Abstracts and Case Studies From the College of American Pathologists 2010 Annual Meeting (CAP ’10)

Abstract and case study poster sessions will be conducted during the College of American Pathologists Annual Meeting (CAP ’10), which is scheduled for September 26 to 29, 2010. The meeting will take place at the Hyatt Regency, Chicago, Illinois. The poster sessions will occur in the Connection Café and Exhibits Hall. Specific dates and times for each poster session are listed below. Also shown below each poster session listing are the subject areas that will be presented during that session.

POSTER SESSION 100: SUNDAY, SEPTEMBER 26, 2010, 10:30 AM—1:00 PM
Gastrointestinal and Liver Pathology; Autopsy and Forensic Pathology; Cardiovascular Pathology
Granular Cell Tumor of the Esophagus With Florid Pseudoepitheliomatous Hyperplasia: A Potential Diagnostic Pitfall
(Poster No. 1)
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Granular cell tumors are relatively uncommon benign neoplasms of neural origin, which are usually found in the skin and tongue. An association with pseudoepitheliomatous hyperplasia at these sites is well recognized. Gastrointestinal tract involvement has been reported, most commonly in the esophagus. We report the case of an esophageal granular cell tumor with florid pseudoepitheliomatous hyperplasia. A 41-year-old woman was found to have a 1-cm, yellow, submucosal esophageal nodule on endoscopic ultrasound. A biopsy was performed. It showed hyperplastic squamous epithelium with squamous nests infiltrating the underlying tissue (Figure 1). The biopsy was read as squamous cell carcinoma. Subsequently, the entire nodule was excised. Microscopic examination revealed sheets of large cells with eosinophilic cytoplasm in the submucosa that were S100 positive. A diagnosis of granular cell tumor was made. The pseudoepitheliomatous hyperplasia overlying the tumor had been misinterpreted on the original biopsy due to the superficial nature of that biopsy. This case illustrates a potential pitfall that can arise from a superficial biopsy showing only the pseudoepitheliomatous hyperplasia that accompanies a granular cell tumor, especially when the tumor arises at rare sites like the esophagus. It is therefore important to keep this entity in mind because granular cell tumors have been reported at a variety of sites, including oral cavity, pharynx, larynx, trachea, bronchi, orbit, gastrointestinal tract, breast, and urogenital tract. Clinical and radiologic correlation and an adequate biopsy will help in arriving at the right conclusion.

Gastrointestinal Stromal Tumors: Not Always Lone Rangers
(Poster No. 2)
Meenakshi Singh, MD (meenakshi.singh@stonybrook.edu); Timothy Pal, MD; Sui Zee, MD. Department of Pathology, Stony Brook University Medical Center, Stony Brook, New York.

Context: Gastrointestinal stromal tumors (GISTs) may not always be solitary lesions and are often discovered incidentally during procedures for other benign or malignant conditions or vice versa.

Design: All GISTs resected at our hospital from 1998 to 2009 were evaluated for the presence of concurrent neoplasia or Helicobacter pylori infection. Clinicopathologic characteristics were also analyzed. The aim was to identify whether there was a pattern to these associations.

Results: From 211,305 total surgical pathology cases, 51 (0.024%) patients with GISTs were identified. Twenty-two (43%) of these cases were associated with other pathologic findings, including 5 (9.8%) cases with multiple associations. Eleven (22%) GISTs were found in patients with other malignancies; one of these patients had both prostate and colon adenocarcinomas. In total, there were 5 gastrointestinal, 2 gynecologic, 2 prostate, and 2 lung malignancies and 1 malignant peripheral nerve sheath tumor. There were 11 benign tumors in patients with GISTs of which the most common were colonic tubular adenomas, breast fibroadenomas, and benign ovarian tumors including fibromas. Five patients had H. pylori infection, one of whom also had a lung adenocarcinoma. CD117 and CD34 immunoreactivity was observed in all GISTs.

Conclusions: Although GISTs can be symptomatic, they may often be encountered while evaluating other disease processes. Although 1 patient had type I neurofibromatosis, most of these cases do not suggest a specific tumor syndrome. Nevertheless, many of the associated tumors did have spindle cell morphology. This study highlights the variety of lesions that can be seen in patients with GISTs. Future studies investigating molecular phenotypes are warranted.

Epstein-Barr Virus–Negative Follicular Dendritic Cell Tumor of the Liver
(Poster No. 3)
Ninu Sharma, MD (ninunaina@yahoo.com); Fouzia Shakil, MD; Myron Melamed, MD; Valentina Vedenin, MD; Umadevi Katta, MD. Department of Pathology, Westchester Medical Center, Valhalla, New York.

Follicular dendritic cell tumor is a rare tumor of follicular dendritic cells that was first reported by Monde et al in 1986. Most cases were identified as lymph node–based neoplasms. Follicular dendritic cell sarcomas of the liver are rare neoplasms with only 6 well-documented
cases. We report an extremely rare case of primary follicular dendritic cell tumor of the liver in a 53-year-old woman. The patient presented with vague abdominal pain, fever, anemia, and jaundice. A computed tomography scan and magnetic resonance imaging revealed an 11.5-cm, lobulated, arterial enhancing mass in the left hepatic lobe. A computed tomography-guided core biopsy revealed a morphologic appearance of spindle and epithelioid cell proliferation associated with a lymphoplasmacytic infiltrate in the background. The tumor cells were immunopositive for CD21, CD35, CD56, claudin, and vimentin, and, most notably, they were negative for Epstein-Barr virus. Based on the immunocytochemical findings, we made a final diagnosis of follicular dendritic cell sarcoma. This case highlights the histologic and ancillary studies that are useful in diagnosing this rare tumor. This information is important because the behavior of these tumors is more akin to that of a low-grade soft tissue sarcoma than a lymphoma. Our case is unique because it represents an Epstein-Barr virus–negative hepatic follicular dendritic cell tumor. After extensive review of the literature, we found only 1 previous case of hepatic follicular dendritic cell sarcoma without Epstein-Barr virus.

Also, to our knowledge this is the first time a patient with such a tumor had jaundice as the initial presentation.

Prostatic Brachytherapy-Related Obstructive Terminal Ileal Stenosis
(Poster No. 4)

Cesar V. Reyes, MD (creyes@morrishospital.org). Department of Pathology, Morris Hospital, Morris, Illinois.

Urinary and rectal complications of brachytherapy are well documented. Up to 17.5% of these patients exhibit acute toxicity and late radiation effect, the latter of which occurs less frequently. Enteric complications following brachytherapy are extremely rare, and obstructive terminal ileal stenosis, which has not been previously reported, is herein described. A 70-year-old man was diagnosed with a localized low-grade prostatic adenocarcinoma that was treated with palladium 103 seed implantation, resulting in remission of cancer for 4 years. An early complication of acute erosive proctitis completely resolved. In a late complication, the patient complained 2 weeks prior to admission to the hospital of nausea, vomiting, and abdominal distention that were secondary to narrowed terminal ileum, the latter of which was noted on endoscopy and computer tomographic scan imaging (Figure 2, with arrow). The clinical impression was either Crohn disease or ischemic ileitis. There was prompt improvement of propria and serosa. Neither chronic inflammatory bowel disease nor mild chronic postirradiation ileitis that was limited to the muscular arrow). The clinical impression was either Crohn disease or ischemic ileitis. There was prompt improvement of propria and serosa. Neither chronic inflammatory bowel disease nor mild chronic postirradiation ileitis that was limited to the muscular arrow). The clinical impression was either Crohn disease or ischemic ileitis. There was prompt improvement of propria and serosa. Neither chronic inflammatory bowel disease nor mild chronic postirradiation ileitis that was limited to the muscular

Differential Expression of Immunohistochemical Markers, p53, Ki-67, iNOS, and eNOS, in Barrett Esophagus Cases With No Dysplasia, With Low- and High-Grade Dysplasia, and in Adenocarcinomas
(Poster No. 6)

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Context: Inducible nitric oxide synthase (iNOS) is a mediator of inflammation and regulator of epithelial growth. Because Barrett esophagus arises in response to chronic injury, the levels of iNOS are expected to be elevated in such cases as compared with controls. One study showed a prominent expression of iNOS and neuronal nitric oxide synthase in the metaplasia-dysplasia sequence of bronchial carcinogenesis. p53 and Ki-67 reports were not consistent due to interpretation errors.

Design: We conducted a retrospective study of archived tissue at St Richard’s Hospital, Chichester, United Kingdom, following internal review board approval. Immunohistochemistry was performed using primary antibodies p53 (BD PharMingen International Cat 15801A), Ki-67 (DAKO, MIB1 Cat M7240), iNOS (BD Transduction Labs Cat 61029), and endothelial nitric oxide synthase (eNOS) (BD Transduction Labs Cat 61027).

Results: Low-grade dysplasia/negative groups had significantly lower p53 levels than those in the high-grade dysplasia and adenocar-
adenocarcinoma and the other groups. Low-grade dysplasia/negative groups had significantly lower Ki-67 levels than those in the high-grade dysplasia and adenocarcinoma groups ($\chi^2 = 42.642, P < .001$). There was a significant difference in iNOS levels across the 4 groups using the Kruskal-Wallis test ($\chi^2 = 56.552, P < .001$). There was a significant difference between deep muscularis propria and pericolonic adipose tissue. Pathologic staging is difficult when desmoplasia blurs the junction accurate cancer staging and determining optimal patient management. Selection versus subserosal invasion by colonic adenocarcinoma is essential for patient management.

Conclusions: Ki-67 and p53 warrant further research using a prospective study design. iNOS should be similarly investigated, as these data may indicate that iNOS has an ability to distinguish between high-grade dysplasia and adenocarcinoma. The data regarding eNOS do not indicate its inclusion in future research.

Caldesmon and Smoothelin as Reliable Markers for Distinguishing Muscularis Propria From Desmoplasmia: Important Implications in Accurate Staging of Colonic Adenocarcinoma

(Poster No. 7)

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Context: Accurate distinction between deep muscularis propria invasion versus subserosal invasion by colonic adenocarcinoma is essential for accurate cancer staging and determining optimal patient management. Pathologic staging is difficult when desmoplasmia blurs the junction between deep muscularis propria and pericolonic adipose tissue.

Design: We reviewed 60 cases of colonic adenocarcinoma resections at The Methodist Hospital from 2006 to 2009. Fifty-one were selected to address challenges in differentiating deep muscularis propria from superficial subserosal invasion on hematoxylin-eosin staining. Immunohistochemical staining using antibodies to smooth muscle actin (SMA), smoothelin, and caldesmon was performed on 51 cases.

Results: Of the 8 T1 tumors, 12 T2 tumors, and 31 T3 tumors, 51 (100%) had diffuse immunoreactivity for caldesmon and smoothelin in the muscularis propria with a cytoplasmic staining pattern. The desmoplasmic areas of these tumors, composed of spindled fibroblasts, showed negative immunostaining in all cases (0 of 51). SMA positively stained the muscularis propria and weakly stained the spindled fibroblasts.

Conclusions: SMA is a commonly used smooth muscle marker that stains fibroblasts in desmoplastic tissue. Caldesmon specifically stains the muscularis mucosa and muscularis propria with minimal staining of the desmoplastic fibroblasts. Smoothelin, a novel smooth muscle–specific contractile protein, is expressed by fully differentiated smooth muscle cells and not by myofibroblasts or noncontractile smooth muscle cells. Compared with SMA, caldesmon and smoothelin are more specific stains that allow better delineation of the muscularis propria. They are reliable markers for distinguishing muscularis propria from desmoplasmia; this is a critical distinction for accurate staging with implications for prognosis and clinical management decisions.

Clonal Plasmacytosis of the Liver in a Patient in Clinical Remission, Mimicking Graft- Versus-Host Disease, Hepatitis C Infection, and Cirrhosis

(Poster No. 8)

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A 62-year-old man in clinical remission for multiple myeloma following an allogeneic bone marrow transplant from a hepatitis C–positive donor 2 years prior presented with imaging consistent with cirrhosis. A previous liver biopsy had shown the hepatic form of graft-versus-host disease, which had been resolved with increased immunosuppression. The current clinical differential was recurrent graft-vers-host disease or chronic hepatitis C progression. A liver biopsy demonstrated diffuse expansion of the portal areas by a clonal plasmacytosis and spotty lobulitis. Immunohistochemical findings were consistent with the patient’s history of lambda-restricted multiple myeloma. Most plasma cells were lambda restricted, with scattered kappa-positive cells. The lobulitis suggested concurrent mildly active chronic hepatitis C. There was no evidence of graft-vers-host disease. A trichrome stain confirmed no significant fibrosis. Follow-up studies revealed quantitative IgG in the blood (4111 mg/dL) with immunofixation negative for the patient’s previous monoclonal immunoglobulin. The gamma-globulin fraction of the total protein demonstrated a polyclonal increase. The patient was discharged in stable condition. Liver involvement by multiple myeloma is common at autopsy but is rarely clinically apparent. This patient’s course was unusual for the recurrence in the liver following autologous stem cell transplant, a previous biopsy showing graft-versus-host disease, infection with hepatitis C acquired at the time of transplant, and a lack of a clonal population in the serum. The nodularity seen on imaging corresponded to diffuse plasmacytosis in the portal tracts and could be a clinical clue to this diagnosis.

Prognostic Significance of High-Grade Dysplasia in Colorectal Adenoma

(Poster No. 9)

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Context: The widespread use of colonoscopic evaluation to detect and remove polyps has contributed to a reduction in colorectal carcinoma. A 3-year follow-up is recommended for patients who are considered at high risk (≥3 adenomas, adenoma ≥1 cm, and villous or high-grade features). Our study is the first to focus on patients diagnosed with high-grade dysplasia regarding initial management and follow-up.

Design: We reviewed 83 cases from 1999 to 2007 with a diagnosis of high-grade dysplasia in adenomatous polyps. The adenomatous polyp diagnosis was either final or intraoperative. Exclusion criteria included less than 1 year, familial polyposis syndromes, prior colon cancer, and a diagnosis of adenocarcinoma within 6 months of initial diagnosis (implying the diagnosis was a result of sampling error).

Results: Fifty-three of 83 (64%) patients developed polyps with a median 4-year follow-up. Among patients with recurrence, 7% developed adenomas with high-grade dysplasia or adenocarcinoma. All cases of recurrent high-grade dysplasia or adenocarcinoma occurred when the initial polyp was ≥1 cm. In initial management, a follow-up colonoscopy was performed on average 7 months following the initial diagnosis. Ten percent of patients underwent prophylactic segmental resection, and 6% received argon laser therapy.

Conclusions: Our study demonstrates that colorectal adenomas ≥1 cm with high-grade dysplasia represent a risk factor for the development of future adenomas with high-grade dysplasia and carcinoma. Careful follow-up is warranted, as these patients appear to require colonoscopies earlier than the current 3-year recommendation.

Clinicopathologic Distinctiveness of Esophageal Adenosquamous Carcinoma

(Poster No. 10)

Dawn Bradly, MD (dawn Bradly@rush.edu); Marlene Gallegos, MD; Ajay Patel, MD; Shriram Jakate, MD. Department of Pathology, Rush University Medical Center, Chicago, Illinois.

Context: Adenosquamous carcinoma (ASC) is an extremely rare tumor of the esophagus. We assessed the morphologic, immunophenotypic, and clinical characteristics of ASC in patients who underwent esophagectomy and compared the results with those found in patients with conventional adenocarcinoma (AC) and squamous cell carcinoma (SCC).

Design: From 1993 to 2009, 127 patients (94 men and 33 women; age range, 25–87 years) underwent esophagectomy at our institution. There were 4 ASCs, all of which were selected. We randomly selected 10 AC and 10 SCC patients for comparison. All cases were reviewed for location, adjacent dysplasia, Barrett metaplasia, and staging. p63, CEA-P, CK7, CK20, CK5/6, and synaptophysin immunostains were performed in all cases.

Results: Four of 127 (3%) patients had ASC, all of whom were men (age range, 47–76 years). All ASCs were located at the gastroesophageal junction and extended into both the anatomic distal esophagus and proximal stomach. All ACs and SCCs were confined to the distal esophagus and middle third esophagus, respectively. All ASCs were advanced stage with 3 or more involved lymph nodes (pT3N1), while only 3 ACs and 2 SCCs were pT3N1. ASCs had at least a 10% squamous or glandular component and showed the following profile: CEA-P positive, CK7 positive, CK20 positive, CK5/6 positive, and p63 negative. In comparison, ACs were CEA-P positive, CK 7 positive, CK20 negative, p63 positive, and CK5/6 negative, and SCCs were CK5/6 positive, p63 positive, CK7 negative, CK20 negative, and CEA-P negative.

Conclusions: ASC is an extremely rare tumor of the esophagus and has no known premalignant precursors. It is morphologically, immunophenotypically, and clinically distinct from SCC and AC.
Risk Factors for Colectomy in Clostridium Difficile Colitis

(Poster No. 11)

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Context: Clostridium difficile colitis (CDC) has emerged as the most common cause of nosocomial, antibiotic-associated diarrhea in adults and is a frequent cause of morbidity and mortality. We examined the clinical and pathologic factors of patients with severe or recurrent CDC requiring colectomy to assess the risk factors in both groups.

Design: We searched the clinical and pathology databases at our medical center for patients with CDC requiring surgical intervention and found 21 cases between the years 2000 and 2009. We reviewed relevant clinical data and microscopic pathology diagnoses.

Results: During this period, 119 patients were diagnosed with CDC, and 21 (18%) of them underwent surgery for initially severe CDC or for concomitant ischemic necrosis, toxic megacolon, or perforation. Thirteen of 21 (62%) patients were immunosuppressed, having a history of lymphoma, carcinoma, inflammatory bowel disease, or transplant. These patients developed initially severe CDC that required colectomy (mean age, 70 years). The remaining 8 of 21 (38%) cases had resistant CDC (mean age, 64 years), and 3 of these also had mixed features of ischemic colitis and CDC. There were 6 deaths: 5 from the recurrent group and 1 from the initially severe group.

Conclusions: Patients with colectomy for CDC may be divided into 2 groups, one with initially severe colitis and the second with recurrent CDC. Patients with initially severe colitis are generally older and immunosuppressed. Patients with recurrent CDC are comparatively younger and more likely to have coexistent ischemic colitis. Mortality is more common in patients with recurrent rather than initially severe CDC, which may be of great importance epidemiologically.

Glucose Transporter 1 Immunostaining Differentiates Intestinal Metaplasia With Dysplasia From Adenocarcinoma in Barrett Esophagus

(Poster No. 12)

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Context: Barrett esophagus (BE) may be associated with adenocarcinoma and a spectrum of premalignant changes. Classification of these dysplastic changes and their distinction from invasive carcinoma may present a diagnostic challenge for pathologists and may be a possible somatic treatment. Glucose transporter 1 (GLUT-1) is a glucose transporter present on erythrocytes. GLUT-1 is aberrantly expressed in a variety of human carcinomas, including adenocarcinoma of the esophagus. This study was performed in an effort to determine the diagnostic value of GLUT-1 immunoreactivity in the differentiation of adenocarcinoma from preinvasive lesions associated with BE.

Design: A tissue microarray containing 100 separate 0.5-mm tissue cores (simulating small endoscopic biopsies), representing 30 BE without dysplasia, 10 BE with low-grade dysplasia, 13 BE with high-grade dysplasia, and 47 adenocarcinoma, was stained with a GLUT-1 monoclonal antibody. Two independent observers scored GLUT-1 immunoreactivity; ≤5% immunoreactivity was considered negative.

Results: Tissue microarray samples of BE without dysplasia and BE with low-grade dysplasia and high-grade dysplasia were all negative for GLUT-1. Tissue microarray samples of adenocarcinoma were GLUT-1 positive in 29 of 47 samples; in 20 samples, the percent GLUT-1 positivity was ≥50%, GLUT-1 staining showed 62% sensitivity and 100% specificity for invasive adenocarcinoma.

Conclusions: GLUT-1 staining is moderately sensitive and highly specific in the differentiation of invasive adenocarcinoma from preinvasive dysplastic lesions in BE. Our study may underestimate sensitivity due to the small tissue samples we examined (0.5 mm). GLUT-1 immunostaining, if positive, may be of clinical utility in diagnosing invasive adenocarcinoma.

Invasive and Growth Patterns of Ductal Carcinoma of the Pancreas: Early Versus Advanced Stages

(Poster No. 14)

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Context: The origin of pancreatic ductal carcinoma is thought to be either the small intralobular duct or the interlobular duct. The tumor begins to invade the stroma only when it exceeds a certain size. However, invasive patterns of ductal carcinoma, especially in its early stage, have not been completely investigated.

Design: We examined 50 cases of pancreatic carcinoma to identify the invasive patterns, especially at the peripheral portion of the tumor. The invasive patterns were divided into 3 patterns: the intralobular pattern, the interlobular pattern, and the mixed pattern according to its tumor replacement pattern. We also paid attention to the histologic type, tumor growth pattern, and lymphatic invasion.

Results: Among 50 cases, 15 were of the intralobular pattern, 13 were of the interlobular pattern, and 22 were of the mixed pattern. In the interlobular pattern, acinar structures were relatively preserved. Both well-differentiated adenocarcinoma and poorly differentiated adenocarcinoma revealed the infiltrative rather than the expansive pattern. In small-sized (<1 cm in size) pancreatic cancer, all cases (2 cases) showed an infiltrative growth pattern. When carcinoma expanded into the interlobular connective tissue, it invaded into the lymphatic channels. On the other hand, advanced-stage pancreatic cancers usually showed a haphazard growth pattern. Lymphatic invasion was closely related to the expansion of the carcinoma into the interlobular connective tissue.

Primary Signet-Ring Cell Carcinoma of the Cecum

(Poster No. 15)

Dian Feng, MD (dian.feng@osfhealthcare.org); Edward Santos, MD; David Laib, MD. Department of Pathology, Saint Anthony Medical Center, Rockford, Illinois.

Primary signet-ring cell carcinoma of the cecum is a very uncommon form of adenocarcinoma of the gastrointestinal tract. We report a case of primary signet-ring cell carcinoma of the cecum with peritoneal metastases in a 53-year-old man. The patient presented with right-sided...
Lymphovascular Invasion and Proliferation Index in Appendiceal Carcinoid Tumors

(Poster No. 16)

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Context: Appendiceal carcinoid tumors are the most common neoplasms of the appendix. They are generally indolent; appendectomy is curative. Size (>2 cm) is considered the most reliable prognostic indicator. We examined other factors that may affect tumor behavior, namely proliferation index and lymphovascular invasion.

Design: Twenty-two cases of appendiceal carcinoid tumors collected from Mount Sinai Medical Center and Loyola University Medical Center from 1999 to 2009 were stained with Ki-67 (proliferation index), D2-40 (lymphatic invasion), and CD31 (vascular invasion).

Results: Twenty of 22 cases were conventional type tumors, and 2 were goblet-cell type. One of 22 cases was >2 cm (measuring 3 cm). Following D2-40 staining, 5 cases showed lymphatic invasion, including the 2 goblet-cell carcinoid tumors (supporting their more aggressive behavior). The remaining 3 cases were conventional type, including the 3-cm tumor. Four of 5 cases with lymphatic invasion also showed increased Ki-67 staining, which ranged from 5% to 40%. The remainder of the cases showed a low Ki-67 index, ranging from 1% to 2%. The 3-cm tumor was the only case to show both vascular and lymphatic invasion (Figure 3). In this case, Ki-67 was positive in 8% of tumor cells.

Conclusions: This study raises the possibility of a positive correlation between Ki-67 staining and lymphatic invasion in appendiceal carcinoid tumors. Size (>2 cm) may be associated with lymphovascular invasion and increased proliferation index. Follow-up studies are needed to better assess the effects of increased proliferation index and lymphovascular invasion on tumor behavior. These factors may serve as indicators for a more aggressive surgical treatment of appendiceal carcinoid tumors.

Severe Melanosis Coli Sparing Adenomatous Polyps: Novel Immunohistochemical Findings Relating to Cleaved Caspase 3

(Poster No. 18)

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A 67-year-old woman with a lifelong history of laxative use underwent right hemicolectomy for a cecal polyp not amenable to endoscopic removal. The gross specimen showed a remarkable black discoloration of the entire colonic mucosa and sharp demarcation of various polyps (Figure 4). Microscopically, the polyps consisted of tubular adenomas, all of which showed marked reduction in lamina propria (LP) pigmentation compared with adjacent melanotic mucosa. One previous study showed decreased apoptosis in the LP of adenomatous mucosa compared with nondysplastic melanotic mucosa by counting apoptotic bodies on hematoxylin-eosin–stained sections, which may not assess apoptosis accurately. We hypothesized that the lack of pigmentation in adenomas is due to reduced apoptosis in the LP of adenomatous mucosa, which can be quantified more accurately by expression of cleaved caspase 3. The latter is an essential apoptotic pathway enzyme. Immunostaining with anti-cleaved caspase 3 antibody was performed on 3 tubular adenomas.
from this specimen. Positive immunohistochemical signals were counted in enough high-power fields (HPFs) (0.55 mm diameter) to cover the entire LP of each polyp and an equal number of HPFs in adjacent nonneoplastic mucosa. Signals in lymphoid follicles and epithelial cells were excluded. Results showed a mean of 1.14 signals per HPF in adenomatous LP and 2.51 signals per HPF in adjacent melanotic LP (P = .02, Student t-test). These findings demonstrate that reduced LP apoptosis, as detected by expression of cleaved caspase 3, contributes to lack of pigmentation of adenomas in melanosis coli. These findings also provide a foundation for further studies to investigate the role of apoptosis in the pathogenesis of melanosis coli.

**Winter Variations in Eosinophil Population in Pediatric Noninflamed Gastrointestinal Mucosal Biopsies: A Review of 29 Cases**

(Hoda Amer, MD; Preeti Jaggi, MD; Rebecca Sherzer, MD; Vinay Prasad, MD. Departments of 1Pathology, 2Infectious Diseases, and 3Allergy & Immunology, Nationwide Children’s Hospital, Columbus, Ohio.

**Context:** The distribution of eosinophils in noninflamed gastrointestinal biopsies varies with seasonal change. We examined 29 cases, evaluating eosinophil distribution in winter months.

**Design:** We studied a total of 29 pediatric cases (15 girls and 14 boys; age range, 1–18 years). Biopsies with pathology were excluded. Eosinophils were counted within the lamina propria in areas of maximum concentration, and the results were averaged over 3 high-power fields. We examined 20 esophageal, 18 gastric, 21 duodenal, 21 terminal ileum, 23 ascending colon, 22 transverse colon, and 22 descending colon biopsies.

**Results:** The mean number of eosinophils was 0.2 in the esophagus, 4.38 in the stomach, 10.57 in the duodenum, 10.57 in the terminal ileum, 23.6 in the ascending colon, 16.5 in the transverse colon, and 14.7 in the descending colon. In the age group of 1 to 10 years, the mean number of eosinophils was 0.2 in the esophagus, 5.3 in the stomach, 13.1 in the duodenum, 13.5 in the terminal ileum, 22.3 in the ascending colon, 15.8 in the transverse colon, and 14.2 in the descending colon. In the age group of 10 to 18 years, the mean number of eosinophils was 0.2 in the esophagus, 3.8 in the stomach, 11.9 in the duodenum, 13.4 in the terminal ileum, 25 in the ascending colon, 18.4 in the transverse colon, and 15.4 in the descending colon.

**Conclusions:** There is a seasonal influence in eosinophilic counts in the pediatric gastrointestinal tract. Detailed larger studies are required to elucidate seasonal variations.

**Discrepancies Between Frozen Section Diagnosis and Final Diagnosis for Donor Livers**

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**Context:** We compared diagnoses from frozen and permanent sections of donor livers to evaluate the effectiveness of frozen section for donor liver biopsy.

**Design:** All donor liver slides (97 cases) from 2005 to 2009 at our hospital were studied. Each case had both frozen section (FS) diagnosis and final diagnosis on permanent sections from right and left lobes of the liver. Nine cases had wedge and needle biopsies; the rest of the cases had needle biopsies only. The following parameters were evaluated: (1) macrosteatosis/microsteatosis: marked (≥30%); (2) fibrosis: portal (mild), perportal (moderate), and bridging (severe); (3) portal inflammation: mild, moderate, or severe; and (4) necrosis: present or absent.

**Results:** For fibrosis, 36 of 97 (37%) cases had discrepancies. Of these, 30 of 36 (83%) were understaged on FS, and 6 of 36 (17%) were overstaged on FS. For portal inflammation, 24 of 97 (24%) cases had discrepancies; severity was equally likely to be greater on FS or final diagnosis. Five of 97 (5%) cases had necrosis; all were correctly identified on FS. Only 2 of 97 (2%) cases had discrepancies (Table).

**Conclusions:** Wedge biopsies typically had more prominent portal inflammation and fibrosis due to closeness to the capsule. FS diagnosis showed a relatively good correlation with final diagnosis for macrostea- tosis, but macrosteatosis was commonly overdiagnosed on FS. Discrepancies for fibrosis and inflammation were common. Fibrosis was frequently underdiagnosed on FS, whereas inflammation was equally undiagnosed or overdiagnosed. Additional training, especially for non-hepatopathologists, should be considered to enhance the accuracy of FS diagnosis of donor liver biopsies.

**Noncirrhotic Portal Fibrosis–Related End-Stage Liver Disease: A Clinicopathologic Study on Explant Livers**

(Deepali Jain, MD; Sanjiv Saigal, MD. Departments of 1Pathology and 2Gastroenterology, Sir Ganga Ram Hospital, New Delhi, India.

**Context:** It has only been recently recognized that noncirrhotic portal fibrosis (NCPF) can progress to clinically manifest end-stage liver disease. In our series of explant livers, we encountered NCPF as the native disease in a proportion of cases having a pre–liver transplant (LT) diagnosis of cryptographic cirrhosis. We assessed the current prevalence of NCPF in our LTs and evaluated clinical and other parameters that might help in making a presumptive pre-LT diagnosis of NCPF cases that carry a high probability of nonrecurrence.

**Design:** We reviewed records from January 2005 to February 2010 (450 adult liver explants) and identified 10 patients with pure NCPF that was clinically diagnosed as cryptographic cirrhosis. Ten other patients showed features of NCPF that overlapped with chronic liver disease of known etiology. Most cases clinically diagnosed as cryptographic cirrhosis were histomorphologically nonalcoholic fatty liver disease (NAFLD) (44 cases). We obtained a detailed comparative analysis of clinical and laboratory parameters for these 2 groups: NCPF and NAFLD patients.

**Results:** Microscopically, there was no cirrhosis; however, portal vein radicals showed fibrotic thickening of their walls in patchy and random distribution. Gastrointestinal bleeding (P = .02), jaundice (P < .001), obesity (P < .001), and other laboratory parameters were statistically significant factors (Table). On follow-up, none of the NCPF patients had recurrence of the disease.

**Conclusions:** Unlike what is generally believed, a proportion of cases of NCPF terminate in irreversible chronic liver failure requiring LT; however, these patients tend to do well after transplantation. There are certain clinical and laboratory features that may be used to predict the pre-LT diagnosis of NCPF.

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**Summary of Results**

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<th>Parameter</th>
<th>Frozen Section Diagnosis, No./Total No. (%)</th>
<th>Final Diagnosis, No./Total No. (%)</th>
<th>Under-diagnosed on Frozen Section, No./Total No. (%)</th>
<th>Over-diagnosed on Frozen Section, No./Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrosteatosis</td>
<td>9/97 (9)</td>
<td>4/9 (44)</td>
<td>6/97 (6)</td>
<td>2/6 (33)</td>
</tr>
<tr>
<td>Microsteatosis</td>
<td>24/97 (25)</td>
<td>27/97 (28)</td>
<td>8/27 (30)</td>
<td>5/24 (21)</td>
</tr>
</tbody>
</table>

**Statistical Analysis of NCPF and NAFLD Patients**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>NCPF, Mean</th>
<th>NAFLD, Mean</th>
<th>P Value</th>
<th>Odds Ratio</th>
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</thead>
<tbody>
<tr>
<td>Prothrombin time, s</td>
<td>15.52</td>
<td>19.67</td>
<td>.003</td>
<td>7.23</td>
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<tr>
<td>International nationalized ratio</td>
<td>1.43</td>
<td>1.91</td>
<td>.002</td>
<td>7.00</td>
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<tr>
<td>Serum bilirubin, mg/dL</td>
<td>1.62</td>
<td>4.85</td>
<td>.03</td>
<td>27.00</td>
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<tr>
<td>Aspartate transaminase, U/L</td>
<td>38.10</td>
<td>62.93</td>
<td>.02</td>
<td>6.35</td>
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<tr>
<td>Serum albumin, g/dL</td>
<td>3.24</td>
<td>2.59</td>
<td>.004</td>
<td>6.99</td>
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<td>Body mass index</td>
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<td>26.81</td>
<td>&lt;.001</td>
<td>22.66</td>
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<tr>
<td>Model for End-Stage Liver Disease Score</td>
<td>13.10</td>
<td>20.11</td>
<td>&lt;.001</td>
<td>70.20</td>
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<tr>
<td>Vascular grade</td>
<td>2.4</td>
<td>3.12</td>
<td>&lt;.001</td>
<td>14.70</td>
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A Rare Case of a 5-Year-Old With VACTERL Association Developing Ulcerative Colitis in an Esophagogastric Interposed Segment of Colon
(Poster No. 22)

Na'im K. Fanaian, MD1 (naimfanaian@gmail.com); Shuan C. Li, MD2; Jeffrey A. Bornstein, MD, MD.2 1Department of Pathology, Orlando Health, Orlando, Florida; 2Department of Pediatric Gastroenterology, Arnold Palmer Hospital for Children, Orlando, Florida.

VACTERL stands for vertebral, anal, cardiac, tracheal, esophageal, renal, and limb abnormalities. The set of abnormalities for each child with VACTERL association may differ. Esophageal atresia is a well-known feature of VACTERL association for which colon interposition can be used to obtain continuity to the stomach. Major complications include ischemia, anastomotic leak, stricture, and fistula formation. We present a case of a male infant with VACTERL association with esophageal atresia who had esophagogastric colon interposition at 9 months of age and who later developed ulcerative colitis in the interposed graft. When the child was age 5, the interposed colonic mucosa was histologically identical to the native colonic mucosa, both showing active chronic colitis with cryptitis, crypt distortion, basal lymphocytosis, and mucosal erosion without granulomas. There are 2 general hypotheses explaining the fundamental pathogenesis of inflammatory bowel disease. One points to dysfunction of the mucosal immune system, which results in aberrant responses to normal gut flora. The other suggests that the mucosal immune system is normal and that the problem is abnormal gut flora and a defective epithelial barrier. There are far fewer microbes in the esophagus than in the colon, with most of the microbes thought to be transient colonizers. In this rare case, the fact that ulcerative colitis developed in a segment of colon placed high in the gastrointestinal tract, where native microbial counts are relatively low, suggests that intrinsic dysfunction of the mucosal immune system is an indispensable component of the development of ulcerative colitis.

Gastrointestinal Stromal Tumor of Stomach with Calcification and Osseous Metaplasia
(Poster No. 23)

Roya Setarehsenas, MD (royasetarehsenas@hotmail.com); Robert V. Jones, MD, FCAP. Department of Pathology, George Washington University Medical Center, Washington, DC.

We present the case of a 64-year-old man who had a history of abdominal pain for a few months. Computed tomographic scan showed a heterogeneous exophytic mass arising from the gastric greater curvature with coarse calcification. Gross examination of the excised specimen revealed a portion of stomach with an exophytic/endophytic, well-circumscribed, 4.2-cm mass with yellow-tan firm cut surface and areas of bony hard consistency. Microscopic sections displayed a cellular spindle cell neoplasm with focal nuclear palisading, suggesting a nerve sheath tumor. In some areas, degenerative calcification and benign osseous metaplasia were identified. Mitotic activity was <1 mitosis per 50 high-power fields. Immunohistochemical findings included strong and diffuse immunopositivity for CD117 and CD34, focal positivity for smooth muscle actin and desmin, immunonegativity for S100 and cytokeratin MAK6, and a low MIB-1 proliferation index. These findings were consistent with a gastrointestinal stromal tumor, probably benign. Calcification is not a usual clinicopathologic feature of gastrointestinal stromal tumors. Occasional examples have been reported in both benign and malignant gastrointestinal stromal tumors and as a response to therapy. We have found no cases so far of gastric gastrointestinal stromal tumors presenting with osseous metaplasia. Further studies may show whether calcification and/or osseous metaplasia can be used as prognostic factors.

Bilateral Pulmonary Metastasis of Pancreatic Mucinous Cystadenocarcinoma: First Case Study and Review of Literature
(Poster No. 24)

Xiangrong Zhao, MD, PhD (xzhao@bhs1.org); Charles L. Abbott, MD. Department of Pathology and Laboratory Medicine, Berkshire Medical Center, Pittsfield, Massachusetts.

Cystic neoplasms of the pancreas account for 1% of pancreatic neoplasms. Approximately 50% of pancreatic cystic neoplasms are mucinous cystic neoplasms (MCNs), for which diagnosis, treatment, and prognosis are yet to be fully determined. Malignant MCNs are often low grade, and metastasis is very rare and not often considered in the differential diagnosis. We report a case of bilateral pulmonary metastasis from pancreatic MCNs in a 69-year-old Caucasian woman who had been receiving palliative chemoradiation therapy for “pancreatic cancer” for 18 months. She was last admitted for bilateral pneumonia, and she died 3 weeks after being discharged symptom-free. At autopsy, 2 mucin-containing, unilocularly cystic tumors were identified in the pancreatic body and tail and were microscopically confirmed as mucinous cystadenocarcinomas. Eleven mucoid masses were found in 4 lobes of the lungs (Figure 5, A). Scrape cytology revealed abundant malignant glandular cells in a mucinous background, containing irregular nuclei with enlarged nucleoli (Figure 5, B, original magnification ×600). Histopathology demonstrated haphazard mucinous glands infiltrating the pulmonary parenchyma and a hypercellular spindly subepithelial stroma typical for pancreatic MCNs (Figure 5, C, original magnification ×40, and D, original magnification ×100). The differential diagnoses of mucinous cystic tumors included those originating from the lung, pancreas, and ovary (in females) and their metastases. A selected panel of immunohistochemical stains, combined with the patient’s medical history, confirmed pulmonary metastases from her primary pancreatic malignancies. This is the first case of pulmonary metastasis of pancreatic MCNs reported in the English medical literature. The metastatic behaviors of pancreatic MCNs and the major differential diagnoses per anatomic site are reviewed in detail.

Signet-Ring Cell Carcinoma of the Gallbladder in a 22-Year-Old Man: Case Report and Literature Review
(Poster No. 25)

Irene Czyszczon, DO (iaczys01@gwise.louisville.edu); Houda Alatassi, MD, Sunati Sahoo, MD. Department of Pathology and Laboratory Medicine, University of Louisville, Kentucky.

Primary gallbladder carcinoma is generally considered a rare neoplasm. Most cases occur in women (5 to 4 women to 1 man) who are older than 50 years. In the United States, the highest incidence is found in individuals of Hispanic and Native American descent. Signet-ring cell carcinoma is a rare and aggressive variant of gallbladder carcinoma and accounts for 0.5% to 2.6% of all gallbladder carcinomas. Risk factors include cholelithiasis, abnormal choledochopancreatic duct junction, obesity, multiparity, and chronic infection with Salmonella and Helicobacter species. Prognosis is generally poor, with a median survival rate of 4 months. We describe an unusual case of signet-ring cell carcinoma of the gallbladder in a 22-year-old African American man who presented with nausea and vomiting and a week-long history of jaundice. His body mass index was 25.7. Computed tomography imaging showed an abnormal gallbladder with contraction and intraluminal edema but no gallstones. The patient underwent cholecystectomy. Histopathology revealed a diffusely thickened and firm gallbladder wall with extensive infiltration by mucin-positive signet-ring cell carcinoma (Figure 6). Review of the literature revealed 8 cases of pure signet-ring cell carcinoma. Average age at diagnosis was 60 years (age range, 22–81 years). Two-thirds of the patients were male. Two cases were limited to carcinoma in situ. Three patients had choleliths. Our case is unusual because the patient was acalculous, young, male, nonobese, and African American and had no family history of gallbladder cancer. Given the absence of any known risk factors, our case emphasizes the need for more research into the pathogenesis of gallbladder cancer for earlier recognition and perhaps prevention.
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Abstracts

Squamous Cyst of Pancreatic Ducts: A Recently Described Entity
(Poster No. 27)

Abha Goyal, MBBS, MD (abgyoyal@yahoo.com); Song Lu, MD, PhD; Benjamin Mathis, MD; Antonia R. Sepulveda, MD, PhD. Department of Pathology and Laboratory Medicine, Hospital of the University of Pennsylvania, Philadelphia.

Cystic pancreatic lesions are increasingly being detected on radiologic imaging and can pose diagnostic challenges to the practicing pathologist. We present a case of a recently recognized cystic lesion of the pancreas. A 2.7-cm cyst in the head and uncinate process of the pancreas was discovered incidentally in a 64-year-old woman. During the next 3 years, the cyst size increased progressively to 3.7 cm. No pancreatic duct dilatation or mural nodules were seen. The cyst fluid showed an elevated carcinoembryonic antigen level (80.1 ng/mL). A Whipple pancreateoduodenectomy was performed. Grossly, the cyst was unilocular and filled with minimally cloudy brown fluid. On hematoxylin-eosin stain, it was lined by cytologically bland multilayered epithelium with a squamoid to transitional appearance (Figure 6). Immunohistochemical stains demonstrated that the lining epithelium was positive for P63, thrombomodulin, CK5/6 (lower half), CK7 (top half), and CK19 (full thickness) and negative for CD20, indicating squamous-transitional (lower half) and ductal (top half) differentiation. Ki-67 highlighted <5% of the lining cells. The cyst wall was thin and fibrous with rare associated lymphoid aggregates. The surrounding pancreas showed occasional dilated ducts with proteinaceous material but otherwise was unremarkable. These findings were consistent with squamous cyst of pancreatic ducts, an uncommon lesion that has been reported only recently. It is postulated to have an obstructive etiology and appears to have benign behavior. It is important to be aware of the distinctive diagnostic features of this unusual entity and to differentiate it from other cystic pancreatic lesions.

Modulation of Nicotinamide Phosphoribosyltransferase Expression in Colorectal Carcinogenesis
(Poster No. 28)

Rodney E. Shackelford, DO, PhD (RdnyShac@aol.com); Ardeshir Hakam, MD; Domenico Coppola, MD. Department of Pathology, H. Lee Moffitt Cancer Center & Research Institute, Tampa, Florida.

Context: The progression from benign colonic epithelium to adenoma to carcinoma is accompanied by multiple genetic changes, occurring at specific stages in carcinogenesis. NAD+ is required for cell survival, angiogenesis, and DNA repair. Nicotinamide phosphoribosyltransferase (Nampt) catalyzes the rate-limiting step of NAD+ synthesis, regulating intracellular NAD+ levels. There are no published studies on Nampt expression in colorectal cancer progression. We examined Nampt expression in benign colonic epithelium, colorectal adenomas, and carcinomas, using semiquantitative immunohistochemistry and tissue microarray technology.

Design: We determined Nampt expression in colorectal adenocarcinoma from 125 patients who underwent colorectal resection for tumor removal, in 23 adenomas, and in 27 normal colonic mucosa samples taken adjacent to the colorectal cancer. Formalin-fixed paraffin-embedded core sections in a tissue array were immunostained with Nampt murine anti-pan-visfatin monoclonal antibody (1:1000; AdipoGen, Incheon, South Korea), using the avidin-biotin-peroxidase method. A semiquantitative measure of Nampt protein expression was determined as the product of immunostain intensity and percent of cells stained, with both scored on a 0 to 3 scale, with 3 being maximal.

Plexiform Fibromyxoma: Report on the Newly Described Mesenchymal Neoplasm of the Stomach
(Poster No. 26)

Rick S. Bains, DO (rickybains@yahoo.com); William G. Watkin, MD. Department of Pathology, University of Chicago (NorthShore), Evanston, Illinois.

A 55-year-old white woman presented to her primary care physician with complaints of dyspepsia. She underwent an upper endoscopy that demonstrated a 2.4-cm submucosal mass in the antrum of her stomach. She underwent a partial gastrectomy. Grossly, the mass was 2 cm, pink-gray, and nodular with areas that were gelatinous. Histologically, the mass was composed of plexiform nodules coursing through the muscularis composed of bland ovoid to spindle cells with a vascular stroma that varied from myxoid to myxofibroid to fibromatous (Figure 7). The lesion extended to the margin of resection. The tumor stained positive for smooth muscle actin and negative for desmin, S100, CD34, and CD117. The diagnosis was plexiform fibromyxoma, which is a unique and recently described entity. It was first described by Takahashi in 2007 as “plexiform angiomyxoid myofibroblastic tumor.” In 2009, Miettinen suggested the term “plexiform fibromyxoma,” highlighting the variation in the stroma that was not described by Takahashi. This tumor, of which there have been only several reported, is a distinct mesenchymal tumor that thus far has only been found to occur in the gastric antrum. It also has a distinct plexiform growth pattern. This tumor can be distinguished from gastrointestinal stromal tumors, particularly myxoid variants, based on its growth pattern and lack of staining for CD117, DOG1, and CD34. Mutational analysis of c-kit and particularly myxoid variants, based on its growth pattern and lack of tumor can be distinguished from gastrointestinal stromal tumors, gastric antrum. It also has a distinct plexiform growth pattern. This mesenchymal tumor that thus far has only been found to occur in the stomach.
Results: Nampt protein expression was weak (immunohistochemistry scores 4 or less) in normal mucosa. Nampt expression increased significantly in adenomas (immunohistochemistry scores between 6 and 9). No significant difference was detected between adenomas and colorectal carcinomas.

Conclusions: Nampt protein expression is increased in colon adenomas and carcinomas compared with benign epithelium. Thus, increased Nampt expression likely plays a role in the early stages of colorectal carcinogenesis. The use of Nampt inhibitors, now in clinical trial, may prove of benefit for colorectal cancer patients.

Value of Immunohistochemical Markers for the Assessment of Dysplasia in Barrett Esophagus

(Poster No. 29)

Eric Himmelfarb, MD (Eric.Himmelfarb@cshs.org); Owen Chan, MD, PhD; Deepit Dhall, MD; David Frisiberg, MD; Stephen Geller, MD; Dan C. Pham, MD; PhD; Hanlin L. Wang, MD, PhD; 2.5 (P < .001) Department of Pathology and Laboratory Medicine, Cedars-Sinai Medical Center, Los Angeles, California.

Context: Degree of dysplasia in Barrett esophagus predicts cancer risk and guides clinical management. Grading dysplasia is primarily by histologic assessment, which is associated with interobserver variability. We examined whether immunohistochemistry aids in the accurate diagnosis of dysplasia.

Design: Seven pathologists reviewed 37 biopsies from cases of Barrett esophagus to establish a consensus diagnosis for dysplasia (negative, indefinite, low grade, or high grade). Agreement among at least 4 pathologists established consensus. Immunohistochemistry was performed on all biopsies using antibodies to 5-methylcytosine A race (AMACR), p53, and insulin-like growth factor 1 mRNA-binding protein 3 (IMP3). Staining was scored as 0 (no staining), 1 (weak staining), 2 (moderate), or 3 (strong) by 1 pathologist blinded to the consensus diagnoses. Histologic and immunohistochemical data were correlated.

Results: We removed 7 cases from the study due to lack of agreement. Cases with a consensus diagnosis of negative for dysplasia (n = 22) demonstrated these average immunostaining scores: AMACR = 0, p53 = 0.4, and IMP3 = 0.5. Cases with a consensus diagnosis of low-grade dysplasia (n = 4) demonstrated these average scores: AMACR = 1.3 (P < .001 compared with cases with no dysplasia), p53 = 2.5 (< .002), and IMP3 = 0.3. Cases with a consensus diagnosis of high-grade dysplasia (n = 4) demonstrated these average scores: AMACR = 1.3 (P < .001 compared with cases with no dysplasia), p53 = 2.3 (P < .02), and IMP3 = 1 (P = .11).

Conclusions: Combined use of AMACR and p53 immunostains may distinguish between cases with or without dysplasia but may not distinguish between low- and high-grade dysplasia. Although IMP3 demonstrated an increased average staining score for high-grade dysplasia, its value in diagnosing dysplasia remains to be established.

Multifocal Lymphangioendotheliomatosis With Thrombocytopenia: An Unusual Presentation

(Poster No. 30)

Rajeswari Nagarathinam, MD (rajeswari-nagarathinam@ouhsc.edu); Candaca M. Marshall, MD; Muhammad Altaf, MD; Paula E. North, MD, PhD; 2. Zhongxin Yu, MD. 1 Departments of 1Pathology and 2Pediatric Gastroenterology, The University of Oklahoma Health Sciences Center, Oklahoma City; 2Department of Pathology, Children’s Hospital of Washington, Milwaukee.

Multifocal lymphangioendotheliomatosis with thrombocytopenia (MLT) is a rare disorder featuring multiple congenital skin vascular papules, severe gastrointestinal (GI) bleeding, and coagulopathy. Until now, no histologic features have been described even with and after GI presentation. We report a case without skin lesions. To our knowledge, MLT without skin manifestations has not been previously reported. The patient was a 3-month-old male infant with a 6-week history of hematemesis and melena. Born at term, he was healthy until this presentation. He presented with anemia, thrombocytopenia, and GI bleeding but without skin lesions. A bone marrow biopsy was normal. An upper GI endoscopy showed multiple, variable-sized erythematous lesions scattered throughout the stomach. Although the architecture was generally well preserved, the gastric mucosa showed discreet but easily overlooked collections of ectatic, thin-walled vessels lined by slightly hobnail endothelial cells that formed complex intraluminal papillary projections with periodic acid-Schiff-positive cores. The lesional endothelial cells were strongly positive for both LYVE-1 and CD31. The distinctive vascular changes observed in the gastric mucosa were characteristics of MLT, as previously reported in other visceral sites (e.g., lung and kidney) and in the skin. A diagnosis of MLT was made, and the patient was treated with ocreotide and steroids. He continued to have occasional GI bleeding, but he never developed skin lesions during the follow-up period of 8 months. In conclusion, MLT may present without skin lesions. The pathologic changes of this lesion can be very subtle. Therefore, being familiar with and vigilant for this lesion is crucial in dealing with GI biopsies from young patients who have severe GI bleeding.

Primary Leiomyosarcoma of the Pancreas

(Poster No. 31)

Mario Rascon, MD (mrascon@nshs.edu); Nora Morgenstern, MD. Department of Pathology, North Shore Long Island Jewish Health System, Glen Oaks, New York.

We present a case of primary pancreatic leiomyosarcoma, a rare mesenchymal neoplasm that has been reported in less than 40 cases worldwide. Furthermore, with the great advances in molecular characterization of stromal tumors in recent years, some of the previously reported cases would now be classified as gastrointestinal stromal tumors. Our patient was a 47-year-old man with general malaise due to a tumor in the pancreatic body. He underwent distal pancreatectomy, partial omentectomy, and splenectomy. On gross examination, the pancreas showed a 4.8-cm, tan, lobulated mass. Histologic examination revealed a markedly pleomorphic neoplasm with a strong spindle cell component arranged in long fascicles and exhibiting brisk mitotic activity. Immunohistochemistry was diffusely positive for desmin, caldesmon, smooth muscle myosin, and smooth muscle actin and negative for CD117, CK7, CAM 5.2, and high-molecular-weight keratin, confirming the smooth muscle lineage of this tumor. Primary pancreatic stromal tumors represent less than 0.1% of all pancreatic tumors, with the 3 main categories being myogenic tumors, gastrointestinal stromal tumors, and neurogenic tumors. Leiomyosarcomas of the pancreas usually exhibit aggressive features and have a dire prognosis. Based on abdominal magnetic resonance imaging, our patient remains free of disease 8 months after treatment, and there is no evidence of metastatic disease. Morphologic, immunohistochemical, and molecular characterizations are important for an accurate diagnosis of primary pancreatic stromal neoplasms.

Epstein-Barr Virus–Related Gastritis: A Rare Clinicopathologic Entity

(Poster No. 32)

Hong Yin, MD 1 (hong.yin@chcmc.org); Lifang Fan, MD; Jun Q. Mo, MD; Owen T. M. Chan, MD; Hanlin L. Wang, MD. 2 1 Department of Pathology, Cincinnati Children’s Hospital, Cincinnati, Ohio; 2Department of Pathology, Cedars-Sinai Medical Center, Los Angeles, California.

Context: Epstein-Barr virus (EBV) has been detected in approximately 7% of gastric carcinomas. The frequency of EBV-related gastritis is unknown, and there are few reports in the literature. This study was designed to investigate the potential role of EBV infection in severe gastritis that was not associated with Helicobacter pylori infection.

Design: Gastric biopsies from 43 patients were selected. All of the biopsies showed severe gastritis and were negative for H. pylori by immunohistochemistry. Paraffin-embedded tissue sections were subjected to EBV-encoded RNA (EBER) in situ hybridization.

Results: The patients ranged from 2 to 90 years (mean age, 40.5 years). Sixteen (37.2%) patients were younger than 25 years. Of these, 14 of 16 (87.5%) patients had Crohn disease (12 cases) or ulcerative colitis (2 cases), and 2 of 16 (12.5%) patients had liver or bone marrow transplantations. Of the 27 patients older than age 25 years, 5 of 27 (18.5%) patients had Crohn disease (4 cases) or ulcerative colitis (1 case), 8 of 27 (29.6%) patients received chemotherapy for various cancers, 6 of 27 (22.2%) patients were clinically thought to have peptic ulcer disease or nonsteroidal antiinflammatory drug–induced gastritis, and 1 of 27 (3.7%) patient was infected with human immunodeficiency virus and had a history of lymphoma in the central nervous system. In situ hybridization demonstrated EBER-positive inflammatory infiltrates in the lamina propria in the 1 (2.3%) patient who was infected with human immunodeficiency virus. This case resembled those seen in graft-vs-host disease, with increased apoptotic activity in glandular epithelium and the presence of eosinophilic debris in the lumens of glands.

Conclusions: EBV-related gastritis is exceedingly rare, even in patients with immune dysregulation. However, testing for EBV may prove useful when a graft-vs-host disease-like histology is encountered in a gastric biopsy without an explainable etiology.
Adult Nesidioblastosis as a Cause of Persistent Hyperinsulinemic Hypoglycemia
(Poster No. 33)

Muhammad A. Raza, MD (muhammad.raza@stjohn.org); Randy S. Tashjian, MD; Paul F. Mazzara, MD, Department of Pathology & Laboratory Medicine, St John Hospital & Medical Center, Detroit, Michigan.

We report a case of a 43-year-old woman with type 2 diabetes mellitus who presented with symptomatic hypoglycemic episodes for 1 year, which were relieved with food intake. The patient was instructed to discontinue all medications, but she continued to experience hypoglycemic episodes. An abdominal computed tomography scan and magnetic resonance imaging were both unremarkable. A selective arterial calcium stimulation test was positive for multiple arteries mitigating against a localized lesion. She underwent subtotal distal pancreatectomy, and no gross lesions were identified. Histologic examination of the resected pancreas revealed diagnostic features consistent with nesidioblastosis, including the presence of ductulo-insular complexes and an increase in the number of islets. Some islets were approaching 4 times their normal size. Following surgery, the hypoglycemic episodes ceased. Nesidioblastosis is a rare cause of persistent hyperinsulinemic hypoglycemia. In contrast to infants who generally present with a discrete nesidioblastoma, adults typically present with more diffuse, grossly inapparent nesidioblastosis. The diagnosis of adult nesidioblastosis requires the exclusion of an insulin-secreting tumor like an insulinoma. Because of the relative rarity of nesidioblastosis in adults, there is a lack of surgical experience with these patients, and no standard treatment recommendations are currently available. Treatment modalities have ranged from distal pancreatectomy to total pancreatectomy.

Nonneoplastic Myxomatous Degeneration of the Appendix: An Entity in Search of Identity
(Poster No. 34)

Lahle Hakima, DO (hakima.lahle@gmail.com); Sambit Mohanty, MD; Elena Selbs, MD; George K. Turi, MD, Department of Pathology, Winthrop University Hospital, Mineola, New York.

Ovarian endocervical-like mucinous adenocarcinoma is a rare tumor with only a dozen cases reported in the literature. Most ovarian mucinous tumors show gastrointestinal type cells and are frequently associated with mucinous neoplasm of the appendix. We report a case of a 51-year-old woman with a well-differentiated endocervical-like mucinous adenocarcinoma of the ovary in association with a borderline endocervical-like mucinous tumor. On gross examination, the ovary showed a multilocular cystic mass containing abundant mucinous material. The appendix was not dilated grossly and serosal implants were absent. On section, the appendix had a circumferential tan-white, gelatinous, glistening area within the wall. Histopathology of the ovary revealed a well-differentiated mucinous adenocarcinoma with uterine serosal implants and peritoneal metastasis. Histologic examination of the gelatinous area within the appendix wall revealed myxomatous degeneration of the muscularis propria with prominent eosinophilic infiltrate. No mucinous neoplastic or metastatic epithelial change was present in the entire examined appendix. Despite the presence of a mucin-producing carcinoma involving a few sites in this patient, we concluded that the mucin present in the appendiceal wall is a nonneoplastic stromal mucin secondary to degenerative changes associated with muscle atrophy and accumulation of myxoid stromal material. To our knowledge, nonneoplastic dissecting mucinous degeneration of the appendix wall has not been reported in the literature to date. The etiology of this process remains unclear.

Epstein-Barr Virus–Positive Gastric Adenocarcinoma in a 14-Year-Old Adolescent Boy
(Poster No. 35)

Matthew F. Fleming, MD (mfleming@mednet.ucla.edu); Samuel French, MD, PhD; David Dawson, MD, PhD; Sarah Dry, MD, Department of Pathology and Laboratory Medicine, University of California, Los Angeles.

We describe a case of Epstein-Barr virus (EBV)-positive gastric adenocarcinoma in a 14-year-old adolescent boy with a family history of stomach cancer. The patient presented with abdominal pain and a clinical suspicion of immunodeficiency syndrome due to prior Giardia infection, cytomegalovirus gastritis, and protein-losing enteropathy. At endoscopy, a mass was detected in the greater curvature of the stomach. Biopsies confirmed a diagnosis of gastric adenocarcinoma, and the patient underwent partial gastrectomy, which revealed moderately differentiated gastric adenocarcinoma (6.2 cm), intestinal-type, arising in the setting of high-grade dysplasia. EBV studies were ordered due to the history of possible immunodeficiency. EBV-encoded RNA in situ hybridization showed positive staining in all tumor cells with negative staining in the adjacent dysplastic epithelium. A link between gastric carcinoma and EBV was originally hypothesized due to a similarity between lymphoepithelioma-like gastric carcinoma and EBV-associated nasopharyngeal carcinoma. Subsequently, lymphoepithelioma-like gastric carcinomas and small subsets of other types of gastric adenocarcinoma were shown to have clonal EBV DNA. Recent novel treatment strategies for EBV-associated tumors have focused on agents that switch EBV from its latent to its lytic form, as viral kinases specific to the lytic phase are able to activate produgs, such as ganciclovir, into active cytotoxic forms that can lead to increased tumor apoptosis. We report a rare case of pediatric gastric adenocarcinoma with diffuse EBV positivity, highlighting the utility of EBV studies in evaluating gastric carcinomas in pediatric and immunocompromised patients, as well as their potential value in predicting the utility of novel EBV-targeted therapies.

Metastatic Hepatocellular Carcinoma to the Bone Occurring in a 13-Year-Old Adolescent Boy
(Poster No. 36)

Jose Gorospe, MD1 (jose.gorospe@ucdmc.ucdavis.edu); John Bishop, MD2; George Rab, MD2; Dariusz Borys, MD. Departments of 1Pathology and Laboratory Medicine and 2Orthopedics, University of California Davis at Sacramento.

Hepatocellular carcinoma is a relatively uncommon condition in children and adolescents with an incidence rate of 0.5 to 1.0 case per million. Few cases of hepatocellular carcinoma with bone metastases in children have been reported, and most studies are adult series. We present a case of metastatic hepatocellular carcinoma in a 13-year-old adolescent boy who initially presented with a pathologic femur fracture. The boy first presented with leg pain after a fall at school with initial x-rays demonstrating a right femur fracture and possible underlying trochanteric bone cyst. To further evaluate the bone cyst, a pelvic computed tomography scan was completed, which incidentally revealed a large hepatic mass. Curettage of the bone lesion was obtained during surgical reduction and fixation of the fracture. Microscopically, the curettage demonstrated neoplastic cells forming sheets and trabeculae (Figure 9) with extensive necrosis, moderate nuclear atypia, and mitotic activity. The immunohistochemical stains for carcinoembryonic antigen, hepatocyte paraffin 1, anti-cytokeratin (CAM 5.2), and α-fetoprotein (focally) were positive. Based on these findings, a diagnosis of metastatic hepatocellular carcinoma to the bone was rendered with agreement from external consultation. To our knowledge, this is the first described case of hepatocellular carcinoma in a child diagnosed on bone biopsy.

Sulfur Granules in Colonic Mucosal Biopsy
(Poster No. 37)

Cesar V. Reyes, MD (creyes@morrishospital.org). Department of Pathology, Morris Hospital, Morris, Illinois.

Sulfur granules are yellow microbial colonies composed of tangled filamentous gram-positive bacilli, admixed gram-negative cocccobacilli,
and irregular golden brown crystals of Splendore-Hoeppli phenomenon in an exudative background. Frequent locations of infection are the lower respiratory tract and the head and neck. The usually isolated microbes in an exudative background. Frequent locations of infection are the lower and irregular golden brown crystals of Splendore-Hoeppli phenomenon are Actinomyces israelii and Actinobacillus actinomycetemcomitans. Effective treatment for a clinically significant infection is massive intravenous penicillin for 6 weeks. Sulfur granules with a background of acute inflammatory exudate in colonic mucosal biopsy were observed during a 6-month follow-up colonoscopy being performed on a 64-year-old woman who was diagnosed with ulcerative, invasive, and moderately differentiated adenocarcinoma with transmural and radial margin involvement and stage T3N0MX. Microscopically, a mucosal suture with attached sulfur granules (Figure 10) and 75-cm transverse colon anastomosis were noted. The infection was clinically asymptomatic; therefore, no treatment was instituted. The probable mechanism in this case was the swallowing of sulfur granules that originated in diseased gingiva, poorly kept teeth, or infected tonsillar crypt. A mucosal suture from a previous colectomy provided a perfect lodging nidus.

**Colonic Lymphangioma Covered by an Adenomatous Polyp**

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Colonic lymphangiomas are uncommon benign submucosal tumors for which etiology and pathogenesis are unclear. Histologically, they contain dilated lymphatic channels and are covered by normal colonic mucosa. We present a unique case of an 87-year-old man with a lymphangioma underlying an adenomatous polyp. We present possible hypotheses regarding the causal relationships between the 2 entities. On colonoscopy, a 4-cm flat polyp was identified. Biopsy showed adenomatous mucosa, and the patient underwent partial colectomy. The gross specimen revealed a cecal broad-based, edematous, glistening, tan mucosal polyp measuring 4.6 cm. The cut surface of the polyp contained no solid component; it was composed of marked, diffuse edema and focal hemorrhage. Histologically, the lesion showed surface changes of a tubular adenomatous polyp without high-grade dysplasia (Figure 11). The surface epithelium also contained a mild inflammatory infiltrate. Beneath the surface there were dilated lymphatic channels with proteinaceous fluid. This is the first reported case of abnormal colonic mucosa overlying a lymphangioma. We question whether local insult to the lymphangioma in the hostile colonic environment initiated adenomatous change. The idea of a link between chronic inflammation and neoplasia has been widely studied since Virchow suggested it in 1863. Alternatively, it is possible that local disturbance can induce formation of lymphangiomas or incite further growth. This raises the possibility that the adenoma was there first, with subsequent development of the submucosa lymphangioma.

**Crohn Disease Presenting as Granulomatous Cervical Lymphadenitis**

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Crohn disease is an inflammatory disorder of unknown etiology predominantly affecting the gastrointestinal tract and rarely other organs. Involvement of mesenteric lymph nodes in the form of granulomatous lymphadenopathy is not uncommon. However, systemic or localized peripheral lymphadenopathy as initial presentation is rare. We report a 23-year-old African American woman who presented with intermittent fevers and marked bilateral anterior cervical lymphadenopathy (up to 3.5 cm) for 18 months. Her symptoms remitted during pregnancy but recurred 4 months postpartum. During the next several months, she developed abdominal pain and diarrhea. Biopsy from her terminal ileum revealed active ileitis with cryptitis, crypt abscesses, focal ulceration, and superficial granulomas consistent with inflammatory bowel disease. Concurrent biopsy of the cervical lymph node showed granulomatous lymphadenitis with well-formed, nonnecrotizing granulomata localized frequently within or near germinal centers and containing numerous multinucleated giant cells. Microbiology workup for mycobacterial and fungal organisms was consistently negative. All of the patient’s symptoms responded to medical treatment directed against Crohn disease, including oral 5-aminosalicylate and oral steroid. Crohn disease needs to be considered in the differential diagnosis in patients with granulomatous lymphadenitis. Granulomatous cervical lymphadenitis can be an initial manifestation of Crohn disease.

**Inflammatory Components of Posttransplant Hepatitis in Hepatitis C Virus RNA-Negative Patients Is Not Different From That in RNA-Positive Transplant Patients**

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**Context:** Hepatitis C virus (HCV) is a major indication for liver transplant; posttransplant recurrence is universal with significant risk of graft loss. Successfully treated patients with negative polymerase chain reaction (PCR) should therefore have good long-term outcomes. However, some treated patients show persistence of hepatitis by histologic criteria and constitute a therapeutic dilemma for the clinical team. Despite their negative viral RNA status, there is evidence that these “idiopathic” hepatitis patients progress with fibrosis. Our goal was to answer the following question: Is the inflammatory infiltrate in HCV-positive hepatitis different from that in HCV-negative hepatitis?

**Design:** Thirty patients in 2 groups were compared. Group 1 (sustained viral response) consisted of 15 posttransplant patients who were HCV negative by PCR. Group 2 consisted of 12 HCV-positive posttransplant (HCV+) and 3 HCV-positive nontransplant (HCV-) patients. The most recent biopsies in all patients were phenotyped for CD3, CD4, CD25, CD8, CD45RO, CD45RA, FoxP3, CD20, CD138, and human leukocyte antigen class II (HLA-DR).

**Results:** CD8+ T cells mostly activated/memory phenotype (CD45RO) constituted most of the cells in all 30 cases. The relative density of T-cell subsets (CD8, CD4 cells), B cells (CD20), and FoxP3+ regulatory T cells was identical in sustained viral response, HCV+, and nHCV patients. Human leukocyte antigen class II was diffusely expressed in lymphocytes but not in bile duct epithelium.
Conclusions: In comparing the density of inflammatory cells, there is no apparent difference between hepatitis in HCV PCR-negative and HCV PCR-positive patients. This supports the notion that viral-negative PCR in peripheral blood does not predict absence of viral particles at the tissue level, implying the need to consider continued antiviral therapy in a proportion of patients despite negative PCR.

Differential Expression of Pancreatic Duodenal Homebox 1 in Pancreatic Nonendocrine Neoplasia
(Poster No. 41)

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Context: The pancreas-specific transcription factor, pancreatic duodenal homeobox 1 (PDX-1), is a key regulator of pancreatic development and function. PDX-1 is expressed in pluripotent progenitor cells during organogenesis and functions in glucose homeostasis in mature pancreas. Because developmental regulatory molecules such as PDX-1 may play a role in pancreatic neoplasia, we broadened our previous work on endocrine neoplasia to define PDX-1 expression in pancreatic nonendocrine neoplasms.

Design: We studied 79 pancreatic neoplasms, including ductal adenocarcinomas, acinar cell carcinomas, pancreatoblastomas, intraductal papillary mucinous neoplasms, mucinous cystic neoplasms, solid pseudopapillary neoplasms, and serous cystadenomas. Immunohistochemical staining for PDX-1 was performed on formalin-fixed paraffin-embedded sections. Nuclear staining intensity for PDX-1 was scored from 0 (negative) to 3+ (strong), with beta cells serving as an internal 3+ reference.

Results: With the exception of solid pseudopapillary neoplasms (0 of 21 cases), PDX-1 was detected in all other pancreatic neoplasms with a variable degree of nuclear expression: 10 of 12 ductal adenocarcinomas (mean intensity, 1.2 ± 0.7), 8 of 9 acinar cell carcinomas (mean intensity, 1.9 ± 0.7), 4 of 4 pancreatoblastomas (mean intensity, 1.6 ± 0.5), 13 of 13 intraductal papillary mucinous neoplasms (mean intensity, 1.8 ± 0.7), 12 of 12 mucinous cystic neoplasms (mean intensity, 1.8 ± 0.4), and 8 of 8 serous cystadenomas (mean intensity, 1.9 ± 0.2).

Conclusions: Most pancreatic nonendocrine neoplasms expressed PDX-1 to a variable degree. Whereas acinar cell carcinoma and serous cystadenoma were associated with moderate PDX-1 expression, ductal adenocarcinoma, intraductal papillary mucinous neoplasm, mucinous cystic neoplasm, and pancreatoblastoma showed mild to moderate PDX-1 expression. There was no detectable expression in solid pseudopapillary neoplasms. These results suggest that PDX-1 may play a role greater than previously recognized in pancreatic neoplasia.

Two Synchronous, Primary, Histologically Distinct Colon Carcinomas in a 29-Year-Old Man With Ulcerative Colitis
(Poster No. 42)

Alexandra E. Kovach, MD (akovach@partners.org); Dora Dias-Santagata, PhD; Mari Mino-Kenudson, MD. Department of Pathology, Massachusetts General Hospital, Boston.

We report a case of a 29-year-old man with a 12-year history of ulcerative colitis and primary sclerosing cholangitis. A surveillance colonoscopy revealed a focus suspicious for intramucosal adenocarcinoma and rare foci of low-grade dysplasia in the background of chronic active colitis. He subsequently underwent a total colectomy that showed 2 synchronous invasive carcinomas (a high-grade neuroendocrine carcinoma in the cecum and a mucinous adenocarcinoma in the sigmoid colon) with lymph node metastases. Multiple foci of conventional dysplasia and hyperplastic-like mucosal changes were also identified within diffusely ulcerated mucosa with pseudopapillae or elevated mucosa. Immunohistochemical study showed preserved expression of mismatch repair proteins in both carcinomas. p53 overexpression was seen in the mucinous adenocarcinoma, its overriding mucosa, and flat high-grade dysplasia; however, p53 was negative in the neuroendocrine carcinoma. The Ki-67 reactivity paralleled the relative degree of dysplasia/neoplasia, but increased proliferation was not seen in most luminal/superficial epithelium. Additional molecular study using a SNaPshot platform in each carcinoma is in progress. This case of 2 histologically and biologically distinct carcinomas and multiple dysplastic lesions together in 1 patient underscores the myriad of possible genetic pathways underlying colorectal cancer arising in association with ulcerative colitis. It also underscores the difficulty in detecting high-grade neoplastic lesions in the background of inflammatory bowel disease and the importance of aggressive management of dysplasia, particularly in high-risk patients.

A patent application for the SnaPshot genotyping methods described herein has been applied for, and these methods are the subject of ongoing licensing discussions. Refer to U.S. Provisional Application Serial No. 61/172, 342, filed on April 24, 2009.

Signet-Ring Cell Carcinoma of the Ampulla of Vater
(Poster No. 43)

Jo Elle G. Peterson, MD1 (jgpeterson@tmhs.org); Aliila Ertan, MD2; Wade R. Rosenberg, MD2; Megan M. Rust, MD3. Departments of 1Pathology, 2Internal Medicine, and 3Surgery, The Methodist Hospital, Houston, Texas.

Carcinomas of the ampulla of Vater comprise 0.5% of all gastrointestinal malignancies. Commonly found in the stomach, signet-ring cell carcinoma (SRCC) originating in the ampulla of Vater is exceedingly rare. We report on a healthy 45-year-old white woman with no family history of cancer who was diagnosed with SRCC of the ampulla of Vater after 1 year of progressively worsening biliary colic. She initially presented with biliary pancreatitis and gangrenous cholecystitis for which she underwent a cholecystectomy. Three months later, endoscopic mucosal biopsies revealed normal papillary mucosa with a stone at the papillary level of the common bile duct. A biliary sphincterotomy was performed, the stone was removed, and a stent was placed. Upon stent removal 1 month later, the papillary mucosa was again noted to be grossly normal. Seven months later, with worsening right upper quadrant abdominal pain and itching, repeat endoscopy showed a prominent papilla with ulceration and distal common bile duct short-segment stricture. Papilla biopsy and distal biliary stricture brushing showed SRCC of the papilla. Subsequent Whipple specimen confirmed SRCC (1.5 cm) originating from the ampulla of Vater with inflammatory change in the wall of the distal common bile duct, pancreatic duct, duodenal muscularis propria, and the local retroperitoneal soft tissue. Perineural and lymphovascular invasion and regional lymph node involvement were seen (pT4bN1M1X, stage III). As the 14th reported SRCC of the ampulla of Vater, this case of a relatively young patient highlights the treacherous infiltrative nature of an SRCC with late-onset mucosal involvement on diagnostic endoscopy.

Intraductal Mucinous Endocrine Neoplasm of the Pancreas
(Poster No. 44)

Kelly L. West, MD, PhD (kelly.west@duke.edu); Rajesh C. Dash, MD. Department of Pathology, Duke University Medical Center, Durham, North Carolina.

A 71-year-old woman presented with recurrent pancreatitis and was found to have a small enhancing lesion in the pancreatic duct. A Whipple procedure was performed, and a 1.1-cm mass was found filling the main pancreatic duct. Microscopically, the tumor was composed of trabeculae of small, undifferentiated papillotubular glands with abundant mucus. The cells uniformly stained with synaptophysin and chromogranin, while the lakes of mucin were highlighted with Alcian blue and mucicarmine. The most common intraductal pancreatic tumor in our series was a high-grade neuroendocrine neoplasm with extensive mucin production. The cells uniformly stained with synaptophysin and chromogranin, while the lakes of mucin were highlighted with Alcian blue and mucicarmine. The most common intraductal pancreatic tumor in our series was a high-grade neuroendocrine neoplasm with extensive mucin production. The cells uniformly stained with synaptophysin and chromogranin, while the lakes of mucin were highlighted with Alcian blue and mucicarmine.

Incidence of Microscopic Colitis in Open Access Colonoscopy Center in the Midwest United States
(Poster No. 45)

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Context: Because most studies are conducted in major medical centers, which have different patient populations than private open-access colonoscopy centers, incidence of microscopic colitis and guidelines for colonoscopy in chronic diarrhea may also differ. This study was designed to determine whether incidence of microscopic colitis is different at an open-access colonoscopy center versus a major medical center.

Design: We conducted a retrospective search of the surgical pathology database for specimens with a diagnosis by SNOMED code of microscopic colitis, lymphocytic colitis, collagenous colitis, spherocytosis, focal active colitis, melanosis coli, or no histopathologic abnormalities seen. Specimens and colonoscopy reports from 497 consecutive patients between January 1, 2004, and May 25, 2006, at a single, private, practice-based, open-access endoscopy center were obtained and reviewed by a single pathologist. Cases were excluded for a clinical history of inflammatory bowel disease, abnormal endoscopic findings, lack of chronic diarrhea, or missing colonoscopy report.

Results: Of 266 consecutive patients with chronic diarrhea and normal colonoscopies during the study period, the incidence of microscopic disease was as follows: lymphocytic colitis (12), collagenous colitis (17), focal active colitis (15), spherocytosis (2), melanosis coli (64), and "no histopathologic abnormality seen" (160) (Table). Four patients had both melanosis coli and focal active colitis.

Conclusions: In this study, the incidence of microscopic colitis at an open-access endoscopy center did not differ significantly from that seen in previous studies.

### Diagnoses in 266 Patients With Chronic Diarrhea and Normal Endoscopic Findings

<table>
<thead>
<tr>
<th>Diagnoses</th>
<th>Number Diagnosed</th>
<th>Percentage of Total</th>
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<tr>
<td>Collagenous colitis</td>
<td>17</td>
<td>6.39</td>
</tr>
<tr>
<td>Lymphocytic colitis</td>
<td>12</td>
<td>4.51</td>
</tr>
<tr>
<td>Spherocytosis</td>
<td>2</td>
<td>0.75</td>
</tr>
<tr>
<td>Focal active colitis/ileitis</td>
<td>15</td>
<td>5.64</td>
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<tr>
<td>Melanosis coli</td>
<td>64</td>
<td>24.06</td>
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</tbody>
</table>

### Primary Gastric Choriocarcinoma With Tripartite Differentiation

Michael Choi, MD; Walter Cha, MD; Joseph Tomasheski, MD; Joram Sawady, MD. Departments of Pathology and Surgery, MetroHealth Medical Center, Cleveland, Ohio.

We present a 76-year-old man who developed vague abdominal pain with subsequent gastrointestinal bleeding. Abdominal computed tomography revealed an abnormal soft tissue density and stricture involving the gastric antrum. An upper endoscopy and biopsy of an antral gastric ulcer revealed poorly differentiated adenocarcinoma. Following partial gastrectomy, gross examination of the stomach disclosed an expansive ulcerated mass along the lesser curvature with transmural invasion. Microscopic examination demonstrated 3 distinct but interwoven histologic patterns, including moderately differentiated adenocarcinoma (Figure 12, A), a component of squamous carcinoma (Figure 12, B), and areas of high-grade carcinoma with distinct choriocarcinoma features (Figure 12, C). Immunohistochemical evaluation revealed human chorionic gonadotropin positivity within the choriocarcinomatous component (Figure 12, D) and p63 and CK5/6 positivity within the squamous component. Intracytoplasmic mucin was documented within the adenocarcinoma component. This case was interpreted as invasive combined choriocarcinoma and adenocarcinoma of the stomach. A separately submitted omental metastasis consisted exclusively of choriocarcinoma. Primary gastric choriocarcinoma, either solitary or in combination with adenocarcinoma, is very unusual but well-documented in the literature. In the spectrum of gastric choriocarcinoma, our case is remarkable for its tripartite differentiation. Trophoblastic differentiation in tumors of the gastrointestinal tract has been reported in the esophagus, stomach, jejunum, and colon. The most plausible theory of histogenesis is that of retro-differentiation or metaplasia. The prognosis of gastric choriocarcinoma with choriocarcinomatous elements is exceedingly poor due to frequent hematogenous metastases. Correlation with serum human chorionic gonadotropin levels may be used to detect recurrent and metastatic disease.

### Fatty Acid Synthase Expression in Extrahepatic Bile Duct Carcinoma and Its Prognostic Implications

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**Context:** Fatty acid synthase (FASN) is an important metabolic enzyme that is associated with synthesis of membrane phospholipids in both normal and cancer cells. Overexpression of FASN is known as a prognostic marker in several other malignant neoplasms, including breast, colorectal, and prostatic cancers. However, the prognostic implications of FASN in patients with extrahepatic bile duct carcinoma have not been systematically evaluated.

**Design:** Tissue microarray was constructed from 184 surgically resected extrahepatic bile duct carcinomas, an independent set of 52 normal biliary epithelia, and 143 dysplasias. Immunohistochemical staining with FASN was performed. A histologic score was determined...
by combining intensity and area that was labeled in the cytoplasmic compartment.

Results: A significant increase in FASN labeling was observed in cancers (score, 2.58) versus in normal biliary epithelia (score, 1.48) and dysplasias (score, 1.72; analysis of variance, \( P < .001 \)). When cases were dichotomized by histologic score into FASN high expression (score > 1) or low/no expression (score ≤1) groups and then compared with other clinicopathologic variables, FASN overexpression was more frequently observed in patients with lymph node metastasis (45 of 58 cases, 77.6%) than in those without metastasis (79 of 126 cases, 62.7%, \( P = .04 \), \( \chi^2 \) test). Patients with FASN high expression had significantly worse survival (\( n = 124; \) median survival, 44 months) than those with low/no FASN expression (\( n = 60; \) median survival, 63 months, \( P = .02 \), log-rank test).

Conclusions: FASN overexpression was observed in a subset of extrapancreatic bile duct carcinoma patients, and its expression status correlates with patients’ overall survival.

Dispersed Endocrine Tumorlets With Abnormal E-Cadherin Arising Within a Serous Cystadenoma of the Pancreas

(Poster No. 49)

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Combined endocrine tumor and serous cystadenoma of the pancreas are very rare. There are only 15 reported cases with female predilection. We recently encountered a 7.4-cm mass at the tail of the pancreas found accidentally in a 67-year-old man. It had typical morphologic features of ductal mucinous low-grade atypia/pancreatic intraepithelial neoplasia (Figure 13, hematoxylin-eosin, original magnification ×100). Small foci of ductal mucinous low-grade atypia/pancreatic intraepithelial neoplasia (PanIN) were also present. Based on morphology, we hypothesized that this tumor derived from pluripotential precursor cells. Pan-cytokeratin and endocrine markers were used to phenotype the 2 components. E-cadherin, which has a high frequency of abnormality in endocrine tumors, was assessed together with another potential endocrine precursor marker, c-kit (CD117). Synaptophysin and chromogranin A were expressed in the endocrine tumor but not in the epithelial components. However, both components had decreased to absent membrane E-cadherin and slightly increased c-kit expression compared with adjacent normal pancreas. This rare pancreatic tumor has endocrine and epithelial components that are distinct in morphology and immunophenotype but that bear the same aberrant expression of E-cadherin. Common precursor origin is implied. Further molecular clarification will be undertaken.

Poorly Differentiated Esophageal Adenosquamous Carcinoma With Cutaneous Metastasis

(Poster No. 50)

Mei Zheng, MD (meizheng12@hotmail.com); Cuong T. Nguyen, MD. Department of Pathology, Medical College of Georgia, Augusta.

Internal malignancies may commonly have cutaneous metastases. However, they are very rarely seen from esophageal neoplasia. Most of these cases involve esophageal adenocarcinoma or even more rarely esophageal squamous cell carcinoma. To our knowledge, cutaneous metastatic manifestation of adenosquamous esophageal carcinoma associated with Barrett esophagus has never been reported. A 69-year-old woman with history of breast cancer was diagnosed with very rare adenosquamous carcinoma arising from Barrett esophagus. She had a preoperative combination of chemotherapy and radiotherapy and underwent thoracoscopy in preparation for esophagectomy. Metastatic disease was subsequently seen in the pleura and lung. More biopsies showed invasive esophageal adenosquamous carcinoma extending to the submucosa with metastatic disease seen in chest wall cutaneous tissue. Immunohistochemistry staining of primary tumor and cutaneous metastatic disease showed predominant positivity for p63 and CK5/6 and focal positivity for CK7/mucin (predominant squamous and minor glandular differentiation). Breast tumor origin was ruled out by negative staining for estrogen receptor, progesterone receptor, and gross cystic disease fluid protein-15. Early biopsy of suspected cutaneous metastasis is important and should be performed in patients with a history of dysphagia or Barrett esophagus and especially in those with a history of cancer. Such evaluation may reveal a distant primary esophageal neoplasm and prompt treatment. The differential diagnosis includes rare primary skin adenosquamous carcinoma, squamous cell carcinoma with abortive glandular differentiation, acantholytic squamous cell carcinoma, mucoepidermoid carcinoma of the skin, cutaneous metastases from other internal malignancies, and others.

Synchronous Pancreatic Adenocarcinoma, Multiple Gastrointestinal Stromal Tumors, and Periampullary Carcinoid in a Patient With Neurofibromatosis Type 1

(Poster No. 51)

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Patients with neurofibromatosis type 1 are at increased risk to develop gastrointestinal tract neoplasms. This disease is reportedly associated with multiple gastrointestinal stromal tumors. In rare cases, it is associated with neuroendocrine tumors and then usually with duodenal somatostatinoma. Pancreatic adenocarcinoma, on the other hand, has not been postulated to specifically associate with neurofibromatosis type 1. Here we report a case of synchronous pancreatic papillary-mucinous adenocarcinoma, multiple gastrointestinal stromal tumors, and periampullary carcinoid in a neurofibromatosis type 1 patient. The patient was a 63-year-old white woman who complained of abdominal pain and weight loss. Computed tomography scan showed a duodenal/pancreatic head mass and multiple gastric, duodenal, and jejunal serosal nodules. The biopsy confirmed adenocarcinoma of the pancreatic mass. Clinically, concern remained that the serosal nodules might be metastasis. Whipple procedure was performed. A 4.2-cm pancreatic head mass was identified as infiltrating pancreatic papillary-mucinous adenocarcinoma. It also had a benign, intraductal, papillary-mucinous neoplasm component. Multiple subcentimeter nodules were found scattered in the gastric and duodenal walls with bland spindle cells and skeinoid fibers. Findings were consistent with multiple gastrointestinal stromal tumors (CD117+, actin positive, and S100 positive focally). A 1-cm periampullary tumor with features diagnostic of periampullary carcinoid was identified. It was nonimmunoreactive for somatostatin. In conclusion, in the workup for an intra-abdominal neoplasm in neurofibromatosis type 1 patients, the differential diagnosis should include not only multiple gastrointestinal stromal tumors and neuroendocrine tumors, which are usually less aggressive diseases, but also aggressive disease forms, such as pancreatic adenocarcinomas. Attention should also be given to multiple synchronous tumors.

Kaposiform Hemangioendothelioma: A Rare But Distinctive Vascular Tumor of Infancy

(Poster No. 52)

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Kaposiform hemangioendothelioma (KHE) of pancreas is an entity that can clinically and radiologically simulate a pancreatoblastoma and other pancreatic tumors of infancy. We identified 2 cases in our files with a diagnosis of KHE in the past 20 years. The histologic material was processed in the usual manner and stained with hematoxylin-eosin.
Immunohistochemistry was performed with antibodies against CD31, keratin, chromogranin, GLUT-1, and Ki-67. Two male infants, a 5-month-old and a 4-month-old, presented with jaundice and abdominal distention. Differential diagnosis was duodenal hemangiomata versus pancreaticoblastoma. A Whipple procedure was performed in both cases. One patient recovered and is well after 17 years. The second patient required multivisceral transplantation. In the first case, the specimen was a hemorrhagic mass involving pancreas and duodenum. In the second case, the mass involved the pancreatic head, common bile duct, mesentery, liver, nerves, lymph nodes, and blood vessels. Histologically, both tumors contained thin-walled vessels surrounding nodules of spindle cells forming small slitlike spaces filled with red blood cells and mixed with round epithelioid cells and capillaries (Figure 14). Neoplastic cells were positive for CD31, focally positive for GLUT-1, and negative for keratin and chromogranin. Ki-67 showed a high proliferative index. A diagnosis of KHE was rendered. KHE is a rare vascular tumor of childhood. Retroperitoneal and pancreatic locations are even more unusual and may represent a diagnostic and therapeutic dilemma. These cases illustrate the importance of considering a vascular tumor, especially KHE, in the differential diagnosis of a pancreatic mass, given the therapeutic implications and prognosis.

Conclusions: Liver fatty acid-binding protein, β-catenin, and glutamine synthetase show different immunostaining patterns between HCA and normal liver, which could aid in distinguishing the 2 apart. Additional investigation is necessary for better use of these surrogate immunomarkers to identify genetic alterations in HCA.

Range and Diversity of Clinicomorphologic Findings and Outcomes in Patients With Primary Biliary Cirrhosis Undergoing Liver Transplant (Poster No. 54)

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Context: A wide range of findings have been reported regarding patients with primary biliary cirrhosis (PBC). Reports on the rate of progression to cirrhosis and liver failure and recurrence in the hepatic allograft are inconsistent. This variability may pose challenges in diagnosis on core needle liver biopsies. We examined 15 cases of advanced PBC in patients with explanted or autopsy livers to document the variable morphologic findings in the available livers and the outcomes after orthotopic liver transplant (OLT).

Design: We searched our medical center’s database (1996–2009) for cases of PBC and found 13 cases in about 1250 OLTs (approximately 1%) and 2 autopsy cases. We reviewed the relevant clinical data, laboratory results, and pathologic findings.

Results: There were 14 women (87% Caucasian) and 1 man. The median age was 59 years (age range, 39–73 years). Histologically, the patients had lymphocytic cholangitis (11 of 15), granulomas (3 of 15), Mallory bodies (3 of 15), and ductopenia (12 of 15). One of 15 patients had hepatocellular carcinoma. Two of 15 patients had recurrence of PBC, one within 2 years and the other within 5 years. Two of 13 patients died within 3 years of having an OLT, and 2 patients without OLTs had autopsies performed.

Conclusions: Advanced PBC is a rare indication for OLT, comprising 1% of all cases. Histologically, as expected, lymphocytic cholangitis and duct loss were the most common findings, whereas granulomas and Mallory bodies were uncommon (20% each). Mortality rate after OLT with a new graft is similar to other cases; recurrence of PBC within 5 years in the new graft is rare.

IMP3 Is a Novel Immunomarker for the Detection of Colonic Adenocarcinoma: Progression Tissue Microarray Study of 123 Cases (Poster No. 55)

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Context: IMP3 is an oncofetal and RNA-binding protein that is found in many malignant tumors, including carcinomas of the pancreas, kidney, and uterine. It has been associated with aggressive tumor behavior. The goal of this study was to identify any differential staining of IMP3 in normal, adenoma, hyperplastic foci, and normal colonic mucosa.

Design: Archival files from the University of Illinois at Chicago Medical Center were searched for colon adenocarcinoma resection specimens. We reviewed 123 cases with CA for areas of CA, AD, hyperplastic foci (HF), and normal colonic mucosa. Duplicate 2-mm cores were obtained from formalin-fixed, paraffin-embedded blocks to create a progression tissue microarray. Immunohistochemical staining were performed on tissue microarray slides using mouse monoclonal antibody specific for IMP3 (L523S, Corixa, Seattle, Washington). Two pathologists independently reviewed the diagnosis by hematoxylin-eosin and the IMP3 immunostaining. IMP3 was graded as negative (0), weakly positive (1 or 2), or strongly positive (3 or 4).

Results: We identified 123 CAs with sufficient tissue for evaluation of AD in 30 and HF in 49 cases. No IMP3 expression was found in HF or AD. IMP3 was overexpressed in CA as compared with AD in 30 and HF in 49 cases. No IMP3 expression was found in HF or AD.

Conclusions: IMP3 was overexpressed in CA as compared with adenoma, HF, or normal colonic mucosa in the same patient group, suggesting that IMP3 may play an important role in colon cancer progression and could serve as a diagnostic biomarker of certain colon cancers.
Histologic features and immunoreactivity patterns were recorded. Cases with 4 or more BE-associated features was associated with CPS1 expression in 37% of cases, and the presence of ≥3 BE-associated features was associated with CPS1 expression in 100% of cases (P = .004) (Table). This is the first study to use the presence of BE-associated features in conjunction with CPS1 expression to evaluate intestinal differentiation in gastroesophageal junction biopsies. In endoscopically suspected cases without histologic evidence of goblet cell loss, the expression of CPS1 antibody in cases with ≥2 BE-associated features can provide evidence of intestinal metaplasia that is consistent with BE.

Eosinophilic/Allergic Esophagitis: Pathologic Comparison of Pediatric and Adult Populations

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Context: The histology of eosinophilic/allergic esophagitis (EoE) is well-described in the pediatric population. The clinical presentation varies between the adult and pediatric populations. However, a comprehensive analysis of the histologic findings in adults as compared with those in the pediatric population is yet to be performed.

Design: EoE patients were determined based on the following definition: 15 eosinophils in at least 1 high power field (HPF) of 1 esophageal biopsy and failed proton pump inhibitor therapy and/or a negative pH probe study. Multiple pretherapy biopsies were reviewed in 27 pediatric patients and 31 adult patients. The following histologic parameters were analyzed: mean/maximal number eosinophils per HPF, eosinophil microabscesses, eosinophil degranulation, surface eosinophil exudate, basal zone hyperplasia, papillae length, distribution of eosinophils within the mucosal thickness (luminal dominant versus diffuse), and eosinophil density with respect to different tissue fragments.

### Differential Expression of CPS1 in Gastroesophageal Junction Specimens

**Positive CPS1 Expression**

<table>
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<tr>
<th>BE-associated morphologic features</th>
<th>Total cases</th>
<th>4/45 (9)</th>
<th>24/65 (37)</th>
<th>54/54 (100)</th>
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<td>Crypt disarray/atrophy</td>
<td></td>
<td>...</td>
<td>2/3 (67)</td>
<td>19/19 (100)</td>
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<td>Multilayered epithelium</td>
<td>0/1</td>
<td>16/39 (41)</td>
<td>9/9 (100)</td>
<td></td>
</tr>
<tr>
<td>Paneth cells</td>
<td></td>
<td>2/3 (67)</td>
<td>13/13 (100)</td>
<td></td>
</tr>
<tr>
<td>Squamous mucosal islands</td>
<td>1/11 (9)</td>
<td>12/31 (39)</td>
<td>24/24 (100)</td>
<td></td>
</tr>
<tr>
<td>Pancreatic metaplasia</td>
<td>0/3</td>
<td>13/26 (50)</td>
<td>3/3 (100)</td>
<td></td>
</tr>
<tr>
<td>Nongoblet columnar cells with blue mucin</td>
<td>1/4 (25)</td>
<td>20/54 (37)</td>
<td>1/1 (100)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: BE, Barrett esophagus; IM, intestinal metaplasia.

* Four additional cases demonstrated focal expression but were considered negative because <5 cells were positive.
* Three cases were in areas of dysplasia/adenocarcinoma.
* Reflux esophagitis with 2 or more morphologic features categorized as suspicious for intestinal metaplasia.
* P < .004. P value based on χ2 analysis.

Conclusions: The histology of eosinophilic/allergic esophagitis (EoE) is well-described in the pediatric population. The clinical presentation varies between the adult and pediatric populations. However, a comprehensive analysis of the histologic findings in adults as compared with those in the pediatric population has yet to be performed.

### Urea Cycle Enzyme Carbamoyl Phosphate Synthetase 1 as a Biomarker for Early Barrett Esophagus Diagnosis

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Context: Barrett esophagus (BE), the major risk factor for developing esophageal adenocarcinoma, is diagnosed following an abnormal endoscopic examination and gastroesophageal junction biopsies with goblet cells. Crypt disarray/atrophy, multilayered epithelium, Paneth cells, squamous mucosal islands, pancreatic metaplasia, and nongoblet columnar cells with blue mucin are well-described BE-associated features. Carbamoyl phosphate synthetase 1 (CPS1), the HepPar1 antibody antigen, is a sensitive marker of intestinal differentiation. We studied the differential expression of CPS1 in BE and reflux esophagitis cases and biopsies suspicious for BE.

Design: We retrospectively collected 54 BE cases, 45 reflux esophagitis cases, and 65 cases suspicious for intestinal metaplasia (SIM) (<2 BE-associated features but without goblet cells). HepPar1 immunohistochemistry was performed on paraffin-embedded tissue for detection of CPS1 expression. Histologic features and immunoreactivity patterns were recorded.

Results: We detected CPS1 expression in 100% BE, 9% reflux esophagitis, and 37% SIM cases. In SIM cases, the presence of ≥2 BE-associated features was associated with CPS1 expression in 37% of cases; the presence of ≥3 BE-associated features was associated with CPS1 expression in 59% of cases, and the presence of ≥4 BE-associated features was associated with CPS1 expression in 100% of cases (P ≤ .004) (Table).
Results: We analyzed 92 biopsies in the pediatric population (age range, 1–17 years; mean age, 9 years). The male to female ratio was 21:6. We also analyzed 47 biopsies in the adult group (age range, 20–69 years; mean age, 38 years). The male to female ratio was 23:8. The mean eosinophil count was 39,318 per HPF in pediatric patients and 67,640 per HPF in adults ($P = .004, \chi^2$ test). In addition, 51% of the pediatric biopsies meeting the criteria for EoE showed a superficial distribution of eosinophils, compared with only 16% of the adult biopsies ($P < .001, \chi^2$ test). The remaining histologic parameters did not show significant differences.

Conclusions: The histology of EoE is generally similar in adults and children. However, the mean number of intraepithelial eosinophils is significantly higher in the adult population, and increased luminal density of eosinophils is significantly more common in the pediatric population.

Melanin-Bearing Pigmented Lesions of the Anorectum (Poster No. 58)

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Melanocytes are known to populate the ananal canal and are more abundant in the African American population. Despite the presence of these melanocytes, melanocytic lesions of the anorectum are rare. Anal melanomas represent 1% of all malignancies in this area, and only 1 case of a submucosal melanocytic nevus within a hemorrhoid has been previously reported. We present 2 cases of melanophages-rich pigmented lesions of the anal verge. Two cases of well-demarcated, flat, pigmented lesions of the anorectum were identified on routine colonoscopy in a 48-year-old African American woman and a 51-year-old African American man (Figure 15). One similar case has been previously reported. Biopsies were obtained and evaluated with hematoxylin-eosin, periodic acid-Schiff, Prussian blue, and Fontana-Masson histochemical stains, as well as CD68 and S100 immunohistochemical stains. Within the submucosa of each specimen were numerous intracytoplasmic clusters of powdery pigment that were suspicious for melanin. There was no evidence of a melanocytic neoplasm. Periodic acid–Schiff and Prussian blue stains were negative for muciphages and siderophages. Fontana-Masson was positive for melanin pigment. S100 was negative for melanocytes, and CD68 was positive in all of the pigment-bearing cells, as is consistent with melanophages. Submucosal anorectal melanophages presenting as CD68 was positive in all of the pigment-bearing cells, as is consistent with melanophages. Submucosal anorectal melanophages presenting as

Hepatic Sarcoidosis Cannot Be Reliably Distinguished From Other Causes of Hepatic Granulomas in Liver Biopsies (Poster No. 60)

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Context: Hepatic granulomas occur in a variety of circumstances. Sarcoidosis is a common cause with the liver following lymph nodes and lungs in frequency of involvement. The present study aimed to determine whether granulomatous hepatitis caused by sarcoidosis can be distinguished from other etiologies in liver biopsies.

Design: We retrieved files for 24 patients with liver biopsies diagnosed as either sarcoidosis or granulomatous hepatitis in the surgical pathology database of Thomas Jefferson University Hospital. Six patients were eliminated because of significant necrosis in the granulomas. Five patients were eliminated due to the absence of clinical data. The clinical records of the remaining 13 patients were reviewed for evidence of sarcoidosis as defined by the ACCESS trial. Their biopsies were analyzed for the density and distribution of granulomas and the extent of nongranulomatous lobular and portal inflammation.

Results: Seven patients were clinically diagnosed with sarcoidosis. In 2 cases, granulomas were accompanied by chronic hepatitis C, whereas no cause was evident in the remaining 5 patients. The sarcoidosis biopsies varied in the extent of nongranulomatous inflammation. In several cases, sharply circumscribed granulomas were randomly scattered throughout the parenchyma. In the other cases, portal and lobular lymphocytic inflammation and interface hepatitis were present. Similar variability was evident in the nonsarcoidosis biopsies. Discrete, well-formed, and isolated granulomas were accompanied by a range of chronic inflammatory infiltrates in both the portal tracts and liver lobules.

Conclusions: Liver biopsies with granulomas caused by systemic sarcoidosis cannot be distinguished from those with other causes. Sarcoidosis as a cause of granulomatous hepatitis must remain a clinical diagnosis.

Two Cases of Lymphoplasmacytic Sclerosing Pancreatitis Associated With Pancreatic Ductal Adenocarcinoma (Poster No. 61)

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Lymphoplasmacytic sclerosing pancreatitis (LPS) is a distinctive type of pancreatitis with a characteristic histology. We present 2 cases of LPS associated with pancreatic ductal adenocarcinoma (DAC). Case 1 was a 59-year-old man who underwent a pancreatectoduodenectomy for a pancreatic mass. Histologic examination revealed that the mass was mainly composed of typical LPS. In addition, a small DAC was observed in the center of the LPS area. Case 2 was a 73-year-old man who underwent a distal pancreatectomy for recurrent pancreatic cancer. Retroperitoneal fibrosis was also suggested by preoperative imaging studies. Histologically, severe lymphoplasmacytic sclerosing pancreatitis inflammation was observed around the aorta and the splenic artery. In addition, DAC was noted around the area of the DAC. Immunohistochemically, many of the infiltrating plasma cells were positive for IgG4 in both cases. So far, only a few cases of LPS accompanied by a pancreatic carcinoma have been reported. These reported cases along with our 2 cases suggest at least 2 possibilities regarding the coexistence of LPS and DAC. First, LPS could be a carcinogenic factor for the pancreas and may develop into DAC in some cases. Second, DAC may trigger the occurrence of LPS in some individuals who have underlying IgG4-related sclerosing disease.

Coexistence of Small Cell Carcinoma and Adenocarcinoma of the Anorectum Associated With Secondary Paget Disease: Case Report and Review of the Literature (Poster No. 59)

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Small cell carcinoma (SmCC) of the anus is an exceptionally rare malignant neoplasm with aggressive behavior. The presence of SmCC is associated with an increased incidence of invasion and metastasis. Even more rarely, SmCC of the anorectal region may coexist with invasive adenocarcinoma or adenocarcinoma in situ. Coexistence of anorectal SmCC and adenocarcinoma associated with secondary Paget disease of the vulva is exceedingly rare. A 61-year-old woman initially presented with Paget disease of the vulva. She underwent vulvectomy and perineal and perianal skin resection with colostomy. Microscopic examination of the specimen showed extensive Paget disease with sweat duct and hair follicle involvement. No invasive carcinoma was identified. Subsequently, the patient developed a perirectal abscess. Abscess drainage and anal biopsy were performed. The biopsy unexpectedly demonstrated coexisting anorectal SmCC and adenocarcinoma in situ. To our knowledge, this is the first case report of coexisting SmCC with adenocarcinoma of the anus and secondary Paget disease of the vulva. The immunohistochemical profile of the tumors will also be discussed.
Hepatocellular Carcinoma Arising in Noncirrhotic Livers

(Poster No. 62)

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Context: Cirrhosis is the main risk factor for hepatocellular carcinoma (HCC). However, HCCs also arise in noncirrhotic livers.

Design: We reviewed clinical and pathologic features of HCC arising in noncirrhotic livers of 143 patients who underwent resections from 1985 to 2003.

Results: Patients included 76 men and 67 women (mean age, 61 years). Risk factors included alcohol in 18 of 143 (13%), hepatitis B virus in 13 of 143 (9%), hemochromatosis in 7 of 143 (5%), and hepatitis C virus in 4 of 143 (3%). Mean tumor size was 103 cm; median tumor number was 1 (range, 1–30). Histopathologic grades were grade 1 in 17 of 143 (12%), grade 2 in 78 of 143 (55%), grade 3 in 45 of 143 (31%), and grade 4 in 4 of 143 (2%) cases. Nonneoplastic tissue was available for review from 98 (69%) patients: 67 had pushing morphology, 17 steatosis, 10 fibrosis (3 with bridging fibrosis; 7 with only portal fibrosis), and 6 steatohepatitis. Seventy-five (52%) patients had recurrence with median disease-free survival of 2.4 years. One- and 5-year survival rates were 85% and 38%, respectively. The median overall survival was 3.3 years. The single factor found to predict recurrence was the presence of 2 or more tumors. Factors predicting decreased survival were presence of 2 or more tumors, tumor grade 3 or 4, perioperative transfusion, >age 65, and male gender.

Conclusions: In addition to chronic hepatitis B, chronic hepatitis C, hemochromatosis, and steatohepatitis are important risk factors for HCC in noncirrhotic livers. Hepatic resection is the best therapeutic choice. However, most of our patients with documented recurrence (71%) had it within the liver, making liver transplantation an interesting option.

Elucidating the Role of JC Virus Infection in Pediatric Crohn Disease: A Search for JC Virus in the Myenteric Plexus of Children With Crohn Disease—A Review of 25 Cases

(Poster No. 63)

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Context: JC polyomavirus (JCV) is a member of the Polyomaviridae family and was first isolated in 1971 in a patient with progressive multifocal leukoencephalopathy. JCV genomic DNA has been isolated from colon polyps, colonic cancer, and normal colonic mucosa adjoicing tumor. Polyomavirus DNA has also been detected in the stool of 46% of hospitalized children. The role of JCV in most gastrointestinal diseases remains unclear. In this study, we attempted to ascertain the presence and extent of JCV protein expression in the intestine of children with Crohn disease (CD). We hypothesized that JCV is present in the myenteric plexus of pediatric patients with active CD.

Design: Twenty-five children with CD were identified; all had clinical and histopathologic evidence of CD. We examined ileum (19 of 25), colon (2 of 25, unspecified), sigmoid (2 of 25), rectum, and cecum (1 of 25 each). Immunohistochemistry was performed to detect JCV viral protein expression and reactivity. A monoclonal antibody to polyomavirus large T–antigen was used. A polyomavirus-infected kidney served as a positive control.

Results: All 25 cases showed variable chronic active colitis, architectural disarray, and granulomas. Ganglion cells within the myenteric plexus were identified. Ganglionitis was not observed. The positive reaction, are required to search for JC virus in childhood CD.

Conclusions: We did not identify JCV protein in tissues studied. Using immunohistochemistry with paraffin-embedded tissue is not the ideal method for identifying JCV virus. Larger studies with molecular techniques, such as in situ hybridization and targeted polymerase chain reaction, are required to search for JC virus in childhood CD.

Parvovirus-Induced Fetal Hydrops: Case Report, Approach to Fetal Autopsy With Nonimmune Hydrops, and Review of the Literature

(Poster No. 64)

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Parvovirus B19 infection is a well-documented preventable and treatable cause of poor pregnancy outcomes. Recognition of the characteristic autopsy findings is crucial in the diagnosis of previously unrecognized infection. We present the case of a stillborn fetus with growth parameters appropriate for gestational age of 28 weeks with no developmental anomalies. Gross examination revealed soft tissue edema, visceral pallor, and bilateral serous pleural effusions. Significant microscopic findings included eosinophilic nuclear inclusions in erythroid precursors in the fetus and the placenta (Figure 16), with prominent extramedullary hematopoiesis in the liver. Immunohistochemical stains for parvovirus were positive, confirming the diagnosis. Parvovirus, a single-stranded DNA virus, is a potent inhibitor of erythropoiesis due to its cytotoxicity to erythroid progenitor cells. Clinical presentation includes fetal anemia, neurologic anomalies, hydrops fetalis, or fetal death. Cardiac tropism of the virus can cause myocarditis and can aggravate the cardiac failure. Antenatal diagnosis is based on testing maternal serum IgM anti–parvovirus B19 antibodies and is confirmed by polymerase chain reaction. If tests are positive, ultrasonographic investigation of the fetus and measurement of the peak systolic flow velocity of the middle cerebral artery are sensitive noninvasive procedures to diagnose fetal anemia and hydrops. Termination of pregnancy is rarely indicated because B19 virus is not teratogenic. Fetal intravascular transfusion can be performed if needed. Kleihauer-Betke test and cytogenetic studies, among others, are additional key studies to rule out other causes of hydrops. Approach to a fetal autopsy with nonimmune hydrops and a review of literature on parvovirus in pregnancy will be discussed.

Ballantyne (Mirror) Syndrome Related to Fetal Laryngeal Stenosis

(Poster No. 65)

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In Ballantyne syndrome, maternal anasarca “mirrors” fetal hydrops. Only about 2 dozen cases have been reported. We encountered a case in which the cause of fetal hydrops was another unusual entity, laryngeal stenosis. The 28-year-old, gravis 4 mother of this 26-week-old male fetus presented with lower extremity swelling for 2 weeks and a headache for 1 day. Earlier, fetal ultrasound showed upper airway obstruction. Maternal history included 3 prior miscarriages. On admission to the hospital, her blood pressure was 145/84 mm Hg. Preeclampsia remote from delivery was diagnosed. A live male infant was delivered by cesarean section. The Apgar scores were 0 at 1 and 5 minutes; the infant was declared dead. Examination of the placenta was not contributory. At autopsy, the infant weighed 1460 g, more than expected for his age. The crown-heel, crown-rump, and foot length were all consistent with the gestational age. The abdomen was protuberant. Internal examination showed 260 mL of clear fluid in the abdomen. The larynx was stenotic. Both lungs were bilobed and enlarged. Both lower lobes were hidden behind the diaphragm. The ribs notch the visceral pleural surfaces. The lungs weighed 65 g, a weight appropriate for a term infant weighing more than 3000 g. Histologic examination of the larynx showed stenosis by striated muscle. Immunohistochemistry confirmed the identification of striated muscle. Muscle-specific actin and myoglobin were present; smooth muscle actin was not present. Laryngeal stenosis by striated muscle was a novel finding that in turn caused the rare mirror syndrome.
Gastroatrial Fistula With Food Embolus Syndrome (Poster No. 66)

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Pericardial and cardiac fistulae associated with esophageal neoplasms are extremely rare. The fistula frequently involves the pericardium, but in some cases, penetration to an atrium or ventricle is present. Most are malignant secondary to tumor extension and arise almost exclusively from esophageal or anastomotic sites. Prior surgery and radiation are predisposing factors. An atrial fistula predisposes the patient to food emboli syndrome and presents with substernal pain, neurologic symptoms, arrhythmia, and hematemesis. We report the case of a 37-year-old woman with T3N1M1 moderately differentiated adenocarcinoma of the gastroesophageal junction who underwent chemotherapy and distal esophagectomy with proximal partial gastrectomy. Five months later, she had seizures and confusion. On admission, a head computed tomography scan showed foci of fat density with edema. An 8-hour electroencephalogram identified 14 seizures. The patient died 9 hours after admission. Postmortem, a chronic gastric ulcer with organisms consistent with Candida species distal to the anastomosis was identified. The ulcer eroded the stomach developing a fistulous tract to the left atrium. Multiple foci of hemorrhage and acute and subacute infarction were observed in the brain. Embolic vegetable matter was strikingly evident in the spleen. To our knowledge, this is the second case of a pseudolipoma of Glisson capsule. The age and sex in this case were atypical. These factors may be less related to etiology and more a consequence of the population examined combined with low awareness and report rates for this lesion. An association between previous abdominal surgery and pseudolipoma of Glisson capsule was again noted.

Pseudolipoma of Glisson Capsule: Case Report and Review of the Literature (Poster No. 67)

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Pseudolipoma of Glisson capsule is a rarely reported benign liver nodule of unknown etiology that is often discovered incidentally at operation or autopsy. The significance of these lesions lies in their ability to grossly mimic metastatic tumors and benign liver nodules, such as solitary necrotic nodules and true hepatic lipomas. Only 25 cases have been reported in the English language literature since 1891; many authors have suggested a relationship to age, sex, previous abdominal surgery, obesity, or alcohol. Only 1 case has been reported in a woman, and all patients have been between 33 and 81 years old. We report an autopsy case of an incidental pseudolipoma of Glisson capsule in a 25-year-old woman who died of acute hydrocoedone and methadone toxicity. On internal examination, the gallbladder was surgically absent. The capsular surface of the right hepatic dome exhibited a grey-white fibrous nodule (diameter, 0.7 cm). Microscopic examination revealed a thick focally hyalinated capsule surrounding mature necrotic fat with calcifications (Figure 17). Fibrous tissue encapsulating the nodule appeared distinct and separate from Glisson capsule. Steatitis and sinusoidal hyperemia were present in the liver parenchyma. The gross and microscopic findings of the hepatic nodule were characteristic of a pseudolipoma of Glisson capsule. The age and sex in this case were atypical. These factors may be less related to etiology and more a consequence of the population examined combined with low awareness and report rates for this lesion. An association between previous abdominal surgery and pseudolipoma of Glisson capsule was again noted.

Mucoid Degeneration of the Umbilical Cord as a Cause of Death in a Late Gestation Fetus (Poster No. 68)

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Bergman et al described mucoid degeneration of the umbilical cord 49 years ago. Nevertheless, there have been only a few reports linking this condition to intrauterine fetal demise. Moreover, such reports have been largely based on first- and second-trimester stillbirths that involved umbilical artery abnormalities and coexisting aneuploidies. We present a 37-week gestation, nondysmorphic stillborn girl. The mother was 35 years old. The pregnancy was uneventful. Gross examination of the umbilical cord showed a focally edematous cord (maximum diameter, 2.0 cm). Cross section of the edematous portion demonstrated 3 translucent and gelatinous vessels (Figure 18). Microscopic examination showed microcyst-like spaces. Colloidal iron and Alician blue stains were positive for mucin in these spaces. The umbilical arteries were partially occluded by thrombi, and the umbilical vein had a focus of complete occlusion. The gross and microscopic findings were those of mucoid degeneration of the umbilical cord leading to umbilical vein occlusion. As a consequence of vascular occlusion, there was severe congestion with hemorrhage in the liver, spleen, kidney, and adrenal glands, which ultimately contributed to fetal demise. To our knowledge, this is the only report of mucoid degeneration of the umbilical cord in a late gestation fetus. Furthermore, the compressive occlusion of the vein is noteworthy because ultrasound assessment of the umbilical cord focuses on determining the number of vessels and the resistance to blood flow in the umbilical arteries. This fetal demise, however, demonstrates an event in which the integrity of the umbilical vein was comparably critical to the well-being of the fetus.
showed microscopic changes consistent with placental vascular insufficiency, infarction, and partial abruption. The umbilical cord structure was complicated by organizing thrombi in the umbilical vessels of 1 cord and increased collagen deposition with deficiency of Wharton jelly in the other hypercoiled umbilical cord. The macerated male fetus with a gestational age of 25.5 weeks had bilateral simian creases. The macerated female fetus with a gestational age of 24.6 weeks had no abnormalities in development. Cytogenetic analysis was not complete due to severely macerated tissues. The cause and mechanism of recurrent umbilical cord stricture remain undetermined. The recurrence risk has been previously reported as low with only sporadic cases of recurrent umbilical cord stricture. A recent study that focused on 2 recurrent episodes and 16 cases involving multiple pregnancies concluded that umbilical cord stricture is not a genetic anomaly. This case of recurrent umbilical cord stricture in subsequent pregnancies in a 1-year period signifies the potentially high recurrence risk and the need for careful fetal surveillance.

**Mesenteric Amyloid Angiopathy Presenting as Ischemic Colitis: Case Study and Review of Literature**

(Poster No. 71)

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Amyloidosis is a disease caused by the misfolding of extracellular proteins, resulting in abnormal deposition in solid organs and abnormal coagulation in bleeding disorders. Amyloidosis-associated gastrointestinal bleeding is rare and is difficult to diagnose: amyloid changes are rarely seen on imaging studies, and the diagnosis is usually made late in the course of the disease. Patients with systemic amyloidosis have been reported to show small vessel fragility resulting in major bleeding. Renal biopsy showed membranous lupus nephritis, class V, and mild acute tubular injury. Significant autopsy findings included acute bronchopneumonia, pleural abscess, significant white pulp depletion in spleen, and chronic pericarditis. The cause of death was acute pneumonia. Our case is exclusive because it highlights the dilemma of using immunosuppressive therapy in this clinical scenario and the rarity of this association in young adult men.

**Overestimation of Invasive Fungal and Parasitic Infections Determined by Autopsy**

(Poster No. 72)

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Context: Invasive opportunistic infections are a major cause of morbidity and mortality for immunocompromised patients. We sought to determine the prevalence of invasive fungal and/or parasitic infections in relation to immune status in a cohort of autopsied patients.

Design: We conducted an 8-year retrospective study of adult autopsied patients. Invasive fungal infections, patient demographics, predisposing risk factors, and coinfections were analyzed.

Results: Clinical or autopsy evidence of invasive fungal and/or parasitic infections were found in 54 of 772 (7%) patients. Eleven (20%) patients had clinical evidence of infection not confirmed at autopsy. Forty-three (5.6%) patients (25 male, 18 female; mean age, 57 years) had postmortem evidence of fungal or parasitic infections. Of these, 25 (58%) had no clinical evidence of infection. The most common invasive infection was *Aspergillus* species (n = 20). All patients except one were immunocompromised. The most common reasons for immunosuppression were transplant (n = 14), malignancy (n = 11), sarcoidosis (n = 4), and human immunodeficiency virus/AIDS (n = 3). One-fourth (n = 11) of the patients had coexisting cytomegalovirus infections.

Conclusions: This study overestimated the number of invasive mycosis found at autopsy likely due to a higher proportion of immunocompromised individuals (especially transplant recipients) than in previous work. This study is unique because in nearly every case, tissue diagnosis was accompanied by positive cultures, demonstrating the importance and validity of postmortem cultures. Opportunistic infections accompany advances in medicine and will continue to challenge us. The autopsy should be regarded as the gold standard for determining the immediate cause of death.

**Nodular Regenerative Hyperplasia Associated With Portal Vein Tumor Thrombosis Due to Metastatic (Male) Breast Cancer**

(Poster No. 73)

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Nodular regenerative hyperplasia (NRH) is an uncommon cause of noncirrhotic intrahepatic portal hypertension. We report the unusual case of a 64-year-old man who had portal hypertension secondary to NRH associated with portal venous embolization caused by metastatic breast cancer. The patient received a cancer diagnosis approximately 10 years prior to his death, and a radiologic diagnosis of cirrhosis deposits in the small-sized blood vessels, as well as solid organ involvement of the liver, kidneys, and heart (Figure 19). Review of the literature revealed amyloid angiopathy leading to ischemic colitis and abnormal bleeding.
7 months prior to his final hospitalization. He experienced various sequelae of his liver disease and was ultimately hospitalized after several days of coffee-ground emesis. Magnetic resonance imaging (performed for transplant evaluation) and bone scan showed possible metastatic lesions throughout the patient’s body. He subsequently died unexpectedly on his 34th day of hospitalization. Autopsy findings included marked ascites, esophageal varices, and widely metastatic adenocarcinoma, all of which were consistent with the patient’s antecedent cancer. Our findings did not support the clinical diagnosis of cirrhosis. Gross examination showed diffusely nodular hepatic parenchyma, and microscopic analysis revealed NRH associated with tumor thrombosis of portal veins (Figure 20). Additionally, the patient’s antemortem laboratory values demonstrated the characteristic profile of NRH. This case illustrates a previously unreported etiology ofobliterative portal venopathy, leading to NRH and portal hypertension. Several reports describe portal vein tumor thrombosis due to metastatic cancer, most frequently of pancreatic, colorectal, or gastric origin. We are not aware of previously reported cases involving portal vein tumor thrombosis due to metastatic breast cancer, and our findings indicate that clinicians should include this condition in the differential diagnosis of noncirrhotic portal hypertension.

A Retrospective Review of the Use and Relevance of Postmortem Microbiology at Boston Medical Center (Poster No. 75)

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Context: A long-standing debate continues regarding the utility of postmortem cultures in medical autopsies. Some pathologists and microbiologists believe that they are not worth the effort or expense they require because any ambiguous results present an unwelcome interpretive conundrum. However, it is acknowledged that when used in a proper context (driven by clinical suspicion or common sense at autopsy) postmortem microbiology can be an important and clinically relevant tool. The utility of postmortem microbiology has not been previously evaluated at Boston Medical Center. A retrospective review of the use and relevance of postmortem microbiology at Boston Medical Center is currently underway. Findings will be compared to peer-reviewed literature and current guidelines. Study data will then be used to inform an institution-specific guideline for postmortem microbiology.

Design: We conducted a retrospective review of data from in-house autopsy cases, electronic medical records, and the laboratory information system.

Results: Preliminary data showed a 79.2% single pathogen isolation rate in autopsy cases in which postmortem cultures were taken. Of these positive cultures, 52.6% of the postmortem ones identified a pathogen identical to that found in antemortem cultures. Statistical analysis showed a positive predictive value of 76.9%, specificity of 66.7%, and sensitivity of 76.9%. Postmortem interval was also assessed as an independent factor in the rate of detection (15.8%, <12 hours; 42.1%, 12–24 hours; 42.1%, >24 hours).

Conclusions: Based on our preliminary findings, one can infer that postmortem cultures when used appropriately are of great utility in medical autopsies. In agreement with published literature, postmortem interval has little, if any, effect on detection rates.

A Case Report of Filamin A Mutation With Periventricular Nodular Heterotopia and Ehlers-Danlos–Like Syndrome (Poster No. 76)

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Filamin A is a unique scaffold and nonmuscle actin-binding protein. This protein cross-links actin filaments with the cytoplasmic domain of integrin proteins. Localized mutations in the filamin gene are linked to cerebral, skeletal, and cardiovascular malformations. We report a case of a 3-year-old girl with a history of pulmonary hypoplasia for which she received a lung transplant in 2006. She received a second heart and lung transplant in 2009, which was complicated with infection and grade 1R
rejection. She also presented with Ehler-Danlos syndrome features, including marked hypermobility of joints and abnormal wound healing. Routine autopsy was performed. The native heart revealed a moderate aneurysmal dilatation of the ascending aorta, perimembranous ventricular septal defect, and polyvalvular dysplasia. Movat stain of the native aorta showed decreased and fragmented elastin fibers and increased deposition of mucopolysaccharides. The brain revealed extensive bilateral periventricular nodular heterotopias with associated hydrocephalus. Microscopically, the nodules contained neuronal cell bodies without ischemic changes. Periventricular nodular heterotopia is a rare malformation of neuronal migration, which is characterized by nodules of neurons in an inappropriate location adjacent to the walls of the lateral ventricles. Periventricular nodular heterotopia can be associated with Ehler-Danlos-like syndrome. The exact relationship between the disruption in connective tissue in Ehler-Danlos syndrome and impaired neuronal migration is not well understood. A possible mechanism could be a decrease in the strength of attachment of the cells to the extracellular matrix or impaired regulation of the cytoskeleton through the filamin binding to integrin proteins.

A Primary Adenocarcinoma With Metastases Originating in a Supernumerary Ovary
(Poster No. 77)

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A 59-year-old woman with a history of distant hysterectomy and bilateral salpingo-oophorectomy was admitted to the hospital with abdominal distention and pain and shortness of breath for 5 days. An omental biopsy was diagnosed as adenocarcinoma, and the peritoneum was suggested as a possible primary site. The identical diagnoses resulted from cytologic examinations of the ascitic and pleural effusions. An ascending colectomy and omentectomy were performed; the same adenocarcinoma was found to be present. The patient died with bilateral bronchial stenosis and pulmonary thromboemboli. At autopsy, the uterus, ovaries, and fallopian tubes were surgically absent, findings that were consistent with the patient's history. Examination of the pelvis disclosed a 3.7 × 1.8 × 1.7-cm, firm-white nodule loosely adherent to the serosal surface of the sigmoid colon. Sections from the nodule revealed ovarian stroma with corpora albicantes, confirming it as a supernumerary of the ovary. Histology also showed a moderately differentiated papillary serous adenocarcinoma of the ovary. The histologic features and special stains were identical to those of the widespread metastases present in the mesentery, colon, pleural effusion, ascites, left hilar and peripancreatic lymph nodes, as well as in the previous omental biopsy and partial colectomy. A supernumerary ovary is a rare gynecologic anomaly. The histologic and cytologic examinations of the metastases confirmed the identity of this supernumerary ovary as the site of the primary tumor.

Liver Agensis With Limb Body Wall Complex in a Twin Fetus
(Poster No. 78)

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Limb body wall complex (LBWC) is a rare malformation syndrome, featuring exencephaly/encephalocele with facial clefts, thoraco- and/or abdominal heterotaxia, and limb defect. We present an interesting case of LBWC and agenesis of the liver in a fetus of a monozygotic/monoamniotic pregnancy. A 24-year-old gravida 5, para 3 woman with sickle cell trait presented with a monochorionic/monoamniotic twin pregnancy and an antenatal diagnosis of LBWC in 1 twin. She elected not to terminate the pregnancy and delivered the twins at 34 weeks gestation. The first twin (without LBWC) was born with an Apgar score of 1 at 1 minute, which quickly improved to 8 at 10 minutes of life. The second fetus was delivered stillborn (Figure 22). This fetus had multiple congenital anomalies, including hypertelorism, cleft nasal bridge, cleft hard palate, vertebral scoliosis, absence of a majority of the upper extremities, and sirenoma with absent lower extremities. Additionally, external genitalia, liver, and portions of the genitourinary and gastrointestinal systems were absent. Internally, the fetus had a solitary cardiac chamber, polysplenia, and an incomplete abdominal aorta without bifurcation. The diaphragm was incomplete. The fetus had cerebral hydrocephalus with non patent aqueduct and agenesis of corpus callosum. Genetically, this fetus was 46,XX. The liver is a major source for hematopoiesis early in embryologic development. The absence of a liver in this fetus therefore suggests the presence of a twin-twin transfusion syndrome and may provide a reasonable cause for polysplenia. The coexisting disruption of the embryonic vessels and surrounding tissue provides the mechanism for placento-abdominal adhesion phenotype LBWC.

Thrombosed Cavernous Hemangioma of Myometrium With Pulmonary Emboli in a 25-Year-Old Postpartum Woman
(Poster No. 79)

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Until now, only 8 cases of diffuse cavernous hemangioma of the uterus have been reported in pregnancy. We performed an autopsy on a patient with this rare entity. A 25-year-old woman (gravida 1, para 2) was admitted to the hospital 1 week after a cesarean section. She had collapsed and was found unresponsive with bloody froth coming from her mouth. Acute respiratory distress syndrome, hypertension, methicillin-resistant Staphylococcus aureus in sputum, leukocytosis, ventilator-dependent respiratory failure, and asystole marked her 12-day hospital course. At autopsy, the uterus was spongy and hemorrhagic and weighed 400 g. The myometrium was filled with thrombi. There were also multiple cystic spaces in the myometrium measuring 0.5 cm × 0.4 cm at greatest dimension. Histologic examination showed several dilated endothelial-lined vessels; some were filled with thrombi with hemorrhage, fibrin, and macrophages. Sections from the endometrium showed proliferative changes, hemorrhage, and endothelial-lined spaces that were similar to those in the myometrium. Histologic examination of the lungs revealed acute and early diffuse alveolar damage that was consistent with the clinical history of acute respiratory distress syndrome. Foci of hemorrhagic infarction and pulmonary emboli in small- and medium-sized vessels were also present. Thrombosed cavernous hemangioma of the uterus was the likely source of the pulmonary emboli, as no thrombi were found in the leg veins. In addition to the significant risk of bleeding during delivery, a pregnant woman may develop cavernous hemangiomas that thrombose and cause embolism, as in this case.

Extraintestinal Entamoeba histolytica Amebiasis Diagnosed at Autopsy
(Poster No. 80)

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Amebiasis due to *Entamoeba histolytica* infection is the second leading cause of death from parasitic disease worldwide but is a very uncommon finding in the United States. Herein, we report a case of extraintestinal amebiasis diagnosed at autopsy. The gross and microscopic findings of the following case were evaluated. The patient was a 35-year-old man who presented with left-sided abdominal pain for 3 months. He was found to have a large cystic mass in the left lobe of his liver, which was thought to be a biliary cystadenoma radiographically. He was transferred to Duke University Medical Center for resection of his mass. However, shortly after arrival, he went into asystole and died. Multiple ulcers were seen in the ascending colon, and histologic sections revealed innumerable *E. histolytica* trophozoites within the submucosa. Extraintestinal manifestations of amebiasis included a 28 × 20 × 15-cm hepatic abscess within the left lobe that contained numerous *E. histolytica* microorganisms. Fibrinous pericarditis with a 350 mL pericardial effusion was found, but *E. histolytica* organisms were not identified, despite extensive sampling of the pericardium. Extraintestinal manifestations of amebiasis are uncommon in the United States and include liver abscesses and pericarditis. Although *E. histolytica* organisms have commonly been identified within the pericardium in the literature, we did not identify any organisms, despite extensive sampling. The liver abscesses of amebiasis can mimic biliary cystadenomas radiographically. Therefore, amebiasis should be in the differential for these lesions, especially if the patient has other symptoms of amebiasis.

**Coronary Artery Intimal Fibrosis With Fatal Myocardial Infarction in a 22-Year-Old Man Who Used Cocaine and Multiple Other Drugs**

(Poster No. 81)

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Accelerated coronary atherosclerosis has been well-documented in cocaine users, whereas diffuse intimal fibrosis histologically resembling graft arteriopathy has been reported only twice. We performed an autopsy on a patient with this rare entity. A 22-year-old man who was admitted to our hospital had collapsed and been subsequently resuscitated. There was a history of drug use, including cocaine and “illy” (also known as “fry”), the latter of which is a marijuana cigarette treated with formaldehyde and often containing phencyclidine. A urine screen showed cocaine, phencyclidine, and opiates. Mechanical ventilation, rhabdomyolysis, acute renal failure, elevated cardiac troponin, bacteremia, and brain death marked the 10-day hospital course. Autopsy findings confirmed the clinical history. Coronary arteries showed diffuse, concentric luminal narrowing almost throughout the left anterior descending, left circumflex, and right coronaries and several of their respective branches. Intimal fibrosis, as described in the previous 2 case reports, was the predominant histologic finding. Lipid-containing atheromas, recanalized thrombi, and calcification were rare. Stenoses varied from 50% to 90% in different sections from each artery. Atherosclerosis was imperceptible in other mid-sized arteries and was only minimal in the large elastic arteries. Myocardial infarctions scattered throughout the left ventricle were likely the immediate cause of brain death. Chronic cocaine use was sufficient to explain all of the findings in this case. However, because of the rarity of the coronary lesions, we did not exclude the possibility of other factors being involved. One such factor could have been “illy” because its pathologic effects have been sparsely documented.

**Concurrent Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma, Influenza A (H1N1) Infection, and Hemophagocytosis: An Autopsy Case Report**

(Poster No. 82)

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Postmortem findings of concurrent chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) and influenza A (H1N1) infection have not been reported to our knowledge. We present an autopsy case of a 50-year-old man with CLL/SLL, influenza A (H1N1) infection, and hemophagocytosis during the 2009 H1N1 pandemic. The patient had been diagnosed with CLL 5 years earlier. He had achieved remission with low tumor burden. He developed acute onset of fever, shortness of breath, chills, nausea, and diarrhea. Upon hospitalization, he was found to have anemia, leukocytosis, and bilateral pulmonary infiltrates and consolidations. His hospital course was complicated by acute respiratory distress syndrome, acute kidney injury, disseminated intravascular coagulation, and ultimately pulseless electrical activity arrest. On autopsy, respiratory findings included a large hemorrhagic infarct in the right lower lung and bilateral acute pneumonitis with extensive hemorrhage, diffuse alveolar damage, microthrombi, and hemophagocytosis (Figure 23, A through C). Immunostains on lymph nodes and flow cytometry analysis of blood showed CLL/SLL, and involvement of the lungs, liver, spleen, and bone marrow was identified. Hemophagocytosis was also present in pulmonary hilar lymph nodes (Figure 23, D). Lung tissue sent to the Centers for Disease Control and Prevention was positive for influenza A (H1N1) by reverse transcriptase-polymerase chain reaction. We postulate that this patient suffered from reactivation of CLL/SLL, which increased his susceptibility to severe H1N1 infection, and the hemophagocytosis was associated with the infection. Patients with hematologic malignancies may be more vulnerable to develop fatal outcomes from H1N1 infection when compared with the general population.

**Intramural Hematoma in a 21-Year-Old Man**

(Poster No. 83)

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The International Registry of Aortic Dissection has been a database of findings in patients with this uncommon disorder. Intramural hematoma, lacking the intimal tear characteristic of dissection, was found in 5% to 20% of the registry cases. Aortic rupture occurred in 20% to 45% of those patients with intramural hematoma; regression was found in only 10% of those patients. The mean age of registry patients was 61.1 years (standard deviation, 14 years). We encountered an unusual case of intramural hematoma. A 21-year-old man presented to another hospital because of 3 days of lower back pain; imaging suggested an abdominal aortic dissection, which prompted transfer to our institution. There were no risk factors for aortic dissection, such as Marfan syndrome, drug use, systemic hypertension, trauma, or prior aortic disease. In the emergency department, before surgery, hemotherax was found, and blood products were administered. Intraoperative findings included 2 to 3 L of blood in the abdomen and a 1.5-cm aortic rupture at the level of the renal arteries. Both subdiaphragmatic and infrarenal aortic crossclamping were performed, but the patient ultimately died. Autopsy showed 750 mL of intra-abdominal blood and clotting; there was also a 3-cm aortic intramural hematoma corresponding to the perforation but with no intimal tear. Histologic examination showed medial degeneration limited to the area of the hematoma. Clinically, the young age of the patient made dissection even more difficult than usual to diagnose. Pathologically, the finding of intramural hematoma in the abdominal aorta is extremely rare, with only 1 such case in the registry.

**Histiocytic Myocarditis and Leukoencephalopathy Following H1N1 Infection**

(Poster No. 84)

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As of October, 2009, the World Health Organization reported more than 440,000 cases of pandemic influenza H1N1 and more than 5700 deaths. The pathogenesis of extrarespiratory complications, such as myocarditis or encephalopathy in influenza, is often attributed to the virus infecting extrapulmonary sites or to cytokines being released into circulation. We report the autopsy case of a 28-year-old previously healthy woman who developed H1N1 influenza pneumonia and died 27 days after hospital admission from encephalitis. During her hospitalization, she received dialysis for renal failure and had elevated myoglobin, creatinine kinase, and troponin levels. She ultimately developed an intercerebral bleed and cerebellar tonsillar herniation. Autopsy revealed brain swelling and an interventricular hemorrhage in the right parietal lobe. Microscopically, there was diffuse alveolar damage at the proliferative and early fibrosing stage with re-epithelialization of alveolar linings. There was no evidence of secondary bacterial pneumonia. The ventricular myocardium contained foci of myocardial necrosis with inflammatory cells that had the immunohistologic phenotype characteristic of activated macrophages (Figure 24, A and B). The right parietal lobe showed discrete hemorrhages and accumulations of fibrin around venules and small veins in the white matter. Many of these vessels contained accumulations of activated macrophages that appeared to have merged with and migrated through vessel walls (Figure 24, C and D). This unique case illustrates postviral encephalitis that appeared to have merged with and migrated through vessel walls.

## Discordant Fatal Gestational Infection Due to Streptococcus agalactiae (Group B Streptococcus) in Monochorionic/Diamniotic Twins

**Poster No. 85**

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A 35-year-old woman presented at 18-weeks’ gestation with premature rupture of membranes. At 13-weeks’ gestation, a scant amount of group B Streptococcus (GBS) was detected in her urine but was not treated. Ultrasound revealed a monochorionic/diamniotic twin pregnancy. Other findings were severe oligohydramnios around twin A, mild oligohydramnios around twin B, and the umbilical cord and lower leg of twin A in the cervical canal. Initially, fetal heart tones were noted from both twins; however, Apgar scores of 0 and 0 were recorded at delivery. Postpartum, the mother was febrile, and blood cultures were positive for GBS. The placenta revealed extensive acute chorioamnionitis and funisitis with gram-positive cocci overgrowing the umbilical cord, membranes, and villi of twin A but not of twin B. At autopsy, twin A had dark, red-brown integument (Figure 25, A) and pleural and pericardial effusions but no congenital anomalies. Microscopically, the organs were well preserved, with gram-positive cocci identified in most tissues. Cultures of the effusions, liver, and lung showed heavy growth of GBS. Autopsy findings in twin B were unremarkable (Figure 25, B), with only scant growth of GBS and no microscopic evidence of bacterial infection. GBS is a frequent cause of neonatal sepsis, and intrapartum antimicrobial prophylaxis is recommended for GBS carriers. Gestational infection among GBS carriers may also occur, but there are no provisions for early intervention. Only 4 cases of discordant gestational GBS infection in twins have been described. Two of these reports specified dichorionic/diamniotic twins. This case is extraordinary because the discordant GBS infection occurred in monochorionic/diamniotic twins.

## Bilateral Symmetric Caudate Hemorrhage

**Poster No. 86**

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Isolated bilateral symmetric caudate hemorrhage is a rare occurrence, with only a few reported cases in the literature. We report a case of symmetric caudate hemorrhage in a 53-year-old woman who had a history of alcoholism. The patient was found unresponsive and without a pulse in her home. She was transported to the emergency department where a pulse was reestablished. At that time, her Glasgow Coma Scale score was 3, and neurologic evaluation suggested severe anoxic encephalopathy. Computed tomography of her brain did not reveal any abnormalities. Despite supportive therapy, she died approximately 6 hours after admission to the medical center. During postmortem examination of the central nervous system, the hemorrhages were discovered in what was otherwise grossly normal formalin-fixed brain. The hemorrhagic areas measured 0.5 cm and were confined to both caudate nuclei with no hemorrhage into the ventricles. Microscopic examination of hematoxylin–eosin–stained slides revealed acute hemorrhage without evidence of thromboembolias or other pathologic processes. The only evidence of neuronal ischemia was focal perineural clearing. Very little neuronal loss was identified in the sections of the cerebral cortex, brainstem, and cerebellum. Trichrome staining was performed to identify any vascular malformations, which were absent. Immunohistochemical staining for β-amyloid was performed to identify amyloid angiopathy, which was also absent. Alcohol use has been linked to spontaneous intracerebral hemorrhage but without this symmetrical pattern. A link has not been made between this type of brain lesion and central nervous system dysfunction to such a great extent.

## Fatal Gastrointestinal Hemorrhage in a Paraplegic Man With Undiagnosed Secondary Amyloidosis

**Poster No. 87**

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In recent decades, paraplegia has declined as a cause of secondary amyloidosis. We performed an autopsy on a 41-year-old paraplegic man in whom the diagnosis was missed despite clinical and anatomic evidence. Furthermore, the immediate cause of death, massive gastrointestinal bleeding due to small vessel involvement, was unusual. The patient was paraplegic for 21 years due to a gunshot wound, which was followed by recurrent urinary tract infections, sacral decubiti, and partial colostomy for unknown reasons; renal and adrenal failure had developed recently; an abdominal fat pad biopsy was negative for amyloid. An urinary tract infection led to the last admission to the hospital. On day 14 of hospitalization, there was hematemesis and blood in the colostomy bag. Angiography did not identify a bleeding site. Blood products were
transfused. Respiratory failure and unresponsiveness preceded death on the following day. At autopsy, the stomach contained 1230 mL of blood. The gastrointestinal tract was erythematous but without focal lesion. Histologic examination showed extensive amyloid deposition in the renal glomeruli and adrenal cortices. Small blood vessels in most organs and tissues, including most of the gastrointestinal tract contained amyloid. Extravasated red blood cells were seen adjacent to a few amyloid-containing gastrointestinal tract small vessels. Staining with crystal violet and Congo red with polarization confirmed amyloid. Immunohistochemistry for amyloid A was strongly positive in renal glomeruli and small vessels. Review of the premortem fat pad biopsy confirmed absence of amyloid. Two other premortem surgical specimens showed abundant amyloid that had not been identified before postmortem review.

An Interesting Hepatic Lesion in a Child With Septooptic Dysplasia
(Poster No. 88)

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Septooptic dysplasia (SOD) is a rare, heterogeneous disorder most commonly associated with the triad of optic nerve hypoplasia, absence of the septum pellucidum (and other midline brain defects), and hypo-function of the pituitary gland. Growth hormone deficiency is the most common manifestation of pituitary hypofunction in SOD; however, any combination of hormones may be deficient. We report the case of a 17-month-old female infant with a history of SOD and panhypopituitarism who despite hormone therapy (including hydrocortisone) died suddenly as a likely result of adrenal crisis in combination with dehydration and central temperature instability. At autopsy, gross findings in the brain were consistent with her diagnosis of SOD. Interestingly, inspection of the decedent’s liver revealed multiple tan masses, measuring between 0.5 to 1.3 cm. Pale, tan, cut surfaces contained central stellate scars. These lesions, on gross and microscopic inspection, were consistent with focal nodular hyperplasia (FNH). This is noteworthy, as it appears to be the first case of FNH associated with SOD. No prior mention was noted in a literature search. FNH is usually asymptomatic. It most commonly occurs as a single mass but may be multiple in 10% of cases. It has been postulated that FNH arises in association with oral contraceptive pills. It is plausible that the decedent’s hydrocortisone therapy (a steroid hormone akin to estrogen/progesterone in oral contraceptive pills) contributed to her multiple FNH. Supporting this idea, reports have shown that a diet high in cholesterol (a steroid hormone precursor) is plausible that the decedent’s hydrocortisone therapy (a steroid hormone precursor) is associated with the development of FNH.

Florid Squamous Metaplasia in a Case of Diffuse Alveolar Damage and Bronchopneumonia
(Poster No. 89)

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Squamous metaplasia of the respiratory tract is frequently seen when respiratory epithelium is subjected to almost any type of injury, including physical, chemical, infectious, ischemic, or inflammatory injury. However, florid squamous metaplasia is rare; when associated with cytologic atypia, it can be confused with squamous cell carcinoma. Therefore, it is extremely important to know about the existence of florid squamous metaplasia and not to confuse it with squamous cell carcinoma. We report a rare case of florid squamous metaplasia in the background of diffuse alveolar damage and bronchopneumonia in a 52-year-old man. He presented with shortness of breath, fever, and dizziness for 1 week and was found to have gram-negative septicemia on admission to the hospital. He subsequently developed respiratory and acute renal failure. He died of ventricular tachycardia 11 days after initial presentation. At autopsy, both lungs showed extensive squamous metaplasia in the areas normally lined with bronchiolar and alveolar epithelium in a bronchioloicentric pattern (Figure 26). Initial impression was clinically unsuspected squamous cell carcinoma. Other findings included diffuse alveolar damage, hyaline membrane formation, fibrin deposition, dilated alveolar spaces, focal thrombus formation, congestion, edema, and diffuse bronchopneumonia involving all lobes. Careful histologic examination revealed a range of cytologic atypia in the squamous cell nests. Given the background of diffuse alveolar damage, we concluded that this case represented an example of very unusual florid and atypical squamous metaplasia of the lung. To our knowledge, this is the third reported case of extensive squamous metaplasia associated with diffuse alveolar damage.

Malignant Perivascular Epithelioid Cell Neoplasm: An Autopsy Case of a 32-Year-Old Woman
(Poster No. 90)

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Perivascular epithelioid cell neoplasms are a family of mesenchymal tumors consisting of perivascular epithelioid cells that express both muscle and melanocytic markers. Clear cell “sugar” tumor of the lung, renal angiomyolipoma, and lymphangioleiomyomatosis are the 3 most common tumors in this group. Other rare perivascular epithelioid cell neoplasms have been reported to occur in various areas in the body, including the uterus, cervix, vagina, abdominal wall, omentum or mesentery, and retroperitoneum. We present an autopsy case of a 32-year-old woman with a perivascular epithelioid cell neoplasm arising from the broad ligament of the uterus. The initial diagnosis was in 2005. The mass continued to grow despite aggressive chemotherapy treatment. At autopsy, there was a 3080-g mass with an additional 1300 g of loose bloody parenchymal tissue. The mass was located in the right lower quadrant without involvement of the uterus, ovaries, or fallopian tubes. Histologically, perivascular sheets of spindle to epithelioid cells with clear to eosinophilic cytoplasm were identified (Figure 27). The nuclei were uniform and round to oval with homogenous chromatin. Brown to black pigment was noted multifocally. There were also areas of acute hemorrhage and necrosis interspersed within the tumor. Vascular proliferation was also present. The tumor cells stained positive for vimentin and actin and negative for S100. We reviewed the literature, and to the best of our knowledge, this is the third case of perivascular epithelioid cell neoplasm arising from the broad ligament. It is also the first case of the aggressive lethal variant causing death.
Diffuse Bronchogenic Adenocarcinoma: A Rare Presentation of Primary Lung Cancer

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Diffuse, bilateral adenocarcinoma is an extremely rare presentation of primary lung cancer, characterized by either widespread nodules involving all lobes or a pattern resembling interstitial pneumonia. We report a case of a 73-year-old man who presented with failure to thrive after a recent hospitalization for postobstructive pneumonia. He was clinically suspected to have lung cancer, although imaging and cytology were nondiagnostic. Computed tomography findings included diffuse airspace opacities, a questionable right infrahilar soft tissue mass (adenopathy versus consolidated lung), and bilateral pleural effusions. Additional findings included a 1.8-cm, left renal mass and multiple blastic lesions in the axial and appendicular skeleton that were suspicious for metastatic disease. A right lower lobe bronchial washing and a fine-needle aspirate of a level 2R lymph node showed atypical cells. The autopsy was limited to the lungs and revealed firm, mottled, and edematous lungs. Grossly, no discrete tumor mass was identified, although the lungs showed tan-yellow discoloration in an interstitial pattern (Figure 28, A). Microscopically, all lobes of both lungs showed extensive infiltration by well-differentiated adenocarcinoma with diffuse stromal, pleural, lymphatic, and vascular wall invasion (Figure 28, B). Immunohistochemical stains revealed the tumor cells were positive for cytokeratin 7 and thyroid transcription factor and negative for stromal, pleural, lymphatic, and vascular wall invasion (Figure 28, B).

Origin of an Anomalous Left Coronary Artery From the Left Hilar Pulmonary Artery Associated With Complex Congenital Heart Disease: An Autopsy Case Study of a Previously Unreported Entity

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The most important clinically significant coronary malformation among the many described to date is the anomalous origin of the left main coronary artery from the pulmonary artery. It is rare and has an incidence of approximately 1 in 300,000 live births. Most of the patients become symptomatic in early infancy with failure to thrive, tachypnea, dyspnea, or angina-like episodes. In most cases, the anomalous coronary arises from either the posterior or the left cusp of the pulmonary artery trunk. We report on an autopsy case of an infant who suffered from complex congenital heart disease that included a rare presentation of anomalous left main coronary artery from the pulmonary artery. The anomalous coronary arose from the distal pulmonary artery at the hilum of the left lung. The other anomalies present were transposition of the great vessels, left ventricular hypoplasia, and mitral and pulmonary atresia. To the best of our knowledge, this is the first case to report this peculiar presentation of the anomalous left coronary artery arising from the pulmonary artery.

Sudden Death Due to Undiagnosed T-Lymphoblastic Leukemia/Lymphoma in a 5-Year-Old Boy

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Undiagnosed neoplasms in childhood are a rare cause of sudden and unexpected death, and most of these cases involve the heart or central nervous system. Unexpected deaths due to undiagnosed hematologic malignancies are limited to a small number of case reports. We present a case of T-lymphoblastic leukemia/lymphoma diagnosed at forensic autopsy in a 5-year-old boy who had no significant medical history and who complained of nausea and vomiting in the subsequent 2 days prior to his death. Meningitis was clinically suspected. Findings at autopsy included 100% cellular bone marrow with greater than 95% blasts. Hemorrhages involving the cerebrum (9 cm), pons, epicardium, lungs, and thymus were present. Prominent leukemic infiltrates and leukostasis were present in the brain, heart, lungs, spleen, hilar lymph nodes, liver, and kidneys. A peripheral blood smear and automated blood count showed a white blood cell count of 435 × 109/L with greater than 80% circulating blasts and mild anemia and thrombocytopenia. Immunohistochemical stains confirmed the diagnosis of T-lymphoblastic leukemia/lymphoma with a precursor T phenotype. Given these circumstances, the diagnosis of acute leukemia should be considered when an intracerebral hemorrhage and/or visceral hemorrhages are identified on internal examination to help ensure appropriate collection of tissue for smears and microscopic examination. This case also highlights the uncommon but serious risks associated with acute lymphoblastic leukemia and hyperleukocytosis.

Reactivation of Histoplasmosis With Sepsis in Clinically Inapparent Human Immunodeficiency Virus Infection

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Histoplasmosis is one of the most common opportunistic infections to attack patients with acquired immunodeficiency syndrome. Many human immunodeficiency virus-infected patients who develop histoplasmosis, disseminated disease occurs in 95% of cases. Although any organ system may be affected, presentation with fulminant gastrointestinal involvement is uncommon. We report an autopsy case of severe involvement of the colon with histoplasma in a 28-year-old female immigrant from El Salvador who was human immunodeficiency virus–positive. She had an unusual presentation of end-stage acquired immunodeficiency syndrome that was clinically inapparent with no significant history of previous infections. She sought medical attention for a sore throat and dysphasia and received treatment for a viral syndrome. Within 4 months of her initial presentation, she was hospitalized and died 4 days later. At autopsy, there was evidence of widespread Histoplasma in most of the body organs, including lungs, esophagus, colon, kidneys, liver, spleen, adrenals, lymph nodes, and cervix. These findings were compatible with Histoplasma sepsis. The lymph nodes and spleen showed very severe lymphoid depletion, supporting the diagnosis of end-stage acquired immunodeficiency syndrome. Mesenteric lymph nodes had numerous hyalinized granulomas, with Histoplasma involvement suggesting reactivation of Histoplasma infection secondary to severe immunodeficient state. In the large intestine, transmural necrosis, hemorrhage, suberosal inflammation,
serosal thickening, and very extensive mucosal and submucosal involvement with histoplasmosis were identified. This autopsy demonstrates that clinically unsuspected human immunodeficiency virus infection may present with severe immunodeficiency at initial presentation.

**Intimal Smooth Muscle Proliferation of Mesenteric Arterial Branches Complicated by Fatal Ischemic Enterocolitis in a Cocaine User**

(Poster No. 95)

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Idiopathic intimal hyperplasia of systemic small arteries has been rarely described. Most cases have involved fibrosis and little or no lipid. Cocaine-related nonatheromatous intimal fibrosis of the epicardial coronary arteries has also been reported but only rarely. We performed an autopsy on a cocaine user who exhibited intimal hyperplasia of multiple small mesenteric arterial branches. A 51-year-old man with a history of nasal and intravenous cocaine use presented with syncope. He was admitted to the hospital for severe congestive heart failure and died suddenly on his third day of hospitalization. A toxicology screen was negative. Autopsy showed acute and chronic ischemic enterocolitis, which had not been clinically suspected as the immediate cause of death. The superior mesenteric artery was normal, but the proximal inferior mesenteric artery had mild to moderate concentric luminal narrowing by intimal fibrosis. Examination of multiple small branches of both mesenteric arteries showed marked luminal narrowing by intimal smooth muscle hyperplasia that was nearly occlusive in some vessels. There was no significant accompanying fibroplasia or thrombosis of these vessels. Similar hyperplastic arterial lesions were found within the pelvis but not in other vascular beds. The lesions were even more unusual than other examples of small arterial intimal enlargement in that they involved smooth muscle hyperplasia rather than fibrosis. Furthermore, previously documented cases of small arterial luminal narrowing due to smooth muscle hyperplasia have usually involved the media rather than the intima. The possibility that prior cocaine use contributed to the development of these arterial lesions was not excluded.

**Hydrometrocolpos Associated With Fetal Vascular Thrombosis in the Placenta**

(Poster No. 96)

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Congenital hydrometrocolpos is characterized by distension and fluid collection in the vagina and uterus and is most commonly caused by an imperforate hymen, a transverse vaginal septum, or vaginal atresia. Most cases are discovered in late gestation or shortly after birth. We report on a fetus with a gestational age of 34 and 2/7 weeks who had an imperforate hymen completely occluding the vaginal opening and causing massive hydrometrocolpos with secondary dilatation of the ureters, distal colon, and rectum (Figure 29). There were no other anomalies such as polydactyly to suggest McKusick-Kaufman syndrome. Placental examination showed multifocal thrombosis of large fetal vessels of the chorionic plate and stem villi. A substantial portion of the placenta (~30%) demonstrated avascular villi indicating obstruction of the fetal arterial tree with other areas of congestion and intravillous hemorrhage indicating obstruction of umbilical venous return. These findings indicated that compromise of placental function played a significant role in causing fetal demise. The umbilical cord was normally inserted and devoid of knots or other potential sources of mechanical obstruction. Review of prenatal magnetic resonance images showed that the intra- abdominal umbilical arteries were displaced toward the abdominal side wall by the distended vagina. We propose that external compression exerted by the massive and enlarging hydrometrocolpos on the umbilical vessels led to vascular stasis in the placental circulation, leading to the fetal vascular thromboses. To our knowledge, this is the first case report of hydrometrocolpos associated with extensive fetal vascular thrombosis in the placenta attributable to obstruction of the intra-abdominal umbilical vessels.

**Undifferentiated Sarcomatoid Gallbladder Carcinoma With Osteoclast-Like Giant Cells and a Black Aorta: An Autopsy Case Report**

(Poster No. 97)

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We present the autopsy results for a 61-year-old African American man with gallbladder carcinoma. One year prior to autopsy, an invasive mass was found on a cholecystectomy specimen. It consisted of a dual population of osteoclast-like giant cells in a mesenchymal background with marked nuclear atypia. The tumor was pancytokeratin-positive and p53-positive and manifested a high proliferation rate by Ki-67. Epithelioid tumor cells were epithelial membrane antigen-positive, and a subpopulation of mononuclear cells were CD138+. This immunohistochemical profile was typical of an undifferentiated carcinoma of the pancreas or biliary tree. However, a transition zone between the tumor and dysplastic epithelium in the gallbladder was seen, confirming a gallbladder primary, which is exceedingly rare. Additionally, at autopsy, a dark black discoloration was grossly present in both the intimal and medial layers of the aorta and coronary arteries (Figure 30). No additional areas of discoloration were noted grossly. No pigment or hemosiderin was visualized with hematoxylin-eosin or Prussian blue. Metal deposition was ruled out by scanning electron microscopy, including secondary electron imaging, backscattered electron imaging, and energy dispersive spectrometry. A side effect of chemotherapeutic agents or minocycline was considered but was not supported by the clinical history. Finally, given the focal distribution, which did not involve the eyes, joints, bones, or cartilage, the lack of arthritis, dark-colored urine, and African American descent, alkaptornuric ochronosis was extremely unlikely. To our knowledge, findings such as these have never been previously reported.
IgG4-Related Sclerosing Disease Simultaneously Affecting Heart and Kidney

((Poster No. 98)

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IgG4-related sclerosing disease is characterized by IgG4-positive plasma cells and fibrosis within affected tissues, as well as elevated serum IgG4. It is a multisystem disease for which clinicopathologic parameters are still being defined. Cardiac involvement by IgG4-related sclerosing disease has not been previously reported. A 55-year-old woman without significant medical history developed complete heart block and was treated with an implanted pacemaker. During the next 8 months, she suffered from intermittent fever, emesis, fatigue, and atrial flutter. Imaging studies revealed a 4.5 x 1.3-cm cardiac mass arising in the left atrium and a 9.2 x 6.5 x 6.0-cm right renal mass. Cardiac and renal biopsies both showed extensive parenchymal destruction by a fibrosing and inflammatory process mainly composed of plasma cells and lymphocytes. Appropriate stains and cultures revealed no bacteria or fungi. Collections of plasma cells showed increased staining for IgG4, with more than 30 IgG4-positive cells per high-power field. Total serum IgG level was normal, but the IgG4 subclass was elevated at 322 mg/dl (reference range, 8-140 mg/dl). Treatment with oral prednisone (60 mg/d) resulted in clinical improvement, and a chest computed tomography scan performed after 6 months showed no residual cardiac mass. This is the first case of an inflammatory, fibrosing, cardiac mass in which IgG4-positive plasma cells and elevated serum IgG4 were documented. Biopsies of the heart and kidney showed very similar findings, indicating that both organs were affected by systemic IgG4-related sclerosing disease. Prednisone may be an effective treatment for cardiac involvement in this condition.

Primary Cardiac Neoplasms: A Review of 298 Archival Cases From a Heart Center

(Poster No. 99)

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Context: Primary cardiac tumors are rare, and thus, there is a paucity of description in published literature. Because most of these tumors present with nonspecific symptoms, an archival review might provide additional data of potentially practical value for future clinical research.

Design: The surgical pathology files during a 33-year period (1976–2009) were reviewed for all archival cases of cardiac tumors. There were 268 of 302 (88.2%) cases that were clinically established as primary.

Results: Of 298 primary cardiac tumors, 279 (93.6%) were classified as benign, while 19 (6.4%) were classified as malignant. There was female sex predilection for both benign and malignant tumors with a male to female ratio of 1:2.5. Of the benign tumors, the most common histologic types were myxoma (94.5%), fibroma (1.4%), rhabdomyoma (1.4%), leiomyoma (0.7%), and hemangioma (0.7%). Locations in decreasing order of frequency were left atrium, right atrium, left ventricle, and right ventricle. Tumor sizes ranged from 0.4 to 8.2 cm. Average age of patient was 51 years. Among the malignant tumors, the most common histologic types were myxofibroblastic sarcoma (15.8%), malignant fibrous histiocytoma (10.5%), myxosarcoma (10.5%), and non-Hodgkin lymphoma (10.5%). Locations in decreasing frequency were left atrium, right atrium, right ventricle, ventricle and atrium, biventricular, and bialtral. Tumor sizes ranged from 0.8 to 10 cm. Average age of patients was 37 years.

Conclusions: Both primary benign and malignant cardiac tumors generally have similar female sex predilection. Interestingly, the limited number of malignant cases occurred in a relatively younger age group than the benign cases.

Cardiac Pathology in a Patient 6-Years Post Stem Cell Transplant for Multiple Myeloma: Case Report and Review of Literature

(Poster No. 100)

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Amyloidosis is an uncommon group of disorders that are characterized by the extracellular deposition of amyloid-forming proteins in 1 or more organs. Cardiac amyloidosis, leading to restrictive cardiomyopathy, is a common feature of myeloma-associated amyloidosis disease. We report a case of multiple myeloma in a patient who received successful stem cell transplantation 6 years prior to cardiac transplantation. This 45-year-old man was diagnosed with multiple myeloma in 2002. He was told he had amyloidosis with restricted heart disease. He underwent a successful stem cell transplant in 2004 with no further chemotherapy. His restrictive cardiomyopathy developed into dilated cardiomyopathy with significant right heart congestive failure in 2007. He received combined heart and renal transplants in 2010. The explanted heart showed amyloid deposition in a loose fibrillar pattern with cardiomyocyte degeneration. Congo red and x light chain staining were positive. Hematopoietic stem cell transplantation in comparison to conventional chemotherapy has been shown to increase survival in myeloma patients. Our patient survived 6 years after a stem cell transplant before needing a heart transplant. Also, there are reports showing amyloid resorption after effective chemotherapy. In this case report, the clinical, cardiac, and pathologic distribution pattern and a restrictive heart condition that became dilated cardiomyopathy seem to suggest amyloid protein resorption. This phenomenon deserves clinical attention; in patients who receive effective chemotherapy or stem cell transplant, dilated cardiomyopathy should be considered as a consequence of amyloid resorption instead of restrictive cardiomyopathy as in nontreated patients.

Diverticulum of the Right Ventricle: Rare Congenital Cardiac Defect

(Poster No. 101)

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Congenital ventricular diverticula are extremely rare anomalies. Fewer than 200 cases have been reported in the literature, and, of these, only 18 have involved the right ventricle. Congenital cardiac diverticula are transmural, localized protrusions within the apical or anterosuperior free wall of the ventricles. They are classified as fibrous or fibromuscular. Their origin is unknown, but may include ischemic myocardial injury, endocardial fibroelastosis, and/or hereditary factors. We report a case of intrauterine fetal death at 24-weeks’ gestation due to a right ventricular diverticulum. The mother was a 26-year-old woman whose pregnancy was complicated by first trimester spotting. Prenatal ultrasound findings at 17 weeks included a small cystic hygroma, a thickened atrioventricular valve with abnormal movement, and an area suspicious for ventricular septum defect. At 24-weeks’ gestation, the mother delivered a stillborn female infant. On autopsy, a right ventricular diverticulum was identified in the membranous interventricular septum with no other cardiovascular abnormalities. Microscopic findings confirmed a fibrous diverticulum. Congenital ventricular diverticula are rare congenital defects, which can present at any age; however, they are usually diagnosed during infancy with a variety of symptoms and associated congenital anomalies, especially ventricular septum defect. Rarely is one seen accidentally as the only cardiovascular anomaly, as in this case. It is important to be aware of congenital diverticula and other cardiovascular anomalies, especially congenital aneurysm, that carry an adverse outcome. The finding of a ventricular diverticulum mandates careful classification of the diverticulum and careful search for associated anomalies for subsequent prenatal counseling.

Idiopathic Giant Cell Myocarditis: Case Report With Autopsy Findings and Literature Review

(Poster No. 102)

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Giant cell myocarditis is a rare disorder seen predominantly in young, healthy adults (average age, 46.2 years). It frequently presents with congestive heart failure. The disease has been associated with other autoimmune disorders, and increased survival has been demonstrated with immunosuppressive therapy. Without treatment, the disease is quickly fatal with a mean survival of 3 months. We report a case of a 73-year-old woman who presented to the emergency department with profound hypotension and altered mental status. The patient rapidly deteriorated and died within 48 hours. She had a 3-month history of congestive heart failure and atrial fibrillation requiring pacemaker insertion. Imaging studies found no evidence of coronary atherosclerotic disease. The patient had amyloidosis and an annual history of congestive heart failure. At autopsy, the patient had cardiomegaly (425 g) with 4-chamber enlargement, biventricular hypertrophy, and fibrotic thickening of the mitral and tricuspid valves. No significant coronary atherosclerotic...
luminal narrowing of the vessels was identified. Histologic examination of the myocardium revealed foci of inflammatory infiltrates composed of lymphocytes, occasional histiocytes and eosinophils, and rare multinucleated giant cells (Figure 31). The inflammation was associated with extensive myocyte injury, including hypereosinophilic myocytes, loss of myocytes, perivascular and interstitial fibrosis, and prominent neovascularization. These findings confirmed the diagnosis of idiopathic giant cell myocarditis. This case is unique due to the elderly age of the patient and serves as a reminder to consider the diagnosis of idiopathic giant cell myocarditis. This case is unique due to the elderly age of the patient in patients presenting with congestive heart failure after more common disorders have been excluded.

Chagas Myocarditis in a 56-Year-Old Woman

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We recently encountered a case of Chagas disease in a 56-year-old woman of Bolivian origin who had a clinical history of Chagas disease that was diagnosed at 6 years of age. She underwent heart transplantation for intractable heart failure. The parasite was found in only 1 section and a single myocyte of the 17 sections submitted with the optimally fixed explanted heart, demonstrating exquisite detail that is rarely seen in autopsy specimens. Histopathologic examination of the explanted heart showed severe chronic myocarditis, most extensively involving the left ventricle. A high-powered view of trypanosomal amastigotes within a single myocyte fiber (hematoxylin-eosin stain) showed kinetoplast (Figure 32). In tissue sections, the kinetoplast distinguished Trypanosoma cruzi from Toxoplasma and Histoplasma, which both lack a kinetoplast, and from Leishmania, which has this structure but usually concentrates in the phagocytic cells, an uncommon site for Trypanosoma cruzi. Adult bugs (reduvid bugs) ingest trypomastigotes when taking blood meals from infected animals. In the alimentary tract of the bug, the parasites multiply and differentiate into transient amastigotes, into epimastigotes, and finally into trypomastigotes. Infection of mammals takes place by ingestion of infected bugs or by contamination of mucus membranes, conjunctiva, or abraded skin with fecal material from infected bugs.

POSTER SESSION 200: SUNDAY, SEPTEMBER 26, 2010, 1:30 PM–4:00 PM

Hematopathology; Kidney and Genitourinary Pathology; Ophthalmic Pathology; Microbiology

An Unusual Case of Primary Central Nervous System Low-Grade B-Cell Lymphoma

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Primary central nervous system (CNS) lymphomas are rare lymphoproliferative disorders that account for 1.6% to 4% of primary CNS tumors. Most primary CNS lymphomas are diffuse large B-cell lymphomas with poor prognosis. Low-grade primary CNS lymphomas are extremely rare. We describe a 70-year-old man who was negative for human immunodeficiency virus; he had a 5-year history of progressive dysnomia with new-onset episodic right arm and leg numbness, dysarthria, and blurry vision. A 3.5 × 2.9-cm infiltrative enhancing mass was visualized on magnetic resonance imaging in the left posterior putamen, posterior subinsular region, and adjacent mid-temporal region. No lesion was found in the thorax, abdomen, scrotum, or pelvis. Results of a concomitant tandem bone marrow biopsy were negative. Serum immunofixation electrophoresis did not reveal paraprotein in the serum. After excision, histologic and immunophenotypic evaluation of the tissue revealed small- to medium-sized CD20+ B cells with surface lambda immunoglobulin light chain restriction with negative CD5, CD10, CD23, and cyclin D1. Interestingly, cytoplasmic lambda immunoglobulin light chain restricted–CD38 bright-positive plasma cells were also detected. A diagnosis of low-grade B-cell lymphoproliferative disorder of the CNS was rendered. The differential diagnosis included extranodal marginal zone B-cell lymphoma and lymphoplasmacytic lymphoma. The patient has achieved good clinical response upon treatment with temozolomide and rituximab. This case illustrates a multimodal approach to diagnosing low-grade primary CNS lymphomas.

Copper Deficiency Presenting With Neurologic Symptoms and Cytopenias

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Copper deficiency is rare and may be clinically confused with myelodysplasia/myeloneuropathy because patients often present with anemia, neutropenia, megaloblastic marrow changes, and neurologic manifestations, which are often seen with B2 deficiency. Copper deficiency may be seen in malnutrition, prematurity, parenteral and enteral feeding, gastrectomy, copper-chelating agents, or excessive zinc. A 31-year-old woman presented with hypothyroidism and a 5-month history of fatigue, weakness, pain, and paresthesia in her back, legs, and feet. Complete blood cell count showed a macrocytic anemia (hemoglobin 4.4 g/dL, mean corpuscular volume 103.9 fL) and neutropenia (absolute neutrophil count 0.18 K/cu mm). Results of laboratory studies for iron deficiency and paroxysmal nocturnal hemoglobinuria were negative; erythropoietin was increased. Bone marrow evaluation revealed a normocellular marrow with left-shifted maturation, megaloblastic erythropoiesis, and cytoplasmic vacuoles in myeloid and erythroid precursors (Figure 33). Despite transfusion and granulocyte colony-stimulating factor, the patient returned 1 month later with no
significant improvement. Repeat complete blood cell count and bone marrow examination showed similar findings; results of additional cytogenetic studies with fluorescence in situ hybridization/myelodysplasia panel were normal. Serum copper (2 µg/dL; reference range, 80–155) and ceruloplasmin (<10 mg/dL; reference range, 20–60) were very low. Zinc was slightly elevated; B₁₂ levels were normal. Parenteral copper was not tolerated; therefore, treatment with oral copper supplement was initiated. Six months later her anemia, neutropenia, and neurologic status improved significantly but did not resolve completely, likely because of ongoing hypothyroidism. Copper deficiency should accompany B₁₂ deficiency and myelodysplasia in the differential diagnosis for patients with persistent cytopenias, especially when accompanied by neurologic signs/symptoms.

**Advia Parameter, Delta MC (MCHC-CHCM) Reliably Correlates With Therapy Responsiveness in Patients With Sickle Cell Disease Treated With Hydroxyurea** (Poster No. 3)

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**Context:** This study examines the utility of Advia parameters in sickle cell disease (SCD) patients treated with hydroxyurea (HU). HU is approved by Food and Drug Administration for treating SCD. Red blood cell (RBC) parameters reported by Advia include mean corpuscular hemoglobin concentration (MCHC), calculated from [Hgb]/RBC * MCV] and corpuscular hemoglobin concentration mean (CHCM) measured by light scatter properties (Figure 34). Advia parameter CHCM is represented in this RBC histogram where the x-axis is hemoglobin concentration and the y-axis is MCV. Dots represent individual RBCs measurements; CHCM represents x-axis distribution. We report that difference between MCHC and CHCM (delta MC) reported by Advia 2120 is different in patients treated with HU, correlating with therapy response.

**Design:** We identified 17 patients (2007–2009) with SCD; 6 patients were treated with HU. Automated RBC parameters from Advia 2120 (MCHC, MCHC, CHCM, delta MC) were compared in treated patients (n = 6) and untreated/normal controls (total n = 18).

**Results:** After therapy with HU, patients with SCD develop macrocytosis and increased HbF. Untreated patients with SCD tend to have microcytosis (unless transfused) and normal levels of HbF. There was no overall difference in MCHC (mean MCHC: HU treated = 34.78; untreated = 34.53). However, CHCM was significantly lower (mean CHCM: HU treated = 33.76; untreated = 34.82; P = .03) and delta MC was significantly higher (HU treated = 0.72; untreated = −0.3; P < .001) in the treated group.

**Conclusions:** We propose that the Advia 2120 parameter CHCM and delta MC can be used in following SCD patients treated with HU. Physiologic changes induced by HU, including macrocytosis and HbF distribution within individual RBCs, may account for decreased CHCM and increased delta MC in HU treated RBCs.

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A subset of hematopoietic neoplasms are characterized by rearrangements of either the platelet-derived growth factor receptor α (PDGFRα) gene, platelet-derived growth factor receptor β (PDGFRβ) gene, or fibroblast growth factor receptor 1 (FGFR1) gene. Neoplasms with these genetic alterations are relatively uncommon and may present as either a myeloid or lymphoid neoplasm and usually with accompanying eosinophilia. Abnormal lymphoblastic populations have been reported previously in association with PDGFRα and FGFR1 rearrangements but, to our knowledge, not with PDGFRβ rearrangement. We report on a 36-year-old man who presented with eosinophilic pneumonia, as well as marked peripheral eosinophilia and neutrophilia. A peripheral blood smear revealed abnormal eosinophils and a small population of blasts (Figure 35). Flow cytometry of the blood showed around 5% of nucleated cells to be a...
small but distinct population of B lymphoblasts. The bone marrow was hypercellular (>95%) with marked neutrophilic and eosinophilic hyperplasia. Karyotype analysis revealed a clone with the following 2 translocations: t(5;12)(q33;p13) and t(1;6)(p36;q12). ETV6 (TEL) (12p13) rearrangement was demonstrated by fluorescence in situ hybridization. Although PDGFRB rearrangement was not detected by fluorescence in situ hybridization, it is not unlikely to be rearranged in this case given the following: the observed translocation involved the PDGFRB locus (5q33), the clinical picture, and the previous reports of false-negative fluorescence in situ hybridization assays for PDGFRB rearrangement. Interestingly, circulating lymphoblasts have not been previously reported in hematopoietic neoplasms associated with t(5;12)(q33;p13); however, this translocation has been detected in cell lines derived from childhood acute lymphoblastic leukemia.

**Coexistence of B-Cell Chronic Lymphocytic Leukemia and Essential Thrombocythemia: A Case Report and Review of the Literature** (Poster No. 5)

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Coexistence of B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma and essential thrombocythemia is extremely rare. We report a case in which these 2 disorders were diagnosed concomitantly. An 80-year-old woman was referred to our hospital for evaluation of an asymptomatic persistent thrombocytosis, which was detected by routine analysis. No lymphadenopathy or hepatosplenomegaly were identified on physical examination and imaging studies. Laboratory studies revealed a platelet count of 672,000/μL and mild leukocytosis of 11.4 x 10^9/L. The diagnosis of essential thrombocythemia was based on typical morphology and immunophenotype on peripheral blood smear, bone marrow aspiration and biopsies, and the presence of Janus kinase 2 V671F mutation. Concurrent flow cytometric immunophenotyping demonstrated a clonal B-cell proliferation with a λ light chain restriction with coexpression of CD19, CD20, CD5, and CD23 but not CD10. Histologic sections of bone marrow biopsies showed a number of nonparatrabecular lymphoid aggregates of small round lymphocytes. Immunohistochemical staining demonstrated that these lymphoid aggregates were positive for CD20 and CD5 and negative for cyclin D1. The morphologic and immunophenotypic characteristics were consistent with B-cell chronic lymphocytic leukemia. Cytogenetic studies demonstrated a normal female karyotype. The patient continues to be asymptomatic in contrast to most of the previously reported cases. Except for chronic treated hypertension, the patient was otherwise healthy. There was no history of any other underlying malignancies or previous exposure to chemotherapeutic agents. In summary, we report a case of B-cell chronic lymphocytic leukemia with a concurrence of the myeloproliferative disorder, essential thrombocythemia, with a unique clinical course.

**A Case of Hereditary Elliptocytosis With Concomitant Glucose-6-Phosphate Dehydrogenase Deficiency** (Poster No. 6)

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A 23-month-old African American boy presented at birth with jaundice, hyperbilirubinemia, and hemolytic anemia, which later transitioned into sporadic hemolysis precipitated by respiratory infection and fever. Peripheral smear revealed marked elliptocytosis with moderate schistocytes, dacrocyes, and occasional blister cells (Figure 36). No distinct red cell inclusions were observed. Iron studies were noncontributory. Osmotic fragility was normal. Red cell enzyme assay showed glucose-6-phosphate dehydrogenase deficiency. Family history was suggestive of hemolytic anemia on the paternal side. To our knowledge, this is only the second reported case of hereditary elliptocytosis associated with glucose-6-phosphate dehydrogenase deficiency. In contrast to the first case, our patient presented with hemolytic anemia at birth with intermittent hemolytic crises afterward. Hemolytic anemia may be prompted by auto- or alloimmunization, red cell enzyme deficiencies, hemoglobinopathies, or red cell membrane defects. Hereditary elliptocytosis, an autosomal dominant disorder, is due to intrinsic red cell membrane abnormalities and occurs in about 1 of 2000 to 5000 individuals. Infantile poikilocytosis is a subset of hereditary elliptocytosis that is often associated with neonatal hemolytic anemia. Resolution of hemolysis typically occurs with age. Glucose-6-phosphate dehydrogenase deficiency, an X-linked recessive condition, is the most common red cell metabolic derangement. Both are common in individuals of African or Mediterranean descent. Concurrent inheritance of both disorders is probable, although incidence is likely unusual, as evidenced by only a single report in the literature thus far. Oxidative stress possibly provokes hemolysis in a subset of patients. Review of blood smear in conjunction with thorough acquisition of history is paramount for accurate diagnosis.

**B-Cell Lymphoma With t(8;14;18)(q24;q32;q21): A Clinicopathologic Study of 3 Cases** (Poster No. 7)

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**Context:** Translocation of c-myc (8q24) occurs in some aggressive B-cell lymphomas, particularly Burkitt lymphoma, in which immunoglobulin heavy gene (14q32) is frequently involved to form t(8;14)(q42;14q32). The t(14;18)(q32;q21) is a genetic hallmark of follicular lymphoma. Occasionally, B-cell lymphomas demonstrate a composite of these genetic abnormalities.

**Design:** We identified 3 cases of aggressive B-cell lymphoma with a de novo t(8;14;18)(q24q32q21) translocation in our database.

**Results:** All patients were men; ages 34, 59, and 61 years. One had a large retroperitoneal mass. He was treated with R-CHOP with no evidence of persistent disease after 6 months. He was lost to follow-up. The second patient had diffuse abdominal lymphadenopathy with a mass in the pancreatic tail. His disease progressed despite chemotherapy and allogeneic stem cell transplant; he died 1 year after diagnosis. The third patient presented with a testicular mass and fatigue. He was treated with chemotherapy, radiation, and allogeneic stem cell transplant but died 15 months after diagnosis. Extensive bone marrow involvement and circulating Burkitt-like lymphoma cells, resembling lymphoblastic leukemia, were seen at presentation in 2 patients and later in the course of disease in the third.

**Conclusions:** These cases suggest that B-cell lymphoma with de novo t(8;14;18)(q24q32q21) carries a dismal prognosis; the patients with follow-up died 12 to 15 months after diagnosis, despite aggressive treatment. The extensive marrow involvement and circulating Burkitt-like cells seen in these cases may cause confusion with lymphoblastic leukemia (L3 type). The 2008 World Health Organization classification categorizes such cases as B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma.

**Intravascular Large B-Cell Lymphoma Mimicking Temporal Arteritis** (Poster No. 8)

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Intravascular lymphoma is a rare type of large cell lymphoma that is characterized by growth of lymphoma cells within vascular spaces. Most of the reported cases are of B-cell lineage; however, rare examples of T-
cell or natural killer cell lineage have also been reported. At the time of diagnosis, this lymphoma is usually widely disseminated in vascular spaces, including those of the skin and bone marrow; lymph nodes are typically spared. The clinical picture depends on the specific organ(s) involved, making the correct diagnosis difficult. We report a case of intravascular large B-cell lymphoma diagnosed postmortem in a 69-year-old African American woman. The patient presented with unilateral propotis and visual loss. He received corticosteroids for presumed temporal arteritis, but he expired with multiorgan failure within 2 months. The autopsy revealed disseminated intravascular lymphoma predominantly involving vessels and focial parenchyma in the heart, kidneys, liver, stomach, lungs, adrenal glands, small intestine, bladder, thyroid, and brain. Interestingly, there was also partial involvement of the retroperitoneal lymph nodes. Immunohistochemically, the lymphoma cells were positive for CD20 and negative for CD3, CD5, CD10, CD56, and MUM-1. This case supports the “mimicking nature” of this rare entity. The unusual presentation included proptosis and visual loss simulating temporal arteritis. It is imperative for this disease to be included in the differential diagnosis. This case also shows that lymph nodes can be partially involved. Increased awareness, early tissue diagnosis (lymph node, bone marrow, or skin), and prompt chemotherapy are crucial for this often lethal disease.

Acute Myelogenous Leukemia Following Untreated Chronic Lymphocytic Leukemia: Cyto genetic Evidence of Separate Entities
(Poster No. 9)

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We report a case of a simultaneous diagnosis of acute myeloid leukemia (AML) with untreated chronic lymphocytic leukemia (CLL). A 74-year-old woman was diagnosed with CLL (RAI stage 0). No treatment was given at that time. Two years later, the patient was referred for evaluation of leukocytosis, anemia, and thrombocytopenia. An indeterminate bone marrow biopsy aspirate were performed, revealing 2 distinct populations of cells; one population was composed of nodules of small lymphocytes consistent with CLL cells, whereas the second population consisted of large immature blast cells infiltrating in an interstitial pattern. The presence of these 2 populations was confirmed by morphology, immunophenotyping, and flow cytometry. The cytogenetic results were also consistent with 2 different neoplastic clones. A deleted 13q clone observed at interphase fluorescence in situ hybridization most likely represented the CLL clone, whereas balanced translocations observed in 24-hour unstimulated culture analyses represented the AML clone. RAI stage 0. No treatment was given at that time. Two years later, the patient was referred for evaluation of leukocytosis, anemia, and thrombocytopenia. An indeterminate bone marrow biopsy aspirate were performed, revealing 2 distinct populations of cells; one population was composed of nodules of small lymphocytes consistent with CLL cells, whereas the second population consisted of large immature blast cells infiltrating in an interstitial pattern. The presence of these 2 populations was confirmed by morphology, immunophenotyping, and flow cytometry. The cytogenetic results were also consistent with 2 different neoplastic clones. A deleted 13q clone observed at interphase fluorescence in situ hybridization most likely represented the CLL clone, whereas balanced translocations observed in 24-hour unstimulated culture analyses represented the AML clone. In this article, we report the clinical, immunophenotypic, and cytogenetic features of untreated CLL followed by the development of AML. Our cytogenetic findings support that this rare occurrence may represent 2 separate disease processes.

A Congenital Myelodysplastic Syndrome in a Patient With Hereditary Hemochromatosis
(Poster No. 10)

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Pediatric myelodysplastic syndrome (MDS) is rarely seen but is often associated with congenital marrow failure syndromes. Our patient is a young white boy who presented at 3 months of age with mild thrombocytopenia, which progressed to profound thrombocytopenia, mild to moderate anemia, and neutropenia within 3 years. In addition, he had feeding delay, chronic diarrhea, episodes of pneumonia, and achalasia. Serial bone marrow biopsies showed progressive hypocellularity, from normocellularity at 3 months to 5% to 10% cellularity at 3 years of age. Cytogenetic analyses detected a low number of monosomy 7 in several bone marrow samples, supporting a diagnosis of hypoplastic MDS. Since then, his cell counts have been rather stable, with platelets around 20,000 to 10,000/μL, and hemoglobin and neutrophils within a mildly decreased range. At age 19 years, an elevated ferritin level (694 ng/mL) prompted a molecular diagnostic test revealing homozygosity of the C282Y mutation, although increased serum iron was noted much earlier. He was thus diagnosed with hereditary hemochromatosis (HH) and treated with phlebotomy/iron chelation with bone marrow transplant as an option if his MDS worsens. HH is an autosomal recessive disorder of dysfunctional iron metabolism with 80% to 90% of patients harboring a C282Y and/or H63D point mutation of the HFE gene. Studies have demonstrated that heterozygous C282Y and/or H63D mutations are significantly increased in subgroups of MDS, especially in those with ringed sideroblasts, compared with healthy controls. Our case highlights an early development of MDS in HH with homozygous C282Y suggesting HH germline mutations’ predisposition to this myeloid malignancy.

Jacobsen Syndrome: A Possible Alternate Mechanism for Thrombocytopenia
(Poster No. 11)

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Paris-Trouseau/Jacobsen thrombocytopenia is a rare genetic syndrome. Patients demonstrate hematologic features ranging from pancytopenia to isolated thrombocytopenia. The proposed mechanism for severe thrombocytopenia is decreased platelet production due to small, immature megakaryocytes that undergo massive intra–bone marrow lysis. We present the case of a 69-year-old man with a past medical history of Jacobsen syndrome. Serial complete blood count examinations were performed using the Sysmex XE-2100, demonstrating anemia and severe thrombocytopenia with an increased immature platelet fraction (IPF). Peripheral blood smear showed macrocytic anemia and thrombocytopenia with large platelets containing giant granules. A cytogenetic study performed 9 years earlier showed 46,XY.del(11)(q23). The bone marrow demonstrated a normocellular bone marrow with prominent dysmegakaryopoiesis, adequate number of megakaryocytes with hypolobated forms, and micromegakaryocytes (Figure 37). His peripheral blood was collected during a 30-day period, and his IPF was measured 6 times. Measurement of IPF has proven to be an important diagnostic tool in determining the etiology of thrombocytopenias. Determination of reticulated platelets helps to differentiate thrombocytopenia due to decreased production from that due to peripheral destruction of platelets. A high IPF has been reported in hyperproliferative thrombocytopenia due to peripheral destruction of platelets. The IPF levels in our patient were consistently elevated. This suggests that, for patients with Jacobsen syndrome, peripheral destruction leads to decreased life span of platelets with release of immature platelets from the affected bone marrow. This could be a concurrent mechanism, accounting for the severe thrombocytopenia seen in Paris-Trouseau/Jacobsen patients.
Megakaryocytes are rarely detected in lymph nodes in the absence of hematopoietic disease. We report a rare case with megakaryocytes present in the parenchyma of the auxiliary lymph nodes without coexisting extramedullary hematopoietic elements. A 75-year-old man presented with a 3-year history of severe anemia secondary to autoimmune hemolysis. He was treated and was essentially disease-free for more than 2 years. Then, the patient presented again with a new onset of autoimmune hemolysis with lymphadenopathy in the axilla. He subsequently underwent lymph node biopsy. Two nodes (1.4 cm in diameter) were received for evaluation. Microscopically, the nodes demonstrated paracortical hyperplasia with reactive immunoblasts, mild follicular hyperplasia, and histiocytic hyperplasia. There were scattered atypical large cells showing irregular dense single to multilobulated nuclei with scant or abundant cytoplasm. The large cells appeared 5 to 20 times larger than the lymphocytes in the background.

To identify the origin of these cells, we used B-cell, T-cell, Reed-Sternberg cell, and natural killer cell markers, all of which were negative. We thought the cells could be megakaryocytes. For verification, we sent the case to Mayo Clinic (Rochester, Minnesota), which confirmed the reactive nature of the nodes and the origin of the cells to be megakaryocytes (positive expression of CD61). However, there was no erythropoietic or myeloepoietic components detected. These megakaryocytes are of no known diagnostic significance, except for possible misinterpretation as malignant cells. Their presence may increase the possibility of misinterpretation as malignant cells.

Blastic Plasmacytoid Dendritic Cell Neoplasm

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Blastic plasmacytoid dendritic cell neoplasm is a rare neoplasm with characteristic clinicopathologic and immunophenotypic features. A patient presented with violaceous skin lesions and generalized lymphadenopathy. Biopsy of skin revealed infiltrates of small- to intermediate-sized lymphocytes that were suggestive of lymphoid malignancy. Flow cytometry studies of lymph node biopsy demonstrated a large population of cells expressing CD4, CD56, and CD123. There was also extensive bone marrow infiltration by mononuclear cells expressing CD4 and CD56 on repeat bone marrow biopsy. We diagnosed blastic plasmacytoid dendritic cell neoplasm based on these findings. The patient received 8 cycles of CHOP chemotherapy from October 2008 to June 2009 with good response clinically and by positron emission and computed tomography scans. In August 2009, he experienced recurrence of the skin lesions, prompting second-line chemotherapy for recurrent disease with bortezomib, thalidomide, and dexamethasone. Immediately after the start of therapy, the patient developed extensive hemorrhagic infarcts of the right and left lungs and the kidneys and high fever that did not respond to antibiotic therapy. The patient died due to renal and respiratory failure. Autopsy showed disseminated blastic plasmacytoid dendritic cell neoplasm in bone marrow, skin, lymph nodes, lungs, and kidney. Literature review shows that this neoplasm does not favorably respond to common chemotherapeutic regimens; however, it shows good outcome in cases where patients received allogeneic stem cell transplant after ablation chemotherapy or received no treatment. We suggest heightened awareness of this neoplasm in the differential diagnosis of malignant lymphomatous skin lesions.

Angioimmunoblastic T-Cell Lymphoma: Phenotypic Characteristics and Recent Evidence on Disease Pathogenesis

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Angioimmunoblastic T-cell lymphoma is a rare entity comprising about 1% to 2% of non-Hodgkin lymphomas and 15% to 20% of peripheral T-cell neoplasms. It is distinguished by systemic findings, such as fever, fatigue, weight loss, mucocutaneous lesions, skin rash, and lymph nodes (Figure 38, A [flow cytometry] and B [reverse transcription–polymerase chain reaction]). In addition, it may affect a man with intermittent low-grade fever, weight loss, pruritic rash, splenomegaly, cervical lymphadenopathy, and clinical evidence of acute Epstein-Barr virus infection on serology. The neck lymph node biopsy revealed a polymorphonuclear infiltrate, which consisted predominately of small- to intermediate-sized lymphocytes, occasional large Reed-Sternberg-like cells, plasma cells, eosinophils, and histiocytes. The neoplastic lymphoid cells mainly expressed T-cell markers CD43, CD4, and CD5, as well as follicular helper T-cell marker CD10, and were negative for CD8, according to immunohistochemistry and flow cytometric analysis. Only a few scattered CD20+, CD79a+, and PAX5+–positive B cells were present. We noted prominent proliferation of high endothelial venules accentuated by CD34 and follicular dendritic cells highlighted by CD23. The clinical, morphologic, and immunophenotypic features were most consistent with angioimmunoblastic T-cell lymphoma. Recent studies have highlighted the role of Epstein-Barr virus infection of these lesions and in the development of angioimmunoblastic T-cell lymphoma. Furthermore, although most lymphomas arising from germinal center lymphocytes are of B-cell origin, recent investigations have postulated that this particular T-cell neoplasm may originate from germinal center follicular helper T-cells expressing CD10, Bcl-6, and CXCL13. CXCL13 is a chemokine that participates in the recruitment and activation of B cells and that facilitates proliferation of follicular dendritic cells.

A Diagnosis of Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Prompted by Cutaneous Perineural Lymphocytic Infiltrates in Squamous Cell Carcinoma

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Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) is one of the more common forms of lymphoproliferations in the United States. Patients with CLL/SLL are at an increased risk for the development of second malignant neoplasms, the most common of which is cutaneous squamous cell carcinoma (SCC). Lymphoma-associated SCC tends to behave more aggressively than without lymphoma. Hence it is important to distinguish between distinct inflammatory versus malignant lymphoid infiltrate associated with SCC. This case reports illustrates a patient with a SCC of the right posterior ear and left neck, who was treated with Mohs micrographic surgery. A dense lymphocytic infiltrate was noted at the periphery of the SCC with a striking perineural distribution. This was suspicious for lymphoproliferative process. Immunohistochemical stains were performed and documented lymphocytes positive for CD5, CD20, and CD23. The diagnosis of CLL/SLL was rendered. This case report demonstrates that SCC with intense infiltrate, especially with perineural distribution, may harbor lymphoproliferations. Immunohistochemistry is helpful with evaluating such infiltrates.

New Insight into CD317, A Multiple Myeloma Antigen

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Context: CD317 is a lipid raft-associated protein with unique topology. It was first identified as an antigen on terminally differentiated human plasma cells, and it can be used as a target for immunotherapy against multiple myeloma. CD317 also functions as a “tetherin” protein that inhibits the release of several viruses, including human immunodeficiency virus. Although not experimentally proven, CD317 has been proposed as a potential regulator of pre–B-cell growth. A B lymph CD317 has been found on some stromal cells, its expression status on early-stage developing lymphocytes, to our knowledge, has yet to be proven.

Design: We used flow cytometry and reverse transcription–polymerase chain reaction to study the expression profile of CD317 among various populations of lymphocytes and stromal cells in murine thymus and bone marrow.

Results: CD317 was highly expressed on some early-stage murine B cells and T cells (Figure 38, A [flow cytometry] and B [reverse transcription–polymerase chain reaction]), as well as on bone marrow and thymic dendritic cells, indicating that CD317 might be involved in lymphopoiesis.

Conclusions: This finding is significant because it suggests that CD317 might be selectively expressed on human lymphoblastic leukemia or lymphoma cells. If this is true, CD317 could be used as a diagnostic marker and/or immunotherapy target for human lymphoblastic leukemia or lymphoma.
Reevaluation of CD15 and MUM-1 Expression in Classic Hodgkin Lymphoma

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Context: Classic Hodgkin lymphoma is a monoclonal B-cell neoplasm that is characterized by frequent expression of CD30 and CD15 and negativity for CD20 and CD79a. However, experience indicates that CD15 is frequently negative or focally positive. This study aims to determine whether CD15 is a sensitive marker for classic Hodgkin lymphoma.

Design: Twenty-three classic Hodgkin lymphomas were identified in our departmental archives from 2007 to 2009. Formalin-fixed, paraffin-embedded tissue sections of each Hodgkin lymphoma were immunostained for CD15 and MUM-1, as well as for other markers, including CD20, CD79a, PAX-5, CD30, CD45, fascin, and CD3.

Results: Patients ranged in age from 22 to 84 years. Of the 23 patients, 13 were men, and 10 were women. The areas involved included lymph node (18), bone marrow (2), retroperitoneum (1), spleen (1), and colon (1). All cases had the typical morphology of classic Hodgkin lymphoma; they were positive for CD30 (100%), MUM-1 (100%), and PAX-5 (100%). CD15 was entirely negative in 10 (43%) cases, focally and usually weakly positive in 8 (35%) cases, and clearly positive in only 5 (22%) cases. Contrary to the disappointing negativity for CD15 as well as for CD123 and are negative for CD3, CD8, CD20, CD34, CD56, and lysozyme. The relationship between these monocytic nodules and the leukemic cells is not fully understood; however, recent studies have demonstrated that the nodules are clonal and closely related to the underlying neoplasm. Additional retrospective studies demonstrate persistence of the monocytic nodules in patients with acute myeloid leukemia who received chemotherapy and obtained complete remission. These findings suggest a possible role of bone marrow monocytic nodules in the continuation and progression of residual disease in patients with myeloproliferative/myelodysplastic diseases and acute myeloid leukemia. We report a case of a 65-year-old man with anemia, monocytosis, and thrombocytopenia who underwent bone marrow aspirate and biopsy that revealed striking myelomonocytic hyperplasia without increased blasts suggestive of chronic myelomonocytic leukemia. Additionally, monocytic nodules expressing CD68 and CD99 were also identified within the bone marrow biopsy. Interestingly, retrospective review of the patient’s previous bone marrow biopsy performed 1 year earlier revealed similar monocytoid-like nodules on routine sections. Bone marrow monocytic nodules are a distinct histologic finding that, with proper identification via immunohistochemistry, can assist in the recognition of myeloproliferative/myelodysplastic diseases and may have potential prognostic implications.

Primary Low-Grade Lymphoma of Bone: Clinical and Pathologic Characteristics in an 18-Case Study From a Single Institute

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Context: Primary low-grade lymphoma of bone (PLGLB) is uncommon with limited published literature. This study retrospectively reviewed clinical and pathologic characteristics of PLGLB.

Design: Cases with pathologic diagnosis of primary bone lymphoma (PLB) from 1999 to 2009 were institutionally retrieved. PLGLB were confirmed by reviewing patient charts, along with laboratory and pathologic results.

Results: Among 151 PLB cases, 18 (11.9%) were PLGLB (average, 60 years; range 20–82 years; M:F = 8:10). Subtypes included marginal zone (3), small lymphocytic (2), low grade (grade 1–2), follicular (11), and not otherwise specified (NOS) (2). PLGLB involved spine (11) and long bones (8) with 10 of 18 cases involving more than one site. Distant spread (4) and low level of bone marrow involvement (5) were seen. Bony lesions were initially detected by imaging study (MRI [9], PET [4], CT [1]), and NOS [4] with the differential diagnosis including metastasis (5), osteoarthritis (1), Faget disease (1), lymphoma (7), and NOS (4). Diagnosis was established by fine-needle aspiration or biopsy, all with additional flow cytometry (FCM) and/or immunohistochemical study (IHC). Most patients were treated with standard therapy and showed relatively good prognosis.
Conclusions: This study demonstrates although PLG LB shares common clinical and radiologic features of a lymphoma, it is often an incidental finding while working up other conditions involving the bone. The low incidence and heterogeneous presentation of PLG LB makes its diagnosis challenging on clinical and radiologic grounds alone. Tissue diagnosis, combined with FCM and IHC, is the gold standard. Staging and systemic evaluation to exclude distant spread and high-grade component greatly influence therapeutic strategies and prognosis of PLG LB.

Complete Clinical Remission of Human Herpes Virus 8–Unrelated Primary Effusion Lymphoma-Like Lymphoma Following Pleurodesis (Poster No. 21)

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Primary effusion lymphoma (PEL) is a rare large B-cell lymphoma that is confined to body cavities without any detectable tumor mass. As defined by the World Health Organization, it is always associated with human herpes virus 8 (HHV-8) and frequently occurs in the setting of human immunodeficiency virus infection; prognosis is extremely unfavorable. Rare cases with negative HHV-8 status have been reported and are referred to as HHV-8-unrelated PEL-like lymphoma. We describe a case of HHV-8-unrelated PEL-like lymphoma with an indolent clinical course. The patient was a 79-year-old man who presented with recurrent left pleural effusion requiring pleurodesis. He had recently undergone reparation of a dissecting aortic aneurysm. Cytology examination showed numerous atypical medium- to large-sized lymphocytes with irregular nuclei, clumpy chromatin, and variably prominent nucleoli. Immunohistochemistry demonstrated positive CD20, CD79a, MUM1, Bcl-6, and Bcl-2 and negative CD3, CD5, CD10, CD30, CD138, HHV-8, latent membrane protein, and Epstein-Barr virus small RNA. Ki-67 revealed a high proliferation index. Polymerase chain reaction detected a monoclonal rearrangement of the immunoglobulin heavy chain gene. Physical examination and computed tomography and positron emission tomography scans found no lymphadenopathy or organ involvement. Results of bone marrow biopsy were normal. The patient tested negative for hepatitis C virus and hepatitis B symptoms. He was put on observation without chemotherapy based on his age and overall condition. The effusion resolved completely after pleurodesis. He is currently alive 8 months after diagnosis. To the best of our knowledge, this is the first reported case of an isolated intravascular ENKTCL uniquely presenting with symptoms of acute abdomen. Intravascular lymphomas usually present with disseminated disease, and, thus, they portend a worse prognosis with most patients succumbing to their disease. Therefore, this unique and rare presentation is clinically relevant.

Plasma Cell Myeloma in a 20-Year-Old Athletic Man (Poster No. 22)

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Plasma cell myeloma is a common hematologic neoplasm that affects the elderly. Median age at initial presentation is 70 years. Of patients diagnosed with plasma cell myeloma, 90% are 50 years old or greater. This disease in younger patients (30 years or less) is extremely rare. A 20-year-old man presented with neck pain for 2 weeks following a fall while playing football. Computed tomography scans revealed a lytic and expansile lesion of the right lateral C1 vertebra. Magnetic resonance imaging demonstrated a diffuse signal abnormality consistent with a pathologic fracture. After an inconclusive fine-needle aspirate examination, the cervical fracture was repaired by a C3 to occiput fusion by neurosurgery without a hematologic referral. Approximately 15 months after surgery, the patient developed intermittent deep groin pain exacerbated by exercise. Coincidentally, the patient fell in the shower, traumatizing his right hip region. Radiologic evaluation of the right hip region revealed a large lytic acetabular lesion and an additional lytic lesion of the left first rib. Subsequent laboratory tests demonstrated serum (160 mg/dL) and urine free k light chain. A biopsy of the acetabular lesion showed sheets of abnormal plasma cells, which expressed CD38 and CD138 and were k light chain-restricted. A diagnosis of plasma cell myeloma was established. This case demonstrates that plasma cell myeloma can occur in an individual as young as 20 years and that hematology referral and diagnostic workup for plasma cell neoplasm are warranted when bone lesions are present, regardless of the patient’s age.

Intravascular Extranodal Natural Killer T-Cell Lymphoma, Nasal Type, in a Patient With Acute Abdomen (Poster No. 23)

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Extranodal natural killer T-cell lymphoma nasal type (ENKTCL) is an aggressive lymphoma that characteristically presents as a mass in the nasal cavity and other soft tissue sites. ENKTCL is associated with angioinvasion, necrosis, and strong Epstein-Barr virus positivity. We report a unique case of ENKTCL with a strictly intravascular presentation. A 37-year-old man presented with acute abdomen with imaging studies highlighting ascites and thickened small bowel wall loops. Emergent laparotomy and a small bowel resection were performed. Gross and histologic examination of the small bowel revealed ischemic changes without any mass lesions or significant lymphadenopathy. Interestingly, some submucosal vessel lumens contained highly atypical lymphoid cells associated with apoptosis and mitosis (Figure 39). These atypical cells showed a natural killer T-cell lymphoma immunophenotype by in situ hybridization: negative for CD20, CD4, CD5, and CD7 and positive for CD3, CD2, CD8, CD56, TIA1, granzyme B, and Epstein-Barr virus–Epstein-Barr-encoded RNA. Staging bilateral bone marrow biopsies showed no evidence of ENKTCL. Full-body imaging and examination confirmed the absence of soft tissue lesions or lymphadenopathy. This patient was treated with the “SMILE” regimen (Decadron, methotrexate, ifosfamide, L-asparaginase, and etoposide) and is currently alive 8 months after diagnosis. To the best of our knowledge, this is the first reported case of an isolated intravascular ENKTCL uniquely presenting with symptoms of acute abdomen. Intravascular lymphomas usually present with disseminated disease, and, thus, they portend a worse prognosis with most patients succumbing to their disease. Therefore, this unique and rare presentation is clinically relevant.

An Unusual Immunophenotype for Precursor T-Cell Acute Lymphoblastic Leukemia (Poster No. 24)

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Precursor T-cell acute lymphoblastic leukemia (pre-TALL) typically expresses CD34 and TdT as markers of early differentiation. Additionally, these leukemic cells show a dimmer CD45 expression that allows separation of the blast population from mature lymphocytes. Clinically, pre-TALL is seen mostly in children and adolescents, especially...
adolescent boys. The patient was a previously healthy 58-year-old man who presented in acute blast crisis with a leukocytosis of 22,000/μL. The aspirate smear showed a population of blasts with a high nuclear to cytoplasmic ratio, fine chromatin, and prominent nuclei. The core biopsy was hypercellular, diffusely replaced by blasts. Flow cytometric analysis showed a CD45 bright population, expressing CD2, surface CD, cytoplasmic CD3, CD5, CD7, and γ/δ T-cell antigen receptor. CD4, CD8, CD34, cytoplasmic TdT, and human leukocyte antigen DR were all negative in this same population. Polymerase chain reaction (PCR) performed on bone marrow showed a clonal T-cell population. Ablerrancy in CD45 expression in the blast population complicated analysis, but morphology supported by clonality studies, as well as CD5 and CD7 expression (the most common markers for pre-TALL), convinced us this was pre-TALL. Indeed, were it not for morphology, this case of pre-TALL could not have been diagnosed by flow cytometry. However, although it is known that 10% to 15% of TALL cases lack CD34, TdT, or human leukocyte antigen DR expression, this is the first case in our review of the literature to show lymphoblasts comparable in CD45 expression to mature lymphocytes.

Primary Gastric T-Cell Lymphomas: A 10-Year Study in a Tertiary Care Institute in Southern United States

(Teacher No. 25)

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Context: Approximately 4% to 18% of extranodal non-Hodgkin lymphomas arise in the stomach, and most are of B-cell phenotype. Primary gastric T-cell lymphoma (PGLTCL) is a rare entity in Western populations. Reports from regions in southeast Asia indicate that two-thirds of cases are HTLV-I associated. Given the prevalence of retroviral infection in our community, we undertook a 10-year review of gastric lymphomas to study the morphology and immunohistochemistry of PGLTCL.

Design: We reviewed gastric lymphoma cases from our database (August 1999–March 2010). Clinical history and laboratory retroviral serology data were also obtained.

Results: Thirty-three cases of gastric non-Hodgkin lymphoma were identified with 30 (90.9%) and 3 (9.1%) cases of B-cell and T-cell phenotype, respectively. All PGLTCL patients were non-Asian males who tested negative for human immunodeficiency virus. B-cell lymphomas were subclassified as mucosa-associated lymphoid tissue (66.7%), large B-cell (16.6%), follicular (6.7%), mantle cell (3.3%), and clonal atypical lymphoid proliferation, unclassified (6.7%). Microscopically, 3 PGLTCL cases showed diffuse proliferation of lymphoid cells with irregular nuclear contour (CK+/CD45) in the mucosa and submucosa. No lymphoepithelial lesions were noted. Case 1 showed intermediate-sized cells strongly CD3/CD30 but CD20/CD79a/ALK negative. Cases 2 and 3 showed large with clear cytoplasm that were CD7/CD30+/CD4+ and ALK negative/granzyme B negative/CD117-. Molecular studies confirmed T-cell monoclonality.

Conclusions: Although the frequency of PGLTCL is very low, it should be considered in the differential diagnosis of diffuse mucosal lymphoid infiltration of intermediate- to large-sized cells, even in the absence of lymphoepithelial lesions. Atypical T-cell infiltrates in the stomach should be evaluated carefully for possible T-cell lymphomas.

Assessment of Platelet Large Cell Ratio: A New Platelet Volume Parameter in Patients With Infectious Events

(Teacher No. 26)

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Context: Platelet function can be conveniently estimated by measuring mean platelet volume (MPV). Although MPV looks at the volume of platelets, the patient population of P-LCR (P-LCR) is able to quantify the percent of large platelets that contribute to the total platelet count. The object of this study is to correlate reactive platelets with ischemic events by using the measurements of P-LCR.

Design: Two hundred thirty-nine patients were evaluated at Danbury Hospital Laboratory with a troponin I test, a marker of cardiac ischemia. The Sysmex X2100 analyzer was used to calculate the P-LCR in EDTA anticoagulated whole blood. The patients were stratified into 3 groups and compared (Table).
pleural effusion as a clinical presentation of $\gamma\delta$ T-cell acute lymphoblastic leukemia: an unusual presentation

(Poster No. 29)

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Pleural effusion as a clinical presentation of $\gamma\delta$ T-cell acute lymphoblastic leukemia (ALL) is a very rare event. We report a case of a 3-year-old boy who initially presented with nonspecific upper respiratory infection at an outpatient clinic where he was diagnosed with pneumonia. Overnight, he developed dyspnea associated with chest pain, requiring a visit to an emergency department. Imaging studies showed pneumonia with large right pleural effusion. He was transferred to the intensive care unit for further care and management, including supplemental oxygen and thoracostomy tube placement. A large amount of fluid was drained and sent for analysis. The review of the cytospin morphology showed many medium- to large-sized pleomorphic blasts including some mitoses. The flow cytometry study of these cells showed $\gamma\delta$ T-ALL. The bone marrow was infiltrated by similar blasts. The prognosis for patients with T-CELL ALL, especially with T-cell receptor $\gamma\delta$ expression, has historically been worse than that for patients with early B-lineage ALL. We discuss the unusual clinical presentation of T-cell $\gamma\delta$ ALL and the diagnostic challenge in this case. We also review the existing literature on the subject.

Automated Cerebrospinal Fluid Cell Counts Using the Sysmex XE-5000: Is It Time for New Reference Ranges?

(Poster No. 30)

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Context: The main objectives of this study were to compare manual and automated white blood cell (WBC) counts on clear cerebrospinal fluid (CSF) samples and to determine the range of automated WBC counts that correspond to manually derived reference values.

Design: Clear CSF samples from 200 adults and children were studied. Cell counts were performed manually using a hemocytometer and were then analyzed on the Sysmex XE-5000 (Sysmex America Inc, Mundelein, Illinois). Spearman correlation for nonparametric data was used for method comparison. Corresponding ranges for Sysmex WBC values were determined for each age-related reference interval. Cytospins were examined on all samples, and manual differential counts were performed. Correlations of automated and manual WBC differential counts were done for samples on which at least 100 cells were retrieved on cytospin. The analyzer flag for abnormal WBC scattergram was evaluated in comparison to predefined morphologic criteria for positive smears.

Results: Manual WBC counts ranged from 0 to 702 cells/μL, and Sysmex counts ranged from 0 to 629 cells/μL. Spearman rank correlation coefficient over the entire range of data was 0.77 (P < .001); however, the correlation was weaker at the low end of the data spectrum. For manual WBC reference ranges of 0 to 5 cells/μL, and 0 to 10 cells/μL, the corresponding Sysmex 0 to 95th percentile ranges were 0 to 23 cells/μL and 0 to 27 cells/μL, respectively. Correlation of WBC differential counts and assessment of WBC flag performance were limited by low cell counts in the samples.

Conclusions: The results suggest that new reference ranges are needed. The automated CSF WBC counts are to replace manual counting methods.

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Frequency of Aneuploidy in Acute Erythroid Leukemia Compared With Nonerythroid Acute Myeloid Leukemia

(Poster No. 32)

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Context: We aimed to determine whether there is a difference between the frequencies of aneuploidy seen in acute erythroleukemia compared with other forms of acute myeloid leukemia.

Design: We reviewed the ploidy status of 108 cases of acute leukemia from the files of US Labs and Ball Memorial Hospital from the previous 2 years (2008–2009). Thirty of these cases were diagnosed as acute erythroleukemia. The erythroleukemias were further subclassified: M6a erythroid/myeloid, based on the presence of at least 50% erythroid precursors in the entire nucleated cell population and at least 20%...
myeloblasts in the nonerythroid nucleated cell population; M6b, based on the presence of proliferation of immature cells with an undifferentiated or proerythroblastic appearance committed exclusively to the erythroid lineage (at least 80% of bone marrow cells) and lacking a significant myeloblastic component; or M6, not otherwise specified, in which none of the previous 2 criteria were satisfied. The remaining cases were defined as nonerythroid acute myeloid leukemias of various types.

Results: Of acute erythroid leukemia cases, 38.5% were aneuploid, while 5% of the nonerythroid acute myeloid leukemia cases were aneuploid. Results were compared using Fisher exact test, which showed a P-value of 0.002.

Conclusions: Acute erythroleukemia is significantly more likely to be aneuploid than nonerythroid acute myeloid leukemia.

**Protein Expression Profile of D Cyclins in Primary Amyloidosis Plasma Cells**

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**Context:** Primary amyloidosis (ALA) results from a clonal expansion of plasma cells (PCs). Unlike multiple myeloma, the volume of the PCs and their proliferative activity in ALA are low, suggesting a different molecular pathogenesis of ALA from myeloma. Gene expression studies have shown that PCs overexpress D cyclins in a majority of multiple myeloma patients. The gene and protein expression profiles of D cyclins in ALA, however, have not been well characterized.

**Design:** Immunohistochemistry studies for cyclin D1, D2, and D3 (all antibodies were from Santa Cruz Biotechnology) were performed on 54 bone marrow biopsies: 34 consecutive cases with a diagnosis of ALA with or without prior treatment, 10 with multiple myeloma, and 10 with benign conditions. The percentage of cyclin D-positive cells was compared with the percentage of CD138+ cells. The identity of positively stained mononuclear cells was further confirmed by overlaying staining with kappa and lambda immunoglobulin light chain in situ hybridization in selective cases.

**Results:** Preliminary results showed that PCs were positive for cyclin D1 in 47% of patients with ALA and 70% of patients with multiple myeloma. In comparison, PCs were positive for cyclin D2 in 70% of patients with ALA, and only 3% of ALA patients had positive PC staining for cyclin D3.

**Conclusions:** Neoplastic PCs in ALA can be categorized according to their aberrant expression of D cyclins. By characterizing the molecular profile of ALA, additional markers can possibly be used to help establish a diagnosis, detect relapse after treatment, and characterize the clinical manifestation and prognosis.

**Acquired Hemophagocytic Lymphohistiocytosis Presenting in the Guise of Myelodysplastic Syndrome**

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Hemophagocytic lymphohistiocytosis (HLH) is an aggressively, life-threatening disease distinguished by systemic hyperinflammation resulting from an overproduction of proinflammatory cytokines. In addition to inflammation, unchecked cytokine production may also lead to necrosis, organ dysfunction, and, ultimately, death. HLH may be either genetic or acquired; acquired HLH has been associated with viral or bacterial infection, autoimmune disease, and malignancy. We report the case of a 15-month-old previously healthy girl who presented with fever, lymphadenopathy, and hepatosplenomegaly. Serologic viral testing revealed recent Epstein-Barr virus and cytomegalovirus infections (IgM positive). Bone marrow aspirate revealed erythroid hyperplasia and dysplasia. Dysplastic features included megaloblastosis, abnormal nucleation, and multinuclearity. The diagnosis of childhood myelodysplastic syndrome was considered; however, further inspection revealed hemophagocytosis of both erythrocytes and leukocytes throughout the specimen. Laboratory testing and clinical and bone marrow findings led to a diagnosis of HLH secondary to recent Epstein-Barr virus and cytomegalovirus infections. This case is notable because 2 of the most common viral illnesses associated with HLH together resulted in HLH. Also significant are the associated bone marrow findings. Hemophagocytosis is absent or a myelodysplastic picture is present. Because this disease can be deadly, it is crucial to take all findings—clinical, laboratory, and bone marrow—into consideration when establishing a diagnosis of HLH.

**Episodic Hemolytic Anemia Secondary to Unstable Hemoglobin Seattle: The Importance of Thorough Investigation for Proper Diagnosis**

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Several factors may contribute to mild, episodic, nonimmune hemolytic anemia, including paroxysmal nocturnal hemoglobinuria and the more common red cell metabolic defects or membrane disorders. A 76-year-old white woman presented with mild normocytic, normochromic anemia and a history of intermittent hematuria. Peripheral blood smear revealed normocytic, normochromic red cells with a mild increase in polychromatophils and rare schistocytes and spherocytes. Results of a direct antiglobulin test were negative. Enzyme analysis showed normal glucose-6-phosphate dehydrogenase and pyruvate kinase activities. Osmotic fragility and high performance liquid chromatography demonstrated unremarkable curve and normal chromatogram, respectively. A subtle, fast migrating β globin chain variant (40%) was detected on alkaline electrophoresis with acid electrophoresis showing a normal pattern. Surprisingly, an isopropanol stability test unveiled the presence of unstable hemoglobin with turbidity within 5 minutes (Figure 41). DNA sequencing confirmed hemoglobin Seattle. Unstable hemoglobins arise from globin chain mutations that result in hemoglobin tetramer instability with subsequent precipitation. There are approximately 200 variants, a number of which may instigate clinically substantial hemolysis or Heinz body hemolytic anemia. The severity and frequency vary and depend on the nature of the unstable hemoglobin. Hemoglobin Bristol induces prevalent hemoglobin precipitation and, thus, results in more severe red cell destruction. Hemoglobin Seattle produces only mild, sporadic hemolytic anemia. This case highlights the significance of a conscientious and systematic approach in detecting and properly diagnosing the presence of unstable hemoglobins, particularly in patients with unexplained hemolytic anemia and relatively normal red cell parameters and chromatographic or electrophoretic findings.

**ALK-Positive Anaplastic Large Cell Lymphomas (ALCLs) Characteristically Express the Myeloid Antigen CD13: A Tissue Microarray Study with Comparison to ALK-Negative ALCL**

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Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) is a B-cell lymphoproliferative disorder with prolonged clinical course. About 2%-8% of patients with CLL develop large B-cell lymphoma, and fewer than 1% develop Hodgkin lymphoma. We report a case of CLL/SLL that underwent classic Hodgkin lymphoma and prolymphocytoid transformation. The patient was observed for 2 years. She then developed high fever, lymphocytosis, and severe anemia. She underwent 1 cycle of chemotherapy (Rituxan, Cytoscan, and fludarabine), and bone marrow revealed the presence of CLL and classic Hodgkin lymphoma with the coexistence of 3 patterns: CLL, Hodgkin cells in a background of CLL, and Hodgkin lymphoma. The diagnosis of classic Hodgkin lymphoma was based on the presence of Hodgkin cells with the immunophenotype CD30+), CD15-, CD45-, CD20+, and PAX-5 (weak) in association with the characteristic polymorphous inflammatory background consisting of numerous small T lymphocytes, histiocytes, rare plasma cells, and rare eosinophils. The CLL nodules consisted predominantly of small lymphocytes morphologically typical of CLL cells with immunophenotype CD5+, CD20+, and PAX-5. Results of in situ hybridization for Epstein-Barr virus were negative. Flow cytometry demonstrated a monoclonal B-cell population with typical CLL phenotype. Cytogenetics demonstrated del(17)(p13.1). The patient underwent chemotherapy (CHOP) and achieved remission. One month later, she relapsed and developed axillary lymphadenopathy. Exciplastic biopsy showed composite lymphoma with focal areas of residual CLL, sheet of prolymphocytes, and classic Hodgkin lymphoma. It is important to recognize Hodgkin lymphoma and/or prolymphocytoid transformation and to distinguish them from diffuse large B-cell lymphoma transformation, since the latter carries a much worse prognosis.

Detection of t(14;18)(q32;q21) in a Case of Small Lymphocytic Lymphoma
(Poster No. 39)

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Chronic lymphocytic lymphoma/small lymphocytic leukemia (CLL/SLL) is a common lymphoid neoplasm accounting for approximately 20% of all B-cell malignancies. The diagnosis of CLL is based on a persistent lymphocytosis of 5 × 10^9/L or more, with nodal and bone marrow involvement by the neoplasm; SLL presents similarly without peripheral blood lymphocytosis. CLL/SLL has characteristic immunophenotypic, immunohistochemical, cytogenetic, and molecular profiles. Deletions of 13q, 11q, 17p, 6q, and trisomy 12 are most frequently detected in CLL/SLL karyotypic analysis. Translocation t(14;18)(q32;q21), typically associated with follicular lymphoma, is exceptionally rare in CLL, but has not been documented in SLL. We report an unusual case of SLL with translocation t(14;18)(q32;q21). The patient is a 66-year-old woman with cervical and axillary lymphadenopathy. Right axillary lymph node and bone marrow biopsy were performed and revealed an extensive nodal and bone marrow involvement by small lymphocytic lymphoproliferative process, but without significant peripheral blood involvement. Flow cytometric immunophenotyping of lymph node and bone marrow revealed lymphoma cells positive for CD45, CD5, CD20, and PAX-5. The patient underwent chemotherapy (CHOP) and achieved remission. One month later, she relapsed and developed axillary lymphadenopathy. Exciplastic biopsy showed composite lymphoma with focal areas of residual CLL, sheet of prolymphocytes, and classic Hodgkin lymphoma. It is important to recognize Hodgkin lymphoma and/or prolymphocytoid transformation and to distinguish them from diffuse large B-cell lymphoma transformation, since the latter carries a much worse prognosis.

Characterization of Bone Marrow Stromal Cell and Matrix Markers Expression in Myelodysplastic Syndrome
(Poster No. 40)

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Myelodysplastic syndrome (MDS) is an ineffective hematopoiesis bone marrow stem cell disorder. The bone marrow stroma is a critical part of the hematopoietic microenvironment that facilitates hematopoiesis. The role of bone marrow stroma in MDS is not clear. We hypothesized that bone marrow stromal marker expression, such as CD34, would be different in MDS cases compared to normal bone marrow biopsies (qualitatively and quantitatively).

Design: We retrieved archived bone marrow core biopsies for confirmed cases of MDS and for cases of normal bone marrow. Immunohistochemistry (anti-CD34, anti-CD45, anti-CD117, anti-CD29, anti-CD36, and anti-collagen IV) was performed on formalin-fixed, paraffin-embedded tissue sections. Staining patterns were analyzed using ImageJ, a public domain Java image processing program.
Results: There were 3 normal bone marrow and 7 MDS cases. There were 7 men and 3 women (age range, 42 to 82 years). All cases, stomal or hematopoietic stem cells, were stained with the antibodies. The Stro-1+ cells and CD34+ cells were significantly higher in MDS cases compared to normal bone marrow (about 30 times higher for Stro-1+ and 2 times higher for CD34+ in MDS), indicating MDS bone marrow is actively responding to more stimulation and a decreased hematopoietic response with a minimal increase of CD34+ cells was noted in MDS cases. As expected, more collagen IV+ areas were detected in MDS cases, especially around marrow sinus areas.

Conclusions: In MDS, bone marrow stroma/microenvironment is very active in facilitating hematopoietic stem cell migration to bone marrow. However, bone marrow stem cells do not respond normally to this stimulation. Additional factors need to be elucidated.

Monomorphic Posttransplant Lymphoproliferative Disorder With Plasmacytic Differentiation: A Case Report With Review of Literature
(Poster No. 41)
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Posttransplant lymphoproliferative disorders (PTLDs) are a diverse group of lymphoid proliferations that arise secondary to immunosuppression after solid organ or bone marrow transplant. The World Health Organization has defined 3 primary PTLD categories: early lesions, polymorphic PTLD, and monomorphic PTLD. Most monomorphic PTLDs resemble diffuse large B-cell lymphoma or Burkitt lymphoma. We describe the pathologic features of a rare case of monomorphic PTLD resembling extramedullary plasmacytoma. A 14-year-old adolescent boy with a past medical history of renal transplant 12 years prior (for polycystic kidney disease) presented with an abdominal mass. He was receiving no immunosuppressive therapy. Computed tomography-guided core biopsy of the mass suggested PTLD. The resected mass measured 7.5 x 7.5 x 5 cm, involved the proximal jejunum circumferentially, and showed mucosal ulceration. Histologic examination showed sheets of plasmacytoid tumor cells, variably plasmorphic nuclei with nucleoli, and focal perisinusoidal staining. Immunohistochemical staining showed tumor cells to be diffusely positive for CD38, CD138, and MUM-1, focally positive for CD79a, and negative for CD20. The Ki-67 proliferative index approached 100%. Flow cytometry showed tumor cells to be CD45 dim, CD38+, and CD138+ with monoclonal cytoplasmic lambda light chain restriction, confirming the diagnosis of plasmacytoma-like PTLD. In situ hybridization for Epstein-Barr virus early RNA was negative. Monomorphic PTLD with plasmacytic differentiation is rare, with fewer than 50 cases reported in the English literature. It arises late after transplantation (mean, 7 years), shows variable association with Epstein-Barr virus, and demonstrates histologic and phenotypic findings that overlap with immunocompetent extramedullary plasmacytomas.

A Case of Chronic Lymphocytic Leukemia With c-Myc Translocation and Osteolytic Bone Lesions
(Poster No. 42)
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An 81-year-old woman with chronic lymphocytic leukemia (CLL) presented with hypercalcemia and osteolytic skull lesions. Biopsy and flow cytometric analysis of iliac crest bone marrow revealed involvement by CLL with usual morphology and immunophenotype. Conventional cytogenetic analysis showed a subtle deletion of the long arm of chromosome 8 with breakpoints at approximately band 8q24 (c-Myc locus). There was additional material of unknown origin on the long arm of both chromosomes 14 and an interstitial deletion within the long arm of chromosome 11 that resulted in loss of ataxia-telangiectasia mutated protein. We report the 85-year-old woman who initially presented with pain, swelling, and loss of vision in her left eye. A left orbital mass was revealed by computed tomography, and a biopsy was performed. On histologic examination, large atypical lymphoid cells were present in blood vessel lumina of the intraorbital adipose tissue. No tumor cells were seen in the surrounding tissue. By immunohistochemistry, the tumor was positive for BCL2, BCL-6, and CD5; they were negative for CD10 and cyclin D1. Ki-67 revealed a proliferation rate of approximately 80%-90%, and CD31 highlighted the vascular endothelium. These findings confirmed the diagnosis of intravascular large B-cell lymphoma. Results of bone marrow and cerebrospinal fluid examinations were negative for involvement, and there was no radiographic evidence of systemic disease. The patient received systemic treatment with etoposide, doxorubicin, vincristine, cyclophosphamide, prednisone, and rituximab in addition to intrathecal methotrexate. The patient had almost complete resolution of her intraorbital mass. While it is understood that this disease can involve any organ, only very rarely does intravascular large B-cell lymphoma present with primary ophthalmologic symptoms. Additionally, this patient’s disease initially appeared to be isolated, with no skin manifestations or other systemic involvement. To our knowledge, this is the first reported case in which this disease manifested as an isolated intraorbital mass without detectable involvement of any other organ.

Sclerosing Angiomatoid Nodular Transformation of the Spleen: A Case Report and Literature Review
(Poster No. 44)
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Sclerosing angiomatoid nodular transformation of the spleen is a vascular lesion composed of multiple confluent angiomatoid nodules that are surrounded by concentric collagen fibers, exhibiting an inflammatory and myofibroblastic response, which are accompanied by numerous erythrocytes and siderophages. The nodules are populated by endothelial cells and phenotypically recapitulating normal splenic sinusoidal capillaries, and small veins. Nuclear atypia is minimal, mitotic figures are extremely rare, and necrosis is consistently absent. This lesion has a unique immunohistochemical profile, which is characterized by CD34+ CD31+ CD8+ sinusoids, CD34+ CD31+ CD8+ capillaries, and CD34+ CD31+ CD8+ small veins. CD68 is positive in macrophages. Occasional cases have shown expression of Epstein-Barr virus RNA. To date, sporadic case reports and occasional series of sclerosing angiomatoid nodular transformation have been described in the literature in association with various systemic diseases. We report the first case of sclerosing angiomatoid nodular transformation described in a patient with essential thrombocythemia.

Primary Central Nervous System Posttransplant Lymphoproliferative Disorder in a Renal Allograft Recipient With IgGλ Monoclonal Gammapathy: Case Report and Literature Review
(Poster No. 45)
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Posttransplant lymphoproliferative disorder (PTLD) is an uncommon lymphoid proliferative disorder or lymphoma. It is associated with immunosuppression in recipients of solid organ transplant or bone
marrow allograft. PTLDs represent a spectrum, ranging from early Epstein-Barr virus–driven polyclonal proliferations resembling infectious mononucleosis to Epstein-Barr virus–positive or Epstein-Barr virus–negative lymphomas. It develops in 1% to 10% of patients, depending on the organ transplant. PTLD occurs in fewer than 1% of renal transplant recipients. PTLD isolated to the central nervous system is rare, and the incidence is unknown. Primary central nervous system localization is associated with poor survival. It is extremely rare in renal transplantation. We report a case of a primary central nervous system PTLD in a renal allograft recipient with IgG monoclonal gammapathy and review the literature.

Correlation of Positive Culture, Semiquantitative Neutrophil CD64 (FcγRI Receptor) Expression, and the Subsequent Effect of Antibiotic Therapy
(Poster No. 46)

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Context: Neutrophil CD64 expression is negligible in a healthy state. It is upregulated on neutrophils during acute inflammatory response. With flow cytometry, CD64 expression can be tested on peripheral blood as a marker of bacterial infection.

Design: We evaluated the expression of neutrophil CD64 in 54 culture-positive patients. Flow cytometry evaluation was performed on ethylenediaminetetraacetic acid anticoagulated blood using the Beckman Coulter CD64 antibody (clone 22) (Beckman-Coulter, Brea, California). CD16 was used to gate the neutrophil population. Neutrophil CD64 expression was analyzed semiquantitatively, and the results were correlated with cultures. Twenty patients with no signs of sepsis (negative control) were used. We tested 22 of 54 patients for CD64 expression at 48, 72, and 96 hours.

Results: Of 54 patients, 47 had a positive culture; 2 of 54 patents had a positive culture and a negative CD64 test result. One of 54 patients had a negative blood culture and a positive CD64 test result. The sensitivity and specificity were 100% and 96%, respectively. Negative and positive predictive values were each 100%. The positive likelihood ratio was 25.0. The negative likelihood ratio was 0.0 (Figure 42).

Conclusions: This study shows that CD64 analysis can be used to identify bacterial infection before the results of a patient’s blood culture are available. The high negative predictive value can be very useful in an emergency or critical care setting. Additionally, 18 of 22 patients who were followed with serial measurements showed a downward trend in the expression of CD64 after the initiation of effective antibiotic therapy. CD64 analysis is useful for detecting an adequate response to antibiotics.

A Case Report of Complete Testicular Feminization Syndrome With B-Cell Lymphoma Involving Breast
(Poster No. 47)

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An 88-year-old woman presented with thrombocytopenia and lymphadenopathy. A computed tomography scan revealed right axillary adenopathy and right pericardiophrenic mass extending to right breast. Past medical history included a diagnosis of Rakitskans-Hauser syndrome, a congenital condition with absence of uterus and vagina in genetically female patients (46,XX). A left lower abdominal mass was removed 10 years ago and revealed Sertoli cell tumor. The patient underwent computed tomography–guided biopsy of the right breast mass and bone marrow biopsy. Microscopic examination of the right breast biopsy showed solid aggregates of mixed small and large lymphoid cells diffusely positive for CD10, CD20, and CD79a, but negative for CD3 and CD5. A CD10– B-cell lymphoma was rendered without further classification owing to limited tumor tissue. Bone marrow showed no evidence of lymphoma. However, cytogenetic study on bone marrow aspirate revealed 46,XY karyotype. Fluorescence in situ hybridization analysis of the breast tissue confirmed an XY sex chromosome complement. Based on the cytogenetic findings and clinical presentation, we diagnosed complete testicular feminization syndrome (genetically male patient). The patient responded fairly well to chemotherapy and was in stable condition 6 months later. Complete testicular feminization syndrome occurs in as many as 1 in 20,000 live births. Testicular cancer is among the most common complications. B-cell lymphoma with breast involvement in these patients has not been reported in the English literature before. It is unknown whether the B-cell lymphoma has any direct causal relationship to the genetic abnormalities or, more likely, is just a coincidence in this patient.

Lymphoepithelioid Variant of Peripheral T-Cell Lymphoma (Lennert Lymphoma) Associated With Common Variable Immunodeficiency in a 25-Year-Old Man
(Poster No. 48)

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Common variable immunodeficiency is a primary immunodeficiency disease, which is characterized by impaired antibody production, recurrent infections, autoimmune diseases, lymphoid hyperplasias, granulomatous diseases, and malignancies, particularly B-cell non-Hodgkin lymphomas. T-cell lymphomas, however, are rare. We report a case of the lymphoepithelioid variant (Lennert type) of peripheral T-cell lymphoma, not otherwise specified, in a 25-year-old man with Evans syndrome and common variable immunodeficiency. His clinical symptoms included fever, abdominal and axillary swelling, night sweats, and a 5-lb weight loss. An axillary lymph node biopsy showed nearly complete effacement by an interfollicular proliferation of mixed epithelioid histiocytes, including multinucleated giant cells, and small T cells with intermixed medium-sized and large forms (Figure 43). The T cells were predominantly CD4+; showed partial loss of CD7, and were negative for CD30 and anaplastic lymphoma kinase. Ki-67 showed an increased proliferation index in these areas. Polymerase chain reaction–based T-cell receptor gene rearrangement studies confirmed the presence of a monoclonal T-cell population. Subsequent imaging studies showed diffuse thoracic and abdominal lymphadenopathy, pulmonary nodules, and hepatosplenomegaly (stage IV-B). The patient was treated with 4 cycles of CHOP and underwent a nonmyeloablative allogeneic stem cell transplant. Imaging studies suggested complete remission. While rare cases of peripheral T-cell lymphoma have been described in patients with common variable immunodeficiency, a case of the rare lymphoepi-
ithelioid subtype has never been reported to the best of our knowledge. Further study is needed to determine optimal therapies and the pathogenesis linking the development of T-cell lymphoma, including the lymphoepithelioid variant, to deficient antibody production.

Sinusoidal Large Cell Lymphoma With Expression of CD30, CD15, and Multiple B-Cell Antigens: A Classic Hodgkin Lymphoma With Sinusoidal Infiltrating Pattern Versus a Sinusoidal CD30-Positive Large B-Cell Lymphoma With CD15

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Classic Hodgkin lymphoma and diffuse large B-cell lymphoma differ substantially in clinical course and optimal therapy, necessitating accurate clinical distinction between the entities. They typically exhibit clear differences in clinical presentation, morphology, and immunophenotype. However, rare hybrid cases can demonstrate marked discordance between morphology and immunophenotype. A 77-year-old woman presented with mediastinal and supraclavicular lymphadenopathy. Her lymph node biopsy revealed nodal architecture distorted by a sinusoidal infiltrate of large, pseudodiscohesive, pleomorphic cells with vesicular nuclei and prominent nucleoli (Figure 44). Based on morphology, the differential diagnosis included anaplastic large cell lymphoma and sinusoidal large B-cell lymphoma. Immunohistochemical stains were strongly positive for CD30, CD15, PAX5, OCT2, BOB.1, MUM1, and BCL2, weakly positive for CD45; partially positive for CD20; and negative for pan T-cell markers, CD4, CD8, CD45RA, ALK1, Epstein-Barr virus, and human herpesvirus-8 stains. Polymerase chain reaction–based B-cell and T-cell receptor gene rearrangement studies detected no clonal rearrangements. The absence of T-cell markers and the expression of multiple B-cell antigens ruled out anaplastic large cell lymphoma. Rather than fully supporting a diagnosis of sinusoidal large B-cell lymphoma, the immunophenotypic and genotypic studies were also suggestive of classic Hodgkin lymphoma. The 2008 World Health Organization classifications introduced a tentative category, “B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and classic Hodgkin lymphoma’,” for cases with overlapping features. This is the first documented case of sinusoidal CD30+ large B-cell lymphoma with expression of CD15 with features overlapping between classic Hodgkin lymphoma and sinusoidal large B-cell lymphoma.

Tissue-Based Variant of Primary Effusion Lymphoma: A Unique and Instructive Case

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Primary effusion lymphoma (PEL) is an aggressive neoplasm accounting for 3% of AIDS-related lymphomas. Tissue-based variant of PEL is a rare lymphoid malignancy morphologically similar to PEL. We present a case of tissue-based PEL presenting as a pelvic mass. Our case is unique and instructive from a clinical perspective as it emphasizes the importance of flow cytometry in the diagnosis of lymphoid disorders. To the best of our knowledge, this is the first case of PEL described in the literature in which flow cytometry is used on a urine specimen to diagnose PEL. The patient is a 45-year-old human immunodeficiency virus (HIV)–positive man who presented with a pelvic mass and worsening renal function. Owing to the presence of atypical cells in urine, a decision was made to use early morning urine sample for flow cytometry. Flow cytometry detected a population of CD45+ cells expressing CD30, CD38, and λ light chains. Figure 45 shows hematoxylin-eosin stain of cell block revealing highly pleomorphic, hyperchromatic cells with high nuclear to cytoplasmic ratio. Immunostaining on urine cell block revealed positivity for CD30, MUM-1, HHV-8, EBER, λ, and Ki-67 (90%). Noticeably, CD38, CD20, CD138, PAX-5, Pan-Keratin, ALK-1, and TdT were found to be negative, among other markers. A diagnosis of tissue-based PEL was made. Chemotherapy was started, and the patient responded with marked improvement in renal function.

Low-Grade Follicular Lymphoma With High Proliferation Index: A Closer Look at the Grading System for Follicular Lymphomas

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Follicular lymphoma (FL) accounts for 20% of all lymphomas. It predominately affects adults and has a male to female ratio of 1 to 1.7. The
lesions and help to accurately classify these lymphomas. A low proliferation index with Ki-67 immunostain is considered a good prognostic indicator because it correlates with the number of large cells and the number of mitoses. The index is significantly higher in high-grade tumors compared to low-grade tumors. The International Prognostic Index and the International Prognostic Index for FL are strong predictors of outcome. Despite the often long survival seen with low-grade lesions (grades 1 or 2), some patients may show a more rapid course of disease with relatively short survival times. This finding is unusual and still to be well studied. We report a case of low-grade FL with a paradoxically high proliferation index (approximately 70% positive cells) arising in the lymph nodes of a 46-year-old woman. Although genetic abnormalities are well documented and impact the outcome in FLs, in our patient no clonal abnormality was detected with routine cytogenetic analysis. It is unclear to us which parameter is more important in predicting biologic behavior of these tumors: histologic grade or proliferation index. In such cases, close long-term follow-up is mandatory for better understanding these lesions. This finding of high proliferative index might explain the adverse behavior in these low-grade lesions and help to accurately classify these lymphomas.

Extranodal Hodgkin Lymphoma in a Child With Hyperimmunoglobulin E Syndrome
(Poster No. 52)

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Hyperimmunoglobulin E syndrome, or Job syndrome, is a rare, heterogeneous group of immune disorders characterized by chronic eczema, recurrent infections, increased serum immunoglobulin E, and eosinophilia. Previous case reports have suggested an increased risk of lymphoma, mainly non-Hodgkin type, in cases of Job syndrome. So far, only 3 Hodgkin lymphoma cases, none of which were extranodal, have been reported in patients with Job syndrome. Primary adenal Hodgkin lymphoma is highly unusual with only 1 case reported. We describe a case of Hodgkin lymphoma involving lung and adenal gland without clear evidence of nodal disease in a 4-year-old girl who presented with adenal and lung masses, eczema, persistent otitis media, chronic diarrhea, growth retardation, and high levels of immunoglobulin E (6000 mg/dL). Grossly, multiple, well-circumscribed white-tan nodules were present within the adenal and lung parenchyma. Microscopically, the adenal mass showed a cellular infiltrate composed of a polymorphous population of cells, including lymphocytes, plasma cells, histiocytes, large numbers of eosinophils, and scattered large atypical, nucleolated, Reed-Sterberg Hodgkin cells. The lung mass showed similar Reed-Sterberg Hodgkin cells in a mixed inflammatory background. Immunohistochemical analysis demonstrated that the Reed-Sterberg Hodgkin cells in both sites were negative for CD45 and CD20, weakly positive for CD15, and strongly positive for CD30 and Epstein-Barr virus. Additional stains for ALK-1, epithelial membrane antigen, cytokeratin, smooth muscle actin, desmin, tyrosine hydroxylase, synaptophysin, S100, acid-fast bacillus, and fungi were all negative. The diagnosis was classic Hodgkin lymphoma, unclassified type. Our case supports a possible link between Hodgkin lymphoma and Job syndrome.

Cannibalistic Phagocytosis in Acute Megakaryoblastic Leukemia (AML-M7) With t(10;17)(p15;q22)
(Poster No. 53)

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Phagocytic activity is occasionally observed in blasts of acute myeloid leukemia in association with certain cytogenetic abnormalities involving chromosomes 8p11, 16p11, or 21q22. In all the reported cases, the interiorized elements are bystander hematopoietic cells/precursors; thus, the term hemophagocytosis has been designated. Our patient, a 52-year-old man with a 15-year history of hemodialysis due to renal failure, developed pancytopenia, and circulating blasts were seen in peripheral blood. A bone marrow biopsy revealed 80% blasts, including some with cytoplasmic vacuoles and others with cytoplasmic blebs. Occasionally, gigantic blasts with multinucleation were seen. Interestingly, blast-versus-blst phagocytosis, also referred to as “cannibalistic” phagocytosis, was frequently observed. This aberrant behavior was typically characterized by a larger blast with a crescentic nucleus enveloping another smaller blast with a round/oval nucleus rimmed by a halo of phagocytic vacuoles. Occasionally, there was multilayer blast “cannibalism” with an onion-skin appearance (Figure 46). Immunohistochemical and flow cytometric analyses demonstrated expression of megakaryocytic antigens (factor VIII–related antigen and CD31) on blasts. Cytogenetic analysis detected a clonal cytogenetic abnormality with t(10;17)(p15;q22). A diagnosis of acute megakaryoblastic leukemia (AML-M7) was established. The patient received standard induction chemotherapy but had a poor response and died 3 months later. While acute megakaryoblastic leukemia with leukemic blast phagocytosis appears to have a dismal clinical outcome, including poor response to chemotherapy, early relapse, and short survival, the underlying mechanism for this aberrant phenomenon is unclear; however, nutritional depletion due to a high proliferation rate of neoplastic cells is postulated.

A Nonrandom Unbalanced Rearrangement (17;20) in Treatment-Related Myelodysplastic Syndrome
(Poster No. 54)

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Dicentric chromosomes, or chromosomes containing 2 centromeres, are formed when translocated material, or material that has been exchanged between 2 separate chromosome areas, retains both respective centromeres on one segment, leaving the second portion void of a centromere (ie, acentric). We describe the effects of a rare dicentric chromosome that was found in the bone marrow sample of a 70-year-old man with a history of nodular sclerosing Hodgkin lymphoma, for which he had received chemotherapy. Previous cytogenetic studies on this patient’s lymph node and bone marrow showed no clonal abnormality. When the patient presented a year later with thrombocytopenia, morphologic and flow cytometric evaluation indicated myelodysplastic syndrome. Cytogenetic analysis on this specimen revealed a new, unbalanced, dicentric translocation [dic(17;20)] between the short arm (p) of chromosome 17 and the long arm (q) of chromosome 20. Only 5 myelodysplastic syndrome cases with this particular rearrangement have been reported internationally. Because dicentric (17;20) rearrangement leads to partial loss of the short arm of chromosome 17 (TP53 gene), patients with this abnormality may have an adverse clinical course, similar to that seen in “17p-syndrome.” Dicentric (17;20) also results in partial loss of the long arm of chromosome 20, where topoisomerase 1, phospholipase C, hepatocyte nuclear factor 4, adenosine deaminase, and KRML transcriptional regulator genes reside. This case stresses the importance of performing conventional cytogenetic analysis on all treated Hodgkin lymphoma patients for the early detection of chromosomal aberrations that indicate the development of therapy-related myelodysplastic syndrome or acute myeloid leukemia.

Secondary Central Nervous System Involvement by Adult Anaplastic Large Cell Lymphoma: Report of 2 Rare Cases
(Poster No. 55)

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Anaplastic large cell lymphoma (ALCL) is a rare T-cell non-Hodgkin lymphoma with distinct pathologic features characterized by CD30-expressing large lymphoid cells with abundant cytoplasm and pleomorphic, often horseshoe-shaped nuclei, with or without a translocation involving ALK gene (ALK- versus ALK+). ALCL could present with primarily cutaneous or systemic involvement. Primary systemic ALCL accounts for 2%-8% of non-Hodgkin lymphomas in adults and 20%-30% of large cell lymphomas in children. The disease can spread to bone marrow (30%), skin (20%), lung or liver (10%), and other sites rarely. Primary central nervous system (CNS) ALCL is noted in pediatric or of large cell lymphomas in children. The disease can spread to bone accounts for 2%-8% of non-Hodgkin lymphomas in adults and 20%–30% primarily cutaneous or systemic involvement. Primary systemic ALCL (CD15

PAX-5. Polymerase chain reaction was performed for heavy- and light-chain gene rearrangements, as indicated.

Morphology and immunophenotyping with CD15, CD20, CD30, and PAX-5. Polymerase chain reaction was performed for heavy- and light-chain gene rearrangements, as indicated.

Results: We identified 14 cases. Average age was 37 years (female to male ratio was 1.3:1). Five cases were distinctly classifiable as PMBL (CD15+/diffuse CD20+); there were 7 CHL cases, 2 of which showed strong CD20+ Reed-Sternberg cells. Two cases classified as DLBCL/HL had features of CHL (CD15+/CD30+ and Reed-Sternberg cells) but also had clusters of CD20+ large cells with clonal heavy- or light-chain gene rearrangements. PMBL had slender fibrosis around individual or small clusters of tumor cells. CHL had prominent thick fibrous bands. CHL had prominent necrosis (10%-50%), which was uncommon in PMBL.

Conclusions: Morphology and immunophenotypic with CD15, CD20, and CD30 can distinguish most PMBL and CHL. Since Reed-Sternberg cells in CHL may be CD20+, subtle/local clustering of CD20+ cells in DLBCL/HL may cause a diagnostic dilemma. Future clarification is needed to determine the percentage of CD20+ cells required to establish accurate diagnosis of DLBCL/HL.

Urothelial Metaplasia of the Seminal Vesicles: Study of 2 Cases

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While urothelial metaplasia has been reported in the fallopian tube, urothelium in the seminal vesicle has been rarely reported. We report 2 cases of urothelial epithelium in seminal vesicles from radical prostatectomy specimens. One case involved a 63-year-old patient with pT2c prostatic adenocarcinoma (Gleason pattern 4+3, total score 7). The other case involved a 60-year-old patient with pT2c prostatic adenocarcinoma (Gleason pattern 4+3, total score 7). The other case involved a 60-year-old patient with pT2c prostatic adenocarcinoma (Gleason pattern 4+3, total score 7). The other case involved a 60-year-old patient with pT2c prostatic adenocarcinoma (Gleason pattern 4+3, total score 7). The other case involved a 60-year-old patient with pT2c prostatic adenocarcinoma (Gleason pattern 4+3, total score 7). The other case involved a 60-year-old patient with pT2c prostatic adenocarcinoma (Gleason pattern 4+3, total score 7).

representation of the left seminal vesicles from both patients demonstrated a circumferential urothelial epithelium consisting of 3 to 8 cell layers, which included superficial (umbrella) cells, intermediate cells, and basal cells. An abrupt transition from the normal single layer of cuboidal cells of seminal vesicle to multilayered urothelium was identified. No urothelial metaplasia was seen in prostatic tissue. The histogenesis of urothelial metaplasia in the seminal vesicle is unclear, but it possibly is a reaction to mechanical irritation, inflammation, or infection, as has been proposed for urothelial metaplasia in the fallopian tube and squamous metaplasia of the pelvic peritoneum. Nevertheless, a rare congenital malformation cannot be ruled out as an etiology. Clinical follow-up of patients with urothelial cell metaplasia of the fimbriae suggests that it bears no biologic significance, yielding no instances of carcinoma. However, whether there will be an impact on fertility awaits further study.

Clinically Undiagnosed Prostate Carcinoma Metastatic to Renal Oncocytoma

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Tumors metastatic to the kidney may at times masquerade as primary renal neoplasms; however, tumors metastatic to a primary neoplasm of the kidney are quite uncommon. The latter scenario may cause diagnostic difficulty, especially if the primary tumor originating the metastasis is clinically undiagnosed at the time of renal resection. Here, we report the case of a kidney resected for a neoplasm (oncocytoma) that harbored metastases from a clinically undiagnosed prostatic adenocarcinoma. The presence of the poorly differentiated metastases within an otherwise typical oncocytoma (Figure 47), in the absence of metastases in the surrounding nonneoplastic renal parenchyma, resulted in a diagnostic dilemma. Immunohistochemistry was invaluable in arriving at the correct diagnosis. To our knowledge, this is the first report of a case in the English literature of a clinically undiagnosed prostatic adenocarcinoma metastatic to a renal oncocytoma identified on examination of the resected renal neoplasm.

Prostate-Specific Antigen–Positive Prostatic Mesonephric Gland Hyperplasia: A First Report

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Mesonephric gland hyperplasia (MGH) of the prostate is a rare, benign lesion that shows an infiltrative pattern. MGH may be mistaken for prostate cancer. It arises from remnants of the mesonephros, which produces testicular efferent ducts, epididymis, vas deferens, and seminal vesicles. MGH has been described as prostate-specific antigen (PSA) negative. We present a case of PSA-positive prostatic MGH and compare its histology and immunohistochemistry to MGH of the uterine cervix.
Indocyanine Green: A Novel Approach to Pelvic Lymph Node Identification in Radical Cystectomy Specimens

Poster No. 60

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Context: Lymph node (LN) count has prognostic implications in bladder cancer patients who are treated with radical cystectomy. Carnoy solution and palpation may not identify all LNs, leading to additional effort and expense for report completion. Indocyanine green (ICG), a nontoxic dye with near-infrared fluorescence properties, is transferred through lymphatics, allowing for identification of LNs. We investigated the ability of intravesically injected ICG to identify pelvic LNs.

Design: We assessed 5 patients for near-infrared fluorescence LN imaging, using ICG intravesical injection. We injected 0.5 to 1 ml of ICG (2.5 mg/ml) at the tumor base or resection margins. LN dissection was performed within 2 to 4 hours. The SPY imaging system (Novadaq, Bonita Springs, Florida) was used to detect ICG fluorescence in pelvic LN specimens. The specimens were placed in Carnoy solution overnight and were then analyzed for additional nodes. The remaining tissue was entirely submitted. Tissue was grouped as ICG LN, Carnoy LN, and residual LN.

Results: In 5 patients, we identified 114 LNs, ranging from 4 to 36 per patient. We identified 16 LNs (14%) with ICG, 38 (33%) with Carnoy, and 60 (53%) with submission of residual tissue. One LN contained metastatic disease and was identified with ICG (Figure 49).

Conclusions: ICG near-infrared fluorescence can identify LNs. Many ICG LNs were <1 mm in size and might have been missed with other techniques. This simple, nontoxic imaging may prove advantageous for LN identification in pelvic LN dissection specimens. Additional investigation is needed to assess this method’s sensitivity, specificity, and predictive values.

Noninvasive Papillary Urothelial Carcinoma, High Grade, With Diffuse Infection by Herpes Simplex Virus 2

Poster No. 61

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We report a unique case of noninvasive papillary urothelial carcinoma, high grade, with diffuse infection by herpes simplex virus (HSV). The patient was a 63-year-old woman with no known history of any sexually transmitted diseases who presented with irritative voiding symptoms and urinary “pressure.” Urine cytology was unremarkable. Cystoscopy revealed 2 exophytic tumors involving the left lateral wall and bladder neck, which were resected. Histologically, the tumors exhibited features of high-grade papillary urothelial carcinoma with widespread geographic areas of necrosis, raising the concern for invasion. Upon close examination, the necrotic foci contained viral cytopathic changes of herpes simplex virus, confirmed by immunohistochemistry for HSV-1/2 and by polymerase chain reaction for HSV-2. No invasion was identified. The adjacent urothelial mucosa exhibited chronic inflammation, but was negative for HSV by hematoxylin-eosin and immunohistochemistry. This case was unique in 2 ways. First, the widespread tumor necrosis was concerning for invasion. The necrosis further mimicked invasion by obscuring the epithelial-stromal interface. Secondly, the selective infection of urothelial carcinoma by HSV raised the question of whether HSV plays a role in urothelial tumorigenesis. A review of the literature revealed no definitive evidence of HSV-induced urothelial neoplasia. However, an increased susceptibility of urothelial carcinoma to infection by HSV was described. While the existing literature supports this patient’s carcinoma being secondarily infected by HSV, it is not possible, based on the histologic findings, to exclude a potential role of HSV in tumorigenesis.

Hepatitis C and Renal Disease: Is It Always Associated With Membranoproliferative Glomerulonephritis?

Poster No. 62

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Context: Membranoproliferative glomerulonephritis (MPGN) consists of a group of renal disorders that can present as either nephrotic syndromes, nephritic syndromes, or a combination of both. Etiology can be either primary or secondary to another systemic disease. Diagnosis is confirmed by renal biopsy. A number of publications have asserted that hepatitis C will present as MPGN. However, in our patient population, we have hypothesized a different outcome. We have found that most of our patients with hepatitis C do not have MPGN and that most patients diagnosed with MPGN have negative hepatitis serology results.

Design: We performed a retrospective review of renal biopsies performed at a major Midwestern medical campus in the last 19 years. We searched for patients with hepatitis C. We also searched for cases of MPGN.

Results: We identified 64 cases of hepatitis C. Of these cases, 17 had MPGN, 15 had diabetic glomerulopathy, and 4 had focal segmental
glomerulonephritis; there were 7 cases of IgA nephropathy and 26 other cases. Of the 63 total renal biopsies with MPGN, 17 were from patients who had hepatitis C.

**Conclusion:** Based on our results, we cannot conclude that hepatitis C presents as MPGN. Of the patients with hepatitis C, 26.5% had MPGN. In addition, of MPGN cases, only 26.9% had hepatitis C. Furthermore, other noninfectious, systemic diseases such as hemodialysis B, systemic lupus erythematosus, and human immunodeficiency virus can cause MPGN. Those patients who have MPGN in the absence of hepatitis C support the assertion that hepatitis C and MPGN do not always present together.

**Expression of Cell Cycle–Related Molecular Markers in Patients With Nonmetastatic Squamous Cell Carcinoma of the Bladder**

**Poster No. 63**

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**Context:** Cell cycle–related molecular markers are commonly altered in squamous cell carcinoma of the bladder. We evaluated the association between p53, p21, p27, and cyclin E1 expression with pathologic features and clinical outcomes of bladder squamous cell carcinoma.

**Design:** Bladder squamous cell carcinoma was identified in 106 patients through immunohistochemical staining of biopsy and radical cystectomy. The breakdown was pT1 (9.4%), pT2 (55.7%), pT3 (30.2%), and pT4 (4.7%). A tissue microarray was prepared with triplicate repeats per patient. Immunohistochemical staining with p53, p27, p21, and cyclin E1 was performed and analyzed with ACIS (Dako, Carpenteria, California).

**Results:** Immunohistochemical expression was positive as follows: p53 in 37 (35%), p27 in 54 (51%), cyclin E1 in 70 (66%), and p27 in 103 (97.2%) cases. p53 expression was significantly associated with abnormal DNA ploidy (P = .01) and higher stage (P = .04). In univariable analyses, p53 was associated with disease recurrence (HR = 2.6; 95% CI, 1.1–6.0; P = .03) and cancer-specific mortality (HR = 2.3; 95% CI, 1.01–6.2; P = .048). In multivariable analyses that were adjusted for the effects of grade, stage, and lymphovascular invasion, p53 was associated with disease recurrence (HR = 2.4; 95% CI, 1.0–5.6; P = .049) but not cancer-specific mortality (P = .35). p21, p27, and cyclin E1 were not associated with pathologic features or clinical outcomes.

**Conclusions:** p53 was the only marker that showed a prognostic role in patients treated with radical cystectomy for nonmetastatic bladder squamous cell carcinoma. No combination of markers was identified as prognostic. Our findings support the need for further evaluation of molecular markers and their signaling pathways.

**Histologic Spectrum of Chromophobe Renal Cell Carcinoma: Cytologic Features and Unusual Growth Patterns**

**Poster No. 64**

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**Context:** Chromophobe renal cell carcinoma (CRC) is a unique type of RCC and its diagnosis confers a more favorable prognosis than other RCCs. Diagnostic considerations arise when some unusual growth patterns such as tubulocytic or even focally papillary patterns are present in a chromophobe tumor. We assessed the differential expression of molecular markers associated with cell cycle (p53, p21, p27, and cyclin E), proliferation (Ki-67), apoptosis (cleaved caspase–3), inflammation (cytokine-2), and growth (epidermal growth factor receptor) between bilateral-related (BUC) and non–bilharzial-related (NBUC) urothelial carcinomas of the bladder.

**Design:** The study included 136 patients treated with radical cystectomy for urothelial carcinoma, with a mean follow-up of 3 years (range, 0 to 8 years). The patients were divided into 2 groups (BUC and NBUC) and were matched for pathologic stage and lymph node involvement. A prognostic score (favorable for ≤4 altered biomarkers; unfavorable for >4 altered biomarkers) was correlated with clinical and pathologic data.

**Results:** The patients included 119 males and 17 females with a mean age of 56 years. Extravesical extension and lymph node involvement was present in 56% and 35% of patients, respectively. Ki-67 and cleaved caspase–3 were the most commonly altered biomarkers in both groups (90% and 88%, respectively). BUC had more p21, p27, and cyclin E alterations (72%, 66%, and 37%, respectively), whereas NBUC had more p53, cova-2, and epidermal growth factor receptor (53%, 40%, and 31%, respectively). Unfavorable prognostic score was associated with advanced tumor stage (P = .04), lymph node involvement (P = .02), and recurrence (P = .03) in BUC but not in NBUC.

**Conclusions:** A panel of multiple biomarkers can predict aggressive biologic behavior and poor outcome for patients with BUC. Altered expression of multiple biomarkers may act cooperatively/synergistically to promote tumor progression.

**Loss of or Reduced Expression of S100P in Invasive Urothelial Carcinoma: Implications for Its Role in Tumor Progression**

**Poster No. 67**

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Context: Our previous study demonstrated that S100P overexpression and loss of expression of pVHL was observed in ductal adenocarcinoma of the pancreas. This study investigates whether there is a correlation of expression for these 2 markers in urothelial lesions. Design: Immunostaining of S100P and pVHL in 129 cases of benign urothelium and urothelial lesions was performed. There were 5 groups: 10 cases of normal urothelium (G1); 25 cases of low-grade papillary urothelial carcinoma (G2); 43 cases of high-grade papillary urothelial carcinoma (G3); 25 cases of invasive urothelial carcinoma (G4A); and 26 cases of urothelial carcinoma with muscle invasion (G4B). The distribution was recorded as negative, 1+, 2+, 3+, and 4+.

Results: The results demonstrated nuclear and cytoplasmic staining of S100P in 100% of cases in groups G1, G2, and G3, with 3+ or 4+ staining in 80% of G1 cases, 92% of G2 cases, and 98% of G3 cases. In contrast, 8 of 25 cases (32%) in G4A and 10 of 26 cases (38%) in G4B showed loss of S100P expression; 9 of 25 cases (36%) in G4A and 6 of 26 cases (23%) in G4B were focally positive for S100P (1+ or 2+); and only 32% of cases in G4A and 38% of cases in G4B were diffusely positive for S100P. No cases demonstrated immunoreactivity for pVHL.

Conclusions: The results demonstrate that loss of or reduced expression of S100P is associated with the progression of noninvasive urothelial carcinoma to invasive urothelial carcinoma. Also, pVHL plays no role in urothelial carcinoma.

Immunohistochemical and Molecular Analysis of Malignant Perivascular Epithelioid Cell Tumor of the Urinary Bladder (Poster No. 68)

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A member of the same family of tumors as angiomyolipoma, perivascular epithelioid cell tumor (PEComa) is an interesting soft tissue neoplasm demonstrating features of melanocytic and smooth muscle differentiation. Cases involving the urinary bladder are very rare, with predominantly individual case reports in the literature; however, PEComa and other soft tissue neoplasms may occur in the urinary bladder. Immunohistochemistry revealed positivity of the tumor cells for melanocytic and smooth muscle markers, combined with absence of desmin, CD117, cytokeratin 20, and p63. Stains for epithelial membrane antigen, and p53 were positive; vimentin, renal cell antigen and vimentin stains were negative. FISH studies demonstrated abnormalities of chromosome 1p, and deletions of 1q in 2 of 2 cases analyzed with UroVysion fluorescence in situ hybridization (FISH) (chromosomes 3, 7, and 17 centromeres and 9p single-copy sequence). Probes for chromosome 1p (1q internal control) and 3p (3q internal control) (Abbott Molecular, Des Plaines, Illinois). Polysomy for ≥ 2 of chromosomes 3, 7, and 17 indicated urothelial origin, while abnormalities of chromosome 1 suggested collecting duct derivation. Tumor 1 had infiltrating nests of clear cells, glandular structures and single cells with pleomorphic nuclei, and an in situ component in the pelvic epithelium. Immunohistochemistry for high-molecular-weight cytokeratin (AE1/AE3), low-molecular-weight cytokeratin (cytokeratin 19, epithelial membrane antigen, and vimentin) stains were negative. FISH studies demonstrated polysomies, confirming the diagnosis of urothelial carcinoma. Tumor 2 was composed of irregular glands and ducts, demisplastic stroma, and cells with pleomorphic nuclei and hobnailing. Stains for mucicarmine, cytokeratin 19/18, high-molecular-weight cytokeratin (cytokeratin 19, epithelial membrane antigen, and p53) were positive; vimentin, renal cell carcinoma, cytokeratin 20, and p63 were negative. FISH studies demonstrated near octaploidy with relative loss of 1p and 3q, favoring a neoplastic neoplasm invading the muscularis propria, composed of spindled and epithelioid cells (Figure 50). Tumor cells exhibited areas of necrosis and focal concentration of the epithelioid component around blood vessels. Immunohistochemistry revealed positivity of the tumor cells for melanocytic markers, smooth muscle actin, and S100. Stains for desmin, CD117, epithelial membrane antigen, and vimentin were negative in the tumor cells. X chromosome inactivation studies performed on paraffin-embedded tissue revealed a clonal proliferative process. This immunohistochemical profile is supportive of classification as PEComa, and tumor size, necrosis, and infiltrative architecture are predictive of aggressive behavior. Expression of melanocytic markers in these tumors may lead to the false impression of metastatic malignant melanoma. Thus, recognition that PEComa and other soft tissue neoplasms may occur in the urinary bladder is important to avoid misdiagnosis.

Primary Carcinoid of the Testes: Do Metastases Always Indicate a Metachronous Primary? (Poster No. 69)

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Carcinoid tumors are well-described entities that are located primarily in the gastrointestinal tract (85%), as well as in the lungs, liver, and genitourinary tract (15%). Primary testicular carcinoids is a rarely described lesion, composing only 0.23% of all testicular neoplasms. We present a case report of a 26-year-old man who presented with an enlarging left testicle and accompanying paresthesias. Radical orchietomy revealed a neoplasm 4.6 cm in greatest dimension, and subsequent retroperitoneal lymphadenectomy revealed metastases. Histopathologic and immunohistochemical staining showed the tumor to be a pure carcinoid arising in the testicle. No other possible primary sites were identified. Subsequent retroperitoneal lymphadenectomy revealed the presence of metastatic disease, a rare finding, as this patient is one of only a few such cases reported in the English literature. Even more rare, this patient had none of the high-risk factors for metastasis, such as large tumor size or carcinoid syndrome. If data suggest that the presence of metastases indicates a metachronous primary, what is the significance of a primary carcinoid tumor with concurrent metastasis? Current standards state that radical orchietomy is the traditional therapy necessary for primary testicular carcinoid tumors, and retroperitoneal lymphadenectomy is usually reserved for patients with evidence of lymphadenopathy or tumors associated with teratomatous elements. Under guidance of these standards, this patient’s lymph node metastases would have been missed. This finding begs the question: should lymph node dissection be adopted as routine in the staging of pure primary testicular carcinoids, not just those associated with teratoma?

Diagnosis of Urothelial and Collecting Duct Carcinoma Using Fluorescence In Situ Hybridization (Poster No. 70)

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High-grade tumors of the renal pelvis and medulla are difficult to classify by histology alone. We examined 2 infiltrative renal pelvic tumors. The first mass replaced the right kidney in a 76-year-old man with hematuria. The second, a left renal hilar mass, was from a 50-year-old man with flank pain. Touch preparations from case 1 and fresh tumor cells from case 2 were analyzed with UroVysion fluorescence in situ hybridization (FISH) (chromosomes 3, 7, and 17 centromeres and 9p single-copy sequence). Probes for chromosome 1p (1q internal control) and 3p (3q internal control) (Abbott Molecular, Des Plaines, Illinois). Polysomy for ≥ 2 of chromosomes 3, 7, and 17 indicated urothelial origin, while abnormalities of chromosome 1 suggested collecting duct derivation. Tumor 1 had infiltrating nests of clear cells, glandular structures and single cells with pleomorphic nuclei, and an in situ component in the pelvic epithelium. Immunohistochemistry for high-molecular-weight cytokeratin, cytokeratin 19, and p63 was positive. Renal cell carcinoma antigen and vimentin stains were negative. FISH studies demonstrated polysomies, confirming the diagnosis of urothelial carcinoma. Tumor 2 was composed of irregular glands and ducts, demisplastic stroma, and cells with pleomorphic nuclei and hobnailing. Stains for mucicarmine, cytokeratin 19/18, high-molecular-weight cytokeratin (cytokeratin 19, epithelial membrane antigen, and p53) were positive; vimentin, renal cell carcinoma, cytokeratin 20, and p63 were negative. FISH studies demonstrated near octaploidy with relative loss of 1p and 3q, favoring a...
diagnosis of collecting duct carcinoma. By performing FISH analysis, the diagnoses were made with increased certainty.

Expression of Ras-Responsive Element Binding Protein 1 in Benign Prostate and Prostatic Adenocarcinoma (Poster No. 71)

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Context: Ras-responsive element binding protein 1 (RREB1) is a transcription factor that binds specifically to the RAS-responsive elements of gene promoters. It was demonstrated that RREB1 interacts with androgen receptor (AR) and serves as a potent AR corepressor, the effect of which is attenuated by activation of Ras. The aim of the current work is to study the expression of RREB1 in malignant versus normal prostate glands.

Design: RREB1 expression in prostate tissue microarray (TMA) sections was determined by immunohistochemistry using anti-RREB1 antibody. The TMA contained 8 cases of different grades of prostate adenocarcinoma and 3 normal prostate cases in duplicate cores per case. Immunopositivity for RREB1 of the glandular epithelial cells was used for scoring as follows: negative, no; +, <10%; ++, 10%-50%; and +++, >50% positive cells.

Results: RREB1 was significantly highly expressed in prostate adenocarcinoma compared to normal prostate (P < .001). Two of 3 benign prostate cases were negative for and 1 case was weakly positive for the expression of RREB1. Analysis of the 8 carcinoma cases for the presence of glands that exhibit RREB1 immunopositivity demonstrated high positivity in all cases (Figure 51, A and B). Negative control slide showed no background reactivity. Good correlation was found between tumor grade, Gleason score, and the expression of RREB1 (r = 0.6).

Conclusions: The present work consistently reveals that RREB1 is always highly expressed in malignant glandular prostatic epithelium compared to benign prostatic glands. The work is in progress to further investigate the role of RREB1 in prostate gland carcinogenesis.

Plasmacytoid Variant Urothelial Carcinoma: E-Cadherin and β-Catenin (Poster No. 72)

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Plasmacytoid urothelial carcinoma (PUC) is a rare histologic variant of urothelial carcinoma. Loss of E-cadherin has been associated with poor prognosis in patients with conventional urothelial carcinoma and few case reports have demonstrated E-cadherin negativity in PUCs. The E-cadherin/β-catenin complex plays a crucial role in epithelial cell-cell adhesion. Perturbation in the expression or function of this complex results in loss of intercellular adhesion, with possible consequent cell transformation and tumor progression. To our knowledge, the expression of β-catenin in PUC has not been reported. We present a case of PUC with concurrent loss of both E-cadherin and β-catenin. A 63-year-old woman complained of postmenopausal bleeding and irritative lower urinary tract symptoms. Cystoscopy noted a flat induration with ulcerated surface. Biopsy revealed high-grade urothelial carcinoma with muscularis propria infiltration. Radical cystectomy was performed and the resected bladder showed a 2.0 × 1.5-cm flat lesion with necrotic surface in the right anterior wall. Microscopically, tumor cells diffusely invaded through muscularis propria and penetrated to perivesical soft tissue with extensive lymphovascular invasion. The infiltrating carcinoma cells showed eccentrically placed nuclei and eosinophilic cytoplasm resembling plasma cells. Immunohistochemistry showed negativity for E-cadherin and β-catenin. β-Catenin signaling has been implicated in the genesis of a variety of tumors; however, the expression and function of β-catenin in PUC are not clear. More cases are needed to further investigate the expression level of β-catenin and the relationship of E-cadherin/β-catenin complex and associated signaling pathways, which may elucidate the pathogenesis and provide a possible therapeutic target for PUC.

Lymphoepithelioma-like Carcinoma of the Urinary Tract Is a Variant of Conventional Urothelial Carcinoma and Is Unlikely to Be of Viral Origin (Poster No. 74)

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Hoon Tan, MD; Mingsheng Wang, MD; Shaobo Zhang, MD; Lee Ann Baldridge, BA, HT(ASCP); Gregory T. MacLennan, MD; Liang Cheng, MD. Departments of Pathology and Pathology and Urology, Indiana University School of Medicine, Indianapolis; Department of Pathology, Cordoba University, Cordoba, Spain; Department of Pathology, University of Michigan, Ann Arbor; Department of Pathological Anatomy and Histopathology, School of Medicine, Polytechnic University of the Marche Region (Ancona), Ancona, Italy; Department of Pathology, Singapore General Hospital, Singapore; and Department of Pathology, Case Western Reserve University, Cleveland, Ohio.

Context: Lymphoepithelioma-like carcinoma (LELC) of the urinary tract is a rare malignancy, which is named for its resemblance to nasopharyngeal lymphoepithelioma (Figure 53). Its origin, association with conventional urothelial carcinoma (UC), and biologic behavior are not well defined. Optimal treatment strategies remain debated. Nasopharyngeal tumors are characteristically associated with Epstein-Barr virus, whereas immunohistochemistry and in situ hybridization have failed to establish this connection in urinary LELC. Human papillomavirus (HPV) positivity, which has been reported in some LELCs of the oropharynx, breast, and uterine cervix, has not been evaluated in urinary tract LELC.

Typically, gross examination reveals a thickened tunica vaginalis studded with tumor. However, in some cases, the gross appearance of the tumor is atypical, making the diagnosis challenging. We report a case of malignant mesothelioma of the tunica vaginalis testis in a 61-year-old man who presented with an ill-defined, firm, and tan-white testicular mass measuring 5.2 cm. The tumor was located in the testicular hilum and involved the testicular parenchyma and paratesticular tissue. Histologically, the tumor was characterized by epithelial cells with papillary, tubulopapillary, solid, and focal spindle-cell features. Malignant mesothelioma, rete testis adenocarcinoma, and less likely germ cell tumors were considered in the differential diagnosis. The tumor stained diffusely and strongly positive for calretinin, focally positive for Wilms tumor–1, inhibin, cytokeratin 5/6, CD15, and D2-40, and negative for carcinoembryonic antigen, epithelial membrane antigen, placental alkaline phosphatase, and OCT4. Ultrastructural examination revealed epithelial cells joined by tight junction complexes with lumen formation. Long, slender, and at times tortuous microvilli were seen on the luminal surface of the tumor cells (Figure 54). The length to diameter ratio of these microvilli was greater than 10, making them distinct from those seen in adenocarcinoma. The diagnosis of mesothelioma of the tunica vaginalis can be challenging given its rarity, and at times, atypical gross features. Immunohistochemical studies may be helpful, but they are not always conclusive. Electron microscopy in such cases is useful to confirm the diagnosis.

Design: We examined 23 cases of urinary tract LELC, using fluorescence in situ hybridization (FISH) with the UroVysion probe set (Abbott Laboratories, Abbott Park, Illinois) and in situ hybridization for HPV. Tumors were classified by percentage of LELC and presence or absence of urothelial CIS and other histologic types of UC.

Results: Age ranged from 54–84 years (mean, 69.5 years) (male to female ratio, 2.7:1). There was concurrent or previous urothelial CIS in 41% of cases. More than half of the tumors were pure LELC, unassociated with conventional UC. UroVysion studies demonstrated frequent chromosomal abnormalities, most commonly gain of chromosome 3. In situ hybridization for HPV was negative in all stained cases.

Conclusions: Although UroVysion FISH abnormalities are not pathognomonic for UC, these findings in a large percentage of urinary LELCs, plus their frequent association with CIS and other histologic types of UC, suggest that urinary LELC is closely related to conventional UC and may develop through similar mechanisms. Urinary LELC appears to be unrelated to Epstein-Barr virus or HPV infection.

Malignant Mesothelioma of Tunic Vaginalis Testis (Poster No. 75)

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Malignant mesothelioma of the tunica vaginalis testis is an extremely rare tumor representing 0.3% to 5% of all malignant mesotheliomas.

Significance of Invasion of Ejaculatory Ducts and Intraprostatic Seminal Vesicle by Prostate Cancer in Radical Prostatectomy (Poster No. 76)

Huiying He, MD, PhD; Cristina Magi-Galluzzi, MD, PhD; Ming Zhou, MD, PhD (zhoum@ccf.org). Department of Pathology, Cleveland Clinic, Cleveland, Ohio.

Context: Seminal vesicle (SV) and vas deferens enter and travel for a short distance in the prostate gland before joining together to form the ejaculatory duct (ED). Invasion of SV by prostate cancer is a well-known negative prognostic factor in radical prostatectomy. However, the significance of intraprostatic SV and ED invasion is unknown.

Design: Radical prostatectomy with cancer involving ED was reviewed for the presence of intraprostatic SV, invasion of intraprostatic SV, extraprostatic SV, extraprostatic extension, Gleason score, and tumor volume.

Results: Seventy-three cases with ED involvement were identified. Gleason score was 6, 7, and ≥8 in 1 (1.4%), 32 (43.8%), and 31 (42.4%) cases, respectively. Nine cases (12.3%) had preoperative hormonal ablation. Tumor volume was 0.5–2 ml in 16 (21.9%) and ≥2 ml in 57 (78.1%) cases. Extraprostatic extension was present in 69 cases (94.5%). Intraprostatic SV invasion was present in 63 cases (86.3%). Intraprostatic SV was identified in 37 cases. Intraprostatic SV invasion was present in 29 of 37 cases (78.4%). Cases with intraprostatic SV invasion all had extraprostatic SV invasion, while cases without intraprostatic SV invasion were all negative for extraprostatic SV invasion.

Conclusions: Invasion of ED is associated with a high probability of extraprostatic extension (94.5%) and SV invasion (86.3%) and should prompt pathologists to submit additional tissue and look for extraprostatic extension and SV invasion if such findings are not seen in the initial
examination of radical prostatectomy. All cases with invasion of intraprostatic SV also had invasion of extraprostatic SV; therefore, invasion of intraprostatic SV should be regarded as SV invasion and staged as pT3b.

Immunohistochemical Study of Prostate Cancer With Glutamate Receptor 2
(Poster No. 77)

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Context: Differentiation between low-grade prostate adenocarcinoma and normal prostate is sometimes difficult. Furthermore, no biomarker to predict behavior exists thus far. Accurate identification of cancer, particularly the aggressive forms, will provide proper risk stratification for optimum patient management. We have performed immunohistochemical staining with a monoclonal antibody designed to detect glutamate receptor 2 (Glur2), a receptor predominantly expressed in the central nervous system.

Design: Immunoreactivity of mAb 6C4 with 46 prostate adenocarcinoma slides, which also contained benign positive glands and/or HGPIN, was assessed.

Results: All the benign prostatic glands displayed strong and uniformly positive membrane staining. Most of the GS6 prostate carcinomas were negative or focally/weakly reactive with Glur2. With the increase in Gleason score, the reactivity of prostate carcinoma with GluR2 increased. The results are summarized in the Table.

Conclusions: MAb 6C4 may be useful to help differentiate between benign epithelium and low-grade lesions in some cases. Increased reactivity in high-grade prostate adenocarcinoma (GS7 and above) may also have prognostic value. However, future study is required, including determination of whether 6C4 is detecting GluR2 or a cross-reacting prostate-specific antigen.

<table>
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<tr>
<th>6C4 Reactivity in Prostatic Carcinoma</th>
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<tr>
<td>Benign</td>
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<tr>
<td>HGPIN</td>
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<tr>
<td>Total</td>
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<tr>
<td>Reactive, %</td>
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<td>Nonreactive, %</td>
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Paraprotein-Associated Crystal Nephropathy With Multiorgan Involvement: A Case of Crystaglobulinemia Syndrome Diagnosed at Autopsy
(Poster No. 78)

Tarush Kothari, MD (tkothari@nshs.edu); Xiaotong Wang, MD; Xinmin Zhang, MD; Jela Bandovic, MD. Department of Pathology and Laboratory Medicine, North Shore University Hospital, Manhasset, New York.

Cast nephropathy due to light chains (LCs) is a known form of renal disease in multiple myeloma. Multigorgan deposition of crystals of an LC-derived substance is seldom reported. We report a case of LC-associated crystal nephropathy in a 66-year-old man who presented with diffuse joint pain, chest pain, and flank pain. He was treated for acute renal failure, and investigations revealed elevated serum-free LCs. His hospital course was complicated by worsening chest pain and terminal metabolic acidosis. At autopsy, significant findings were necrotizing vegetation on tricuspid and pulmonary valves with bilateral enlarged kidneys. Microscopic examination revealed massive deposition of extracellular hyaline crystals of varying shapes in kidney tubules with associated severe inflammatory and granular cell reaction. Similar crystalline material was identified in the glomerular capillaries and intrarenal arteries. Immunohistochemistry showed crystals positive for λ and negative for k. Crystals were seen in the myocardium, pulmonary and tricuspid valve vegetations, alveolar capillaries, thyroid, prostate, and bone marrow. Interestingly, bone marrow showed increased focal collections of plasma cells that were positive for CD38 and cyttoplasmic λ. The extraordinary clinical burden with widespread extracellular deposition of crystalline paraproteins makes this case unique. Diagnosis of a systemic lymphoplasmacytic disorder known as crystaglobulinemia syndrome was made. This is a very rare paraproteinemic syndrome in which LCs spontaneously crystallize in the microvasculature and may be the initial manifestation of myeloma. Older patients with renal insufficiency and proteinuria should be evaluated for paraprotein-related disorders. Kidney and bone marrow biopsies may render an early diagnosis in such cases.

Renal Cell Carcinoma With Rhabdoid Differentiation: A Clinicopathologic and Immunohistochemical Study of 62 Cases
(Poster No. 79)

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Context: Renal cell carcinomas (RCCs) compose more than 80% of primary renal neoplasms. Rhabdoid RCC is relatively rare. We reviewed 62 cases of rhabdoid RCC and evaluated 2 novel markers, PAX2 and PAX8, as well as CD10 and RCC, to determine the sensitivity of these markers in the rhabdoid component.

Design: We reviewed 62 RCCs with rhabdoid differentiation to obtain the following: age, gender, tumor size, percentage of rhabdoid cells, tumor necrosis, renal vein invasion, stage, and survival. Unstained slides from 40 cases were immunostained with CD10, RCC, PAX2, and PAX8.

Results: The mean age was 61 years, the average tumor size was 8.3 cm, and the average percentage of rhabdoid differentiation was 28% (range, 1%–100%). The associated nonrhabdoid component included clear cell RCC (n = 52), papillary RCC (n = 3), sarcomatoid RCC (n = 2), and unclassified RCC (n = 5). On average, 24% tumor necrosis occurred in 54 of 62 tumors. Vascular invasion was present in 44 of 62 cases; 26 also showed renal vein invasion. Tumors presented as T1 in 9 (14%), T2 in 5 (8%), T3A-C in 42 (69%), and T4 in 5 (8%) cases. Ten patients had lymph node or distant metastasis at diagnosis. Mean survival for those who died (N = 47) was 1.9 years (range, 1 month–10 years). The rhabdoid component showed positive staining for PAX2 in 3 of 40 (8%), PAX8 in 32 of 40 (80%), CD10 in 31 of 40 (78%), and RCC in 17 of 40 (45%) cases.

Conclusions: RCCs with rhabdoid differentiation typically present at a high pathologic stage, often with tumor necrosis and renal vein involvement. PAX8 and CD10 showed the highest sensitivity for the rhabdoid component.

Biopsy Versus Whole Mount Location of Prostatic Tumors: Potential Impact on Surgical Technique
(Poster No. 80)

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Context: Selection of candidates for nerve sparing during robotic radical prostatectomy (RRP) involves multiple clinical and pathologic variables. Some surgeons use mapping biopsies to aid in selection with the expectation that tumor in lateral organs could impact ability to perform the closer excision needed to spare erectile nerves. We investigated whether tumor involving lateral biopsy cores predicts laterally located cancer or is associated with presence of extraprostatic extension (ECE), thereby potentially threatening cancer control if nerve sparing is performed.

Design: Biopsy and whole mount tumor location were compared in 63 patients undergoing RRP who had preoperative 12-zone mapping biopsies.

Results: A total of 113 laterally located cancers were identified. Of those, 66 had a positive lateral biopsy on the same side (58.4% sensitivity for lateral cancer). Of the 70 sides with positive lateral biopsies, 66 had lateral disease on the same side in the resection specimen (94.3% positive predictive value of biopsy for lateral cancer). Of the 56 sides with no lateral cancer on biopsy, only 9 did not have lateral disease on resection (16.1% negative predictive value of biopsy for lateral cancer). Of 13 sides with ECE, 10 (77%) had a positive lateral biopsy.

Conclusions: Positive lateral prostate biopsies highly predicted presence of lateral tumor on the same side, and most patients with ECE had positive lateral biopsies. However, absence of cancer on lateral biopsies did not rule out lateral tumors on the same side on final pathology. Mapping biopsies may underestimate lateral location of tumors, which may have implications for selection of patients for nerve sparing.

WT-1–Negative and CK5/6-Negative Mesothelioma With Atypical Features
(Poster No. 81)

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Abstracts
A 36-year-old man complained of left testicular enlargement of 4 to 5 months' duration. He was found to have a hydrocele. Magnetic resonance imaging showed a 3.8 × 3.5 × 1.4-cm mass arising from the scrotal wall and 3 other nodules measuring 4 mm or less. The patient underwent resection of the dominant mass arising from the tunica vaginalis. The overall architecture of the tumor was papillary with complex branching. There were areas consisting of solid sheets with necrosis and focal spindled areas intermixed (Figure 55). Cytologic features were notable for atypia and prominent nucleoli. Immunohistochemical studies were performed on a representative slide and showed strong positivity for pancytokeratin and calretinin but negative staining for WT-1 and CK 5/6. Despite the latter results, calretinin and D2-40 positivity was consistent with mesothelial origin. The tumor cells were also negative for CD15, Ber-Ep4, and TTF-1. The mesothelial elements were present in a linear arrangement in the submesothelial stroma of the tunica vaginalis with associated hemorrhage and chronic inflammation. They were interpreted as entrapped rather than invasive. The absence of definitive invasion precludes a diagnosis of malignant mesothelioma; however, the finding of atypical cells forming solid sheets with necrosis led to the final diagnosis of mesothelioma with atypical features. Following the resection of the mass, the patient underwent orchectomy, which showed no evidence of invasion, and retroperitoneal lymph node dissection. Further imaging studies were conducted to exclude concurrent mesothelial lesions involving the pleura or peritoneal cavities. At 1-year follow-up, no recurrences were identified.

Urinary Bladder Squamous Cell Carcinoma With Osteosarcoma: Case Report and Literature Review

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Urinary bladder carcinosarcoma is a rare highly malignant tumor with an intimate admixture of carcinoma and sarcoma. Usually, the carcinoma component is urothelial carcinoma. Only 3 cases of bladder carcinosarcoma composed of squamous cell carcinoma and osteosarcoma have been previously reported. Here we report the fourth case. A 67-year-old man complained of left testicular enlargement of 4 to 5 months’ duration. He was found to have a hydrocele. Magnetic resonance imaging showed a 3.8 × 3.5 × 1.4-cm mass arising from the scrotal wall and 3 other nodules measuring 4 mm or less. The patient underwent resection of the dominant mass arising from the tunica vaginalis. The overall architecture of the tumor was papillary with complex branching. There were areas consisting of solid sheets with necrosis and focal spindled areas intermixed (Figure 55). Cytologic features were notable for atypia and prominent nucleoli. Immunohistochemical studies were performed on a representative slide and showed strong positivity for pancytokeratin and calretinin but negative staining for WT-1 and CK 5/6. Despite the latter results, calretinin and D2-40 positivity was consistent with mesothelial origin. The tumor cells were also negative for CD15, Ber-Ep4, and TTF-1. The mesothelial elements were present in a linear arrangement in the submesothelial stroma of the tunica vaginalis with associated hemorrhage and chronic inflammation. They were interpreted as entrapped rather than invasive. The absence of definitive invasion precludes a diagnosis of malignant mesothelioma; however, the finding of atypical cells forming solid sheets with necrosis led to the final diagnosis of mesothelioma with atypical features. Following the resection of the mass, the patient underwent orchectomy, which showed no evidence of invasion, and retroperitoneal lymph node dissection. Further imaging studies were conducted to exclude concurrent mesothelial lesions involving the pleura or peritoneal cavities. At 1-year follow-up, no recurrences were identified.

Primary Renal Carcinoid Tumors: Evaluation of PAX-2 and PAX-8 Expression With Emphasis on Novel Immunohistochemical Findings

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Context: Primary renal carcinoid tumors are rare. The cell of origin of renal carcinoid tumors is uncertain, unlike those arising in the gastrointestinal tract and lung. Immunohistochemistry for renal cell lineage transcription factors PAX2 and PAX8 may be useful in determining renal origin of tumors. Expression of PAX2/PAX8 has not been determined in renal carcinoid tumors. We sought to determine if renal carcinoid tumors expressed PAX2/PAX8 in an effort to elucidate the cell of origin and delineate pathologic and immunohistochemical findings of these rare tumors.

Design: The clinical, morphologic, and immunohistochemical features were evaluated in 9 primary renal carcinoid tumors from multiple institutions. The expression of PAX2/PAX8 was evaluated in all cases; additional markers relevant in the differential diagnosis (CD99, synaptophysin, chromogranin, and CD56) and organ-specific transcription factors expressed in extrarenal carcinoid tumors (CDX2, TTF1) were also evaluated.

Results: The clinical and pathologic results are summarized in the Table. The renal-associated (PAX2/PAX8), gastrointestinal (CDX2), and pulmonary/thyroid (TTF1) transcription factors were not expressed in any case (0 of 9). All cases expressed neuroendocrine markers. Of interest, CD99 was expressed in 8 of 9 cases, the 1 negative case representing atypical carcinoid/neuroendocrine carcinoma.

Conclusions: Renal carcinoid tumors are rare tumors; perinephric extension, nodal and distant metastases are common. The absence of expression of PAX2 and PAX8 suggests these tumors may be derived from nonrenal elements; association with horseshoe kidneys (2 of 9 cases) may be derived from entrapped nonrenal elements. CD99 was expressed in almost all cases (8 of 9); recognition of this could prevent misdiagnosis of a renal primitive neuroectodermal tumor.

<table>
<thead>
<tr>
<th>Case</th>
<th>Gender</th>
<th>Tumor Size, cm</th>
<th>Pathology</th>
<th>Immunohistochemistry</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65/M</td>
<td>4.0/capsular</td>
<td>SYN+, CHR−, CD99+</td>
<td>CK7+, CD10−, EMA+, P504s−, CD20+, WT1−, TTF1−, CDX2+, PAx2+, CD99+, EMA−, P504s+</td>
</tr>
<tr>
<td>2</td>
<td>53/M</td>
<td>6.0/metastatic to perirenal adipose tissue and retrorenal lymph nodes</td>
<td>SYN+, CHR+, CD56+, CD99+, CD57+, TTF1+, CDX2−, PAx2−, CD99−, EMA+, P504s+, CD20+, WT1−, TTF1−, CDX2+, PAx2+, CD99+, EMA−, P504s+</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>76/M</td>
<td>9.5/metastatic to liver (pT3PNxPm1)</td>
<td>SYN+, CHR+, CD56+, CD99+, CK7+, RCC−, CD10−, TTF1−, CDX2−, PAx2−, CD99+, EMA+, P504s+, CD20+, WT1−, TTF1−, CDX2−, PAx2+, CD99+, EMA−, P504s+</td>
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<tr>
<td>4</td>
<td>53/F</td>
<td>Unknown size/horseshoe kidney</td>
<td>SYN+, CHR+, CD99+, VIM+, AE1/3+, CAM 5.2+, RCC−, EMA+, CD7−, c-kit−, P504s−, CD10−, CD56−, TTF1−, CDX2+, PAx2−, CD99+, EMA−, P504s+</td>
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Clinicopathologic and Immunohistochemical Findings in Primary Renal Carcinoid Tumors

Downloaded from http://meridian.allenpress.com/doi/pdf/10.1043/3010-0317-AB.1 by guest on 27 September 2020
A Rare Case of Sclerosing Angiomatoid Nodular Transformation of the Spleen: A Clinical and Radiologic Mimicker of Metastasis in Renal Cell Carcinoma

(Stehura et al.; Poster No. 85)

Shree G. Sharma, MD (drshreegopal@gmail.com); Husain Muhammad, MD. Department of Pathology, University of Arkansas for Medical Sciences, Little Rock.

Our case report describes a unique vascular tumor of the spleen with characteristic morphologic, immunophenotypic, and benign clinical behavior. The patient was a 56-year-old man with history of left kidney mass, which was found after he was evaluated for hypercalcemia. He was also found to have possible metastasis in the spleen and small indeterminate lesions on the liver. Results of magnetic resonance imaging of brain were normal. The patient’s left kidney was embolized a day before open radical left nephrectomy and concurrent open splenectomy. The surgeon noticed a firm mass on palpation in the inferior portion of the spleen, but it was not apparent on observation. Upon examination, the kidney had an 11-cm, grade 4 clear cell conventional renal cell carcinoma. The spleen lesion was very unique grossly; it was solitary, unencapsulated, tan-yellow, and lobulated with distinct cell borders (Figure 56). No areas of necrosis or hemorrhage were identified. On microscopy of the spleen lesion, the nodular architecture was revealed in which the angiomatoid nodules were separated from each other by fibrous stroma; the vascular nature of the lesion was proven by CD34 stain (Figure, inset). The present case is reported not only because of its rarity but also to increase the awareness about this entity so that it is not confused with metastasis and other vascular lesions in the spleen.

<table>
<thead>
<tr>
<th>Case</th>
<th>Gender</th>
<th>Tumor Size, cm</th>
<th>Pathology</th>
<th>Immunohistochemistry</th>
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<tr>
<td>5</td>
<td>44/F</td>
<td>4.5/capsular</td>
<td>invasion with extension into the perinephric adipose tissue (pT3pNX)</td>
<td>SYN+, CHR+, VIM+, AE1/3+, CD99+, TTF1−, CDX2−, PAX2−, PAX8−</td>
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<td>6</td>
<td>51/F</td>
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<td>invasion with extension into the perinephric adipose tissue and hilar lymph nodes (pT3pN1)</td>
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<tr>
<td>7</td>
<td>55/F</td>
<td>2.2/capsular</td>
<td>invasion with extension into the perinephric adipose tissue and metastasis to liver (pT3pNXpM1), at least atypical carcinoid, ? neuroendocrine carcinoma</td>
<td>SYN+, CHR+, NSE+, AE1/3+/−, CD31−, CD34−, VIM−, CD99−, TTF1−, CDX2−, PAX2−, PAX8−</td>
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<tr>
<td>8</td>
<td>50/F</td>
<td>9.7/horseshoe</td>
<td>kidney, associated with a cystic teratoma and concurrent adenocarcinoma</td>
<td>SYN+, CHR+, CD56+, CK7+, CD10−, PS104−, CD99+, TTF1−, CDX2−, PAX2−, PAX8−</td>
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<tr>
<td>9</td>
<td>44/F</td>
<td>2.5/multifocal</td>
<td>with capsular invasion with extension into the perinephric adipose tissue (pT3pNX)</td>
<td>SYN+, CHR+, CK7+/−, EMA−, CD99+, TTF1−, CDX2−, PAX2−, PAX8−</td>
</tr>
</tbody>
</table>

Abbreviations: AE1/3, cytokeratin AE1/3; CHR, chromogranin; CK7, cytokeratin 7; CK20, cytokeratin 20; EMA, epithelial membrane antigen; RCC, renal cell carcinoma antigen; SYN, synaptophysin; TTF1, thyroid transcription factor 1; VIM, vimentin; +, positive immunoreactivity; −, nonimmunoreactive; +/−, focal immunoreactivity.

A Rare Case of Sclerosing Angiomatoid Nodular Transformation of the Spleen: A Clinical and Radiologic Mimicker of Metastasis in Renal Cell Carcinoma

(Stehura et al.; Poster No. 85)

Shree G. Sharma, MD (drshreegopal@gmail.com); Husain Muhammad, MD. Department of Pathology, University of Arkansas for Medical Sciences, Little Rock.

Our case report describes a unique vascular tumor of the spleen with characteristic morphologic, immunophenotypic, and benign clinical behavior. The patient was a 56-year-old man with history of left kidney mass, which was found after he was evaluated for hypercalcemia. He was also found to have possible metastasis in the spleen and small indeterminate lesions on the liver. Results of magnetic resonance imaging of brain were normal. The patient’s left kidney was embolized a day before open radical left nephrectomy and concurrent open splenectomy. The surgeon noticed a firm mass on palpation in the inferior portion of the spleen, but it was not apparent on observation. Upon examination, the kidney had an 11-cm, grade 4 clear cell conventional renal cell carcinoma. The spleen lesion was very unique grossly; it was solitary, unencapsulated, tan-yellow, and lobulated with distinct cell borders (Figure 56). No areas of necrosis or hemorrhage were identified. On microscopy of the spleen lesion, the nodular architecture was revealed in which the angiomatoid nodules were separated from each other by fibrous stroma; the vascular nature of the lesion was proven by CD34 stain (Figure, inset). The present case is reported not only because of its rarity but also to increase the awareness about this entity so that it is not confused with metastasis and other vascular lesions in the spleen.
common, metastatic spread from one malignancy to another is a rare occurrence. As of this report, there were fewer than 160 reported cases of tumor-to-tumor metastasis. Although renal cell carcinoma is a common recipient tumor and melanoma is among the most common donor tumors, a similar case has not been reported since the 1950s, and no case has ever included immunohistochemical analysis.

An “Alternate Slice” Method for Processing Radical Prostatectomies Is Comparable to Total Embedding

(Poster No. 86)

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Context: Radical prostatectomy specimens are relatively commonly received in both community hospitals and major academic centers. No standard method for processing these tissues is generally agreed upon, although a number of widely different protocols can be found in grossing manuals and published reports. We evaluated 2 methods of processing radical prostatectomy specimens for key pathologic parameters.

Design: Forty-eight radical prostatectomy specimens were totally embedded, using a standard protocol, resulting in an average of 30 blocks per case. Subsequently these cases were reevaluated with selected limited sampling, which included apex, bladder neck, seminal vesicles, and alternate slices from the anterior, middle, and posterior thirds of the gland (15 blocks). The apical section was inked and submitted on edge to allow evaluation of resection margins. Seminal vesicles, apical, and bladder neck margins were evaluated similarly in both protocols. Gleason scores, extraprostatic extension, margin status, presence of perineural invasion, and pathologic staging were compared by using both methods.

Results: Using the limited sampling method, 87.5% of the cases correlated to within 1 to the Gleason sum of the totally embedded radical prostatectomy. A single case showed a focus of possible extraprostatic extension in the totally embedded material versus the limited sampling method, resulting in a change of pathologic staging in this case from pT2c to pT3a. Status of the resection margins and presence or absence of perineural invasion were essentially unchanged.

Conclusions: A limited sampling protocol for radical prostatectomy specimens provides comparable key pathologic parameters when compared to total embedding. The method is simple and conserves valuable resources.

Peritumor Changes in Renal Cell Carcinomas

(Poster No. 87)

Ying Pei, MD, PhD (ypei@lsuhsc.edu); Ami Bhalodia, MD; Stephen Bonsib, MD. Department of Pathology, Louisiana State University Health Science Center, Shreveport.

Context: Interactions between tumor and surrounding tissues may affect tumor biology and explain differences in invasive and metastatic behavior. This study investigates peritumoral alterations in renal cell carcinoma (RCC).

Design: Nephrectomies from 31 patients with RCC, 17 clear cell (CC) and 14 papillary (Pap RCC), were reviewed. Tumor-related alterations in the peritumoral cortex were studied by hematoxylin–eosin- and immunohistochemistry for CD31, collagen type IV (coll-IV), and α-SMA.

Results: All 17 CC RCCs were invested by a fibrous pseudocapsule that varied mainly in thickness, ranging from 1–3 mm. The pseudocapsule was more variable in Pap RCC. Four showed little capsule; the tumor grew in harmony with the cortex, while 4 showed nodular fibrous bundles at interface with cortex. The remaining cases had a uniform pseudocapsule like CC RCC. All capsules showed a gradient in tubule atrophy that worsened at the tumor interface and variable inflammation with relative preservation of glomeruli. α-SMA showed myofibroblastic proliferation. CD31 showed preservation of peritubular capillaries (PTCs) throughout the pseudocapsule. Coll-IV stain showed absent tubular basement membrane with cells free within the matrix.

Conclusions: Tumor-related alterations in RCC include a pseudocapsule produced by myofibroblastic and/or tubular cells with deposition of coll-IV and preservation of PTCs. These changes may result from vascular and/or tubular obstructive effects of tumor and/or interactions between tumor and cortex. The capsular differences between tumor types may correlate with behavior differences.

Label-Free Cancer Detection in Prostate Biopsies

(Poster No. 88)

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Context: Unstained tissue slices (Figure 58, B) are transparent and usually provide limited diagnostic values, owing to their negligible absorption of visible light, especially when compared to hematoxylin–eosin–stained slices (Figure, C). However, they do change the phase of the illumination and thus term as phase object. We developed spatial light interference microscopy (SLIM) as a quantitative phase imaging method capable of measuring optical path-length changes within 0.3 nm and thus measuring a refractive index change of 0.00075. The refractive index for thin tissue is a measure of the tissue dry mass, that is, nonaqueous content (eg, proteins). Therefore, this optical property is an intrinsic measure of tissue architecture, which in turn provides diagnostic power.

Design: Using SLIM, the refractive index maps of unstained prostate biopsies were retrieved (Figure, A). The resulting images contain information about the tissue organization from submicron to centimeter scales.

Results: In a SLIM image of an unstained biopsy slice, we are able to detect single cells and their individual nuclei and even nucleoli, as well as macroscopic tumor areas, all in one measurement. We examined prostate tissues with both malignant and benign areas. The histogram of the refractive index values shows clear differences between cancerous and benign areas (Figure, D). Furthermore, the spatial correlations of refractive index indicate that cancer progression significantly alters the tissue organization.

Conclusions: Refractive index information provided by SLIM reports on the onset and progression of cancer and is an intrinsic marker for cancer diagnosis. Our preliminary results show a sensitivity and specificity that approach 100%.

In Situ Mucinous Cystadenocarcinoma of the Urachus

(Poster No. 89)

Sylvia Hayek, MD (sylvia.hayek@beaumont.edu); Mohanpal S. Dulai, MD; Maryam A. Farinola, MD. Department of Pathology, William Beaumont Hospitals, Royal Oak, Michigan.

Urachal adenocarcinoma (UA) is a rare neoplasm that accounts for 0.17%–0.34% of all bladder malignancies. It arises from the urachal remnants that occur commonly in the dome and the anterior wall of the bladder. Management of UA consists of partial or radical cystectomy and resection of the umbilicus. Prognosis is considered poor owing to a frequency of locally advanced disease on presentation. We report a case of in situ adenocarcinoma arising from urachal remnant in a 72-year-old woman with a history of prostate adenocarcinoma who presented for a surveillance computed tomography scan that showed a complex cystic mass measuring 3.7 × 3.5 cm in the region of the urachus, abutting the anterior superior aspect of the bladder, raising the concern of urachal...
Lipomatous hemangiopericytoma is a morphologically unique and rare variant of hemangiopericytoma, initially described in 1995, in which mature adipose is an integral part of the soft tissue tumor. Fewer than 50 cases of lipomatous hemangiopericytoma have been reported in the literature, with most arising within the deep soft tissue of the extremities and retroperitoneum. Visceral involvement is exceedingly rare and to our knowledge only 3 cases have been reported that documented involvement of the lung, kidney, and thyroid. We report a case of lipomatous hemangiopericytoma that arose within the renal hilum of a 35-year-old woman who had a history of progressive, intermittent epigastric pain. Abdominal ultrasonography and subsequent computed tomography revealed a $7.0 \times 5.5 \times 5.3$-cm echogenic mass with varying degrees of density. Radical nephrectomy demonstrated a well-defined, multinodular, and heterogenous yellow to pink-gray mass. Microscopically, the mass consisted of a heterogenous population of spindled cells arranged around staghorn-shaped vascular channels, admixed closely with mature adipocytes. Immunohistochemically, the neoplastic cells stained strongly and diffusely for CD34 and were negative for cytokeratins, HMB-45, S100 protein, smooth muscle actin, Melan-A, and CD31. The neoplasm was diagnosed as a lipomatous hemangiopericytoma. This rare variant of hemangiopericytoma is also described as a fat-containing variant of solitary fibrous tumor, classified on a spectrum of solitary fibrous tumor. When involving the kidney, lipomatous hemangiopericytomas must be distinguished from angiomylipoma, sarcomatoid renal cell carcinoma, and other mesenchymal neoplasms.

**Adult Orbital Xanthogranulomatous Disease: Report of 2 Cases and Review of Literature**

(Paper No. 92)

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Adult orbital xanthogranulomatous disease is a rare heterogeneous group of lymphoid tumors that represents 4 recognized entities: adult orbital xanthogranuloma, necrobiotic xanthogranuloma, adult-onset asthma, and periocular xanthogranuloma and Erdheim-Chester disease. This group of diseases is characterized by infiltration of foamy histiocytes and Touton-type giant cells along with lymphocytes, and in some cases, fibrosis and necrosis. We report 2 cases of adult orbital xanthogranulomatous disease. The patients were admitted with a chief complaint of progressive proptosis, swelling of upper lids, and deterioration of vision. Pathologic evaluation of the orbital masses in both cases revealed a diffuse infiltrate of histiocytic cells, xanthoma cells, and Touton giant cells. In 1 of our cases a prominent lymphoid infiltrate with extensive germinal center formation, along with the other characteristic features of xanthogranulomatous disease, led to the diagnosis of adult-onset xanthogranuloma. The second case, with extensive fibrosclerosis, more dispersed Touton giant cells and xanthoma cells, and less prominent lymphoid infiltrate, was diagnosed as Erdheim-Chester disease in this case report, we discuss the clinical, pathologic, and immunohistochemical findings in these 2 cases, along with previously reported cases, and discuss criteria for subclassification into the 4 disease entities comprising this group.

**Wegener Granulomatosis Isolated to the Orbit**

(Paper No. 93)

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Wegener granulomatosis is a vasculitic syndrome of unknown etiology that typically involves the upper airway, lung, and kidney. Involvement of the orbit by Wegener granulomatosis is unusual and typically presents in a limited form with more favorable prognosis. We describe the case of a 64-year-old man who presented with marked proptosis of the right eye. Imaging demonstrated an infiltrative soft tissue mass within the right orbit, which eroded the surrounding bony structures, obliterated the optic nerve, and extended into the ethmoid air cells and maxillary sinus. The radiologic differential diagnosis included an aggressive neoplasic process, such as lymphoma. Results of serologic studies for anti-neutrophil cytoplasmatic antibodies were negative. The patient underwent orbital decompression, and the lesion was noted to be diffusely infiltrative and highly vascular with intraoperative hemorrhage. Microscopic examination revealed confluent granulomatous inflammation with zones of necrosis and acute inflammation; there was necrotizing infiltration of surrounding medium-sized vessels by neutrophils and multinucleated giant cells.
giant cells. There was no evidence of malignancy, and no organisms were seen. The patient subsequently experienced progressively decreased vision and proptosis, but he declined orbital exenteration. He required a repeated debulking procedure, with little symptomatic improvement, and he died shortly thereafter. This case highlights the potentially aggressive course of Wegener granulomatosis affecting the orbit.

Metastatic Prostatic Adenocarcinoma to the Iris and Ciliary Body
(Poster No. 94)

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Prostatic adenocarcinoma metastasizes to sites such as the vertebral column, hip bone, bladder, and lung. Here we present a unique case of metastatic prostatic adenocarcinoma to the eye, with the uvea being the solitary and initial site of metastasis. A 70-year-old man presented with complete loss of vision in his left eye. His past history was significant for prostatic adenocarcinoma. He underwent an enucleation procedure. Cross examination revealed an 8-g enucleated eyeball measuring 25 × 24 × 24 mm with a normal appearing iris, lens, and retina. There was a diffuse thickening of the choroid, but no mass was identified. Microscopic examination showed metastatic adenocarcinoma, which involved the iris, ciliary body, and choroid in a circumferential manner and occluded the angle with corresponding cupping of the disc (Figure 60). The tumor cells were pleomorphic, had abundant clear cytoplasm and prominent nucleoli, and numerous atypical mitoses were identified. They were positive for pancytokeratin, prostate-specific antigen, and prostatic acid phosphatase, but were negative for cytokeratin 7, thyroid transcription factor 1, Melan-A, and renal cell carcinoma immunohistochemical stains. Metastatic carcinoma to the uvea is uncommon. Within the uvea, the choroid is the most common site of metastasis, with the ciliary body and iris being rare sites of involvement. The most common primaries are breast, lung, gastrointestinal, skin, kidney, neuroendocrine, and prostate. Breast and lung form 65% of all cases. Prostatic adenocarcinoma constitutes 1% of all cases. These patients have poorer prognosis, as uveal involvement usually indicates very advanced disease.

Multidrug-Resistant Acinetobacter baumannii in Long-Term Care Facilities
(Poster No. 95)

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Context: Acinetobacter baumannii, an anaerobic gram-negative bacillus, has emerged within the last 15 years as one of the most important health care–associated pathogens. Its increasing resistance to commonly prescribed antimicrobials makes it the major threat to the current antibiotic era. Multidrug-resistant Acinetobacter baumannii is recognized as one of the most difficult infections to control and treat.

Design: Cultures collected from residents in long-term care facilities for a period of 3 years were analyzed for the presence of A baumannii. All positive cultures were subcultured, then identified using MicroScan Walkaway 96 conventional panels. The isolate was considered multidrug resistant if it was resistant to 3 or more classes of antimicrobial agents.

Results: Four hundred seventy-six isolates in 2007, 573 in 2008, and 752 in 2009 were identified as A baumannii; 35.1% in 2007, 36.5% in 2008, and 44% in 2009 were multidrug resistant (Table). Most multidrug-resistant isolates were from wounds. Almost all multidrug-resistant isolates had full resistance to the most commonly prescribed antibiotics; a decrease in the susceptibility over time was noted (imipenem susceptibility dropped from 35% in 2007 to 5% in 2009).

Conclusions: An increase in the prevalence of multidrug-resistant A baumannii and the decline in antimicrobial susceptibility in long-term care facilities highlight the importance of infection control practices including staff education, enhanced hand hygiene, contact isolation, surveillance cultures, and daily chlorhexidine baths. In addition, it emphasizes the necessity for newer antimicrobial agents with activity against these organisms.

Are Turnaround Times for Antimicrobial Susceptibility Testing Different for “Plate-and-Send” Versus “Plate-and-Read” Inpatient Urine Cultures? (Poster No. 96)

Gabriel Z. Larsen, MStat (gabe.larsen@imail.org); Sterling T. Bennett, MD, MS. Department of Central Laboratory, Intermountain Healthcare, Murray, Utah.

Context: Two medium-sized community hospitals in an integrated health care system, with similar scopes of clinical services and equidistant from a central laboratory, use the central laboratory for organism identification and antimicrobial susceptibility testing. For urine cultures, hospital A follows a “plate-and-send” process, incubating culture plates and incubating them until routine courier pickup. Full incubation and detection of growth occur in the central laboratory. Hospital B follows a “plate-and-read” process, incubating and reading cultures on-site, and sending only positive cultures to the central laboratory for identification and susceptibility testing.

Design: Inpatient urine culture data from hospitals A and B were extracted from the data warehouse for 2009. The turnaround times from culture setup to completion of susceptibility testing were retrospectively analyzed. The cumulative distributions of turnaround times were tabulated and the statistical significance of differences in distributions was assessed by using the 2-tailed Mann-Whitney-Wilcoxon test.

Results: Susceptibility testing was performed on 507 of 2541 cultures (20%) from hospital A and 478 of 2942 cultures (16%) from hospital B. The turnaround times for the plate-and-read process were longer at all percentiles (P < .001), averaging 13% longer, with a maximum difference of 25% (13 hours) at the 78th percentile. Selected percentiles are shown in the Table.

Conclusions: Times to completion of susceptibility testing were statistically and practically significantly longer with the plate-and-read process.

Antimicrobial Susceptibility Test Turnaround Times, hours

<table>
<thead>
<tr>
<th>Percentile</th>
<th>Hospital A: Plate-and-Send</th>
<th>Hospital B: Plate-and-Read</th>
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<tr>
<td>10th</td>
<td>36.9</td>
<td>39.4</td>
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<tr>
<td>25th</td>
<td>39.4</td>
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<td>90th</td>
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Congenital Infection by *Haemophilus Influenzae* Biotype IV
(Poster No. 97)

Carlos E. Parra-Herran, MD (cparraherran@med.miami.edu); Maria M. Rodriguez, MD; Timothy J. Cleary, PhD. Department of Pathology, University of Miami-Jackson Memorial Hospital, Miami, Florida.

We report the case of a male baby born at 24 weeks of gestation. The mother was a 25-year-old woman who presented with vaginal discharge, contractions, and fever. She had a urinary tract infection 4 weeks prior to admission. She presented with bulging membranes in the perineum; the cervix was completely dilated and effaced. Her white blood cell count was 4000/µL with 79% neutrophils and 14% bands. At delivery, Apgar scores were 1, 4, and 6. The baby was resuscitated and transferred to the neonatal intensive care unit. Blood cultures were positive for *Haemophilus influenzae* biotype IV and negative for serotypes a through f. A blood sample was sent to the Florida Department of Health for confirmation. The baby expired 14 hours after birth. Postmortem examination revealed an extremely premature newborn with no morphologic anomalies. The lungs showed intrabronchial and peribronchial and bronchiolar neutrophilic inflammation with intra-alveolar hyaline membranes. Congenital and neonatal pneumonias occur in the setting of maternal infection and chorioamnionitis. Nontypeable (lacking a polysaccharide capsule) *H influenzae* is a relatively infrequent pathogen. About 20% of urogenital nontypeable *H influenzae* are biotype IV. This biotype is found almost exclusively in the urogenital tract. Some strains identified as biotype IV comprise a monophyletic cryptic biotype IV. This biotype is found almost exclusively in the urogenital tract. Blood cultures were positive for *Haemophilus influenzae* biotype IV and negative for serotypes a through f. A blood sample was sent to the Florida Department of Health for confirmation. The baby expired 14 hours after birth. Postmortem examination revealed an extremely premature newborn with no morphologic anomalies. The lungs showed intrabronchial and peribronchial and bronchiolar neutrophilic inflammation with intra-alveolar hyaline membranes. Congenital and neonatal pneumonias occur in the setting of maternal infection and chorioamnionitis. Nontypeable (lacking a polysaccharide capsule) *H influenzae* is a relatively infrequent pathogen. About 20% of urogenital nontypeable *H influenzae* are biotype IV. This biotype is found almost exclusively in the urogenital tract. Some strains identified as biotype IV comprise a monophyletic cryptic biotype IV. This biotype is found almost exclusively in the urogenital tract.

Niloofar Nasseri-Nik, MD (niloofar_nik@yahoo.com); Anthony Walsh, PhD; Nawaal Nasser, MD. Department of Pathology, Orlando Health, Orlando, Florida.

We report the case of *Nocardi a cyriacigeorgica* pneumonia in a 17-year-old adolescent boy who had recently begun high-dose prednisone for ulcerative colitis. Two weeks following the start of therapy, he presented with worsening cold symptoms and night sweats. Imaging studies revealed severe bilateral pneumonia with innumerable nodules, extensive cavitations, and necrosis. Sputum cultures were obtained and IV antibiotic therapy was initiated. Blood, chocolate, and Middlebrook agar plates grew dry, chalky, wrinkled, white-yellow colonies (Figure 61). Staining demonstrated numerous gram-positive delicate filamentous beaded rods that were also partially acid-fast. DNA sequencing performed at an outside reference laboratory identified the organism as *N cyriacigeorgica*. This diagnosis prompted subsequent evaluation for chronic granulomatous disease, which was confirmed by an oxidative burst test. *Nocardi a* is the most important genus among the aerobic actinomycetes with a complex taxonomy and numerous species reported. The morphologic and phenotypic characterization of these species is difficult, and they have been grouped based on their pattern of drug resistance (types I–VI). *Nocardi a asteroides* drug pattern type VI has been identified as *Nocardi a cyriacigeorgica* by use of the 16S rRNA gene amplification method. To our knowledge, only 7 cases of *N cyriacigeorgica* have been reported in the literature. This case is exceptional in that the finding of *N cyriacigeorgica* pneumonia led to the serendipitous diagnosis of chronic granulomatous disease.

*Nocardia Cyriacigeorgica* Pneumonia in a 17-Year-Old Adolescent Boy With Ulcerative Colitis and Subsequent Diagnosis of Chronic Granulomatous Disease
(Poster No. 98)

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Community-acquired *Klebsiella pneumoniae* with a hypermucoviscosity phenotype is a rare cause of pyogenic liver abscess in the United States. Although typically implicated in pneumonias, *Klebsiella* has an increased prevalence in hepatic abscesses in Asia. This phenotype, however, is relatively unknown in the United States. Recognition of this entity is of the utmost importance because of the potential 10% to 30% mortality rate. At our facility, a 52-year-old white man who was a truck driver presented to the emergency department with a 10-day fever of unknown origin, chills, and night sweats. He had not traveled outside of the United States. He was prescribed azithromycin for 5 days; however, he returned and was admitted to the hospital owing to nonresolution of symptoms. Six blood cultures were drawn during the patient’s stay, one of which revealed the presence of a gram-negative rod that was isolated and subtyped as *Klebsiella pneumoniae* (Figure 62). Ultrasongraphy and computed tomography imaging of the abdomen revealed a 4.3-cm multiloculated hepatic abscess replacing the right hepatic lobe. The lesion was drained, and 15 mL of pus from the cystic lesions was sent for culture. *Klebsiella pneumoniae* was isolated from the abscess with antibiotic sensitivities comparable to the positive blood culture. Polymerase chain reaction of the organism was positive for both MagA and rpmA, and was negative for wzyK2. Both isolates were sensitive to ampicillin, ceftazolin, ceftriaxone, ciprofloxacin, gentamicin, piperacillin/tazobactam, and trimethoprim-sulfamethoxazole. The patient was treated with ceftriaxone IV and was discharged on ciprofloxacin by mouth with resolution of symptoms.

Pyogenic Liver Abscess Caused by Atypical *Klebsiella pneumoniae*
(Poster No. 100)
Mycobacterium kansasii Bursitis of the Elbow Following Orthotopic Heart Transplantation
(Foster No. 101)

Omar Habeeb, MD (ohabeeb@lumc.edu); Paul C. Schreckenberger, PhD. Department of Pathology, Loyola University Medical Center, Maywood, Illinois.

A 62-year-old man presented to Loyola University Medical Center in October 2009 with increasing erythema of a swollen right elbow. He had incidentally bumped his right elbow along a doorway 1 week earlier. Pertinent medical history included orthotopic heart transplant (January 2009), with immunosuppressive medications for transplant rejection, and gout. Physical examination revealed a nontender, fluctuant right elbow with an intact range of motion; the left elbow demonstrated gouty tophi. An x-ray of the right elbow showed soft tissue bulging and a joint effusion but no fracture. The patient was diagnosed with septic arthritis of the right elbow and an empiric regimen of antibiotics and colchicine were initiated. On hospital day 1, rheumatology was consulted and a white, chalky fluid from the ensuing joint aspiration was submitted for culture and analysis. The Gram stain demonstrated a florid population of nongram-staining, rod-shaped organisms, accompanied by the presence of numerous negative images. Kinyoun and modified acid-fast bacilli stains (Figure 63) were performed and showed numerous, beaded, “tiger-tail” acid-fast bacilli. Identification of Mycobacterium kansasii was confirmed using the AccuProbe Mycobacterium kansasii Culture Identification Test (Gen-Probe Incorporated, San Diego, California). Fewer than 50 cases of M kansasii septic arthritis have been noted, and our case represents only the third report of olecranon bursitis. In addition, it is the second case of this kind in which a patient also had gout and orthotopic heart transplant. Subsequent implications for patient care and follow-up are discussed.

The authors wish to thank Paul J. O’Keefe, MD, Department of Infectious Disease, Loyola University Medical Center and Dominic Bufalino, MD, Stritch School of Medicine, Loyola University Medical Center for their contributions to this case study.

Respiratory Viral Panel—A New Molecular Test for Detecting 12 Different Respiratory Viruses: Danbury Hospital’s Experience
(Foster No. 102)

Aarti Goswami, MD (goswami.aarti@danhop.org); Vishy Chaudhary, MD; Tricia Cavallaro, MT (ASCP); Stephen Majoros, MT (ASCP); Laura Ovittore, BS, MT (ASCP); Leonel Edwards, MD; Jessica Dodge, MD. Department of Pathology, Danbury Hospital, Danbury, Connecticut.

Context: Respiratory viral panel (RVP) is a qualitative nucleic acid multiplex test that can detect 12 respiratory viruses from a single nasopharyngeal swab specimen. The virus types and subtypes include the following: influenza A, influenza A subtype H1, influenza A subtype H3, influenza B, respiratory syncytial virus subtype A, respiratory syncytial virus subtype B, parainfluenza 1, 2, and 3, human metapneumovirus, rhinovirus, and adenovirus. Influenza A/B test was less sensitive and less specific for seasonal influenza (66.7% and 86.7%, respectively). Compared to RVP, the rapid Remel Xpect EIA Influenza A/B test was less sensitive (72.2%) and showed the same specificity (100%) for 2009 H1N1. Compared to the Connecticut State Laboratory’s polymerase chain reaction test for 2009 H1N1, RVP was 100% sensitive and 100% specific (Table).

Conclusions: RVP is a powerful tool for detecting 12 respiratory viruses. Use of RVP will enhance the diagnosis of acute respiratory viral infection and decision making in patient management.

Universal Human Immunodeficiency Virus Screening for Pregnant Women in a Remote Area in Xinjiang Uyghur Autonomous Region of China
(Foster No. 103)

Heng Hong, MD1 (huhong@yahoo.com); Yuning Sun, MD2; Karlene Hewan-Lowe, MD2; Jiang Yu3; Yali Han4; Janati Bolathian5; Ping Xu, MD6; Xinminuer Hoshiharbai7. 1Department of Pathology and Laboratory Medicine, East Carolina University, Greenville, North Carolina; 2Department of Microbiology, Xinjiang Medical University, Urumqi, Xinjiang, China; 3Altay Red Cross, Altay, Xinjiang, China; 4Jeminay County Red Cross, Jeminay, Xinjiang, China; 5Department of Clinical Laboratory and Jeminay County Women and Children Health Center, Jeminay, Xinjiang, China; and 7Department of Clinical Laboratory, Burqin County Women and Children Health Center, Burqin, Xinjiang, China.

Context: The incidence of human immunodeficiency virus (HIV) infection in China has increased dramatically in recent years, especially in Xinjiang Uyghur Autonomous Region. A universal HIV screening for pregnant women was performed in a remote area in Xinjiang to help identify unsuspected maternal HIV infection and prevent perinatal transmission.

Design: All pregnant women in Burqin and Jeminay counties in Xinjiang were offered a free voluntary HIV screening. Local midlevel medical staff were trained to use Determine HIV-1/2 (Inverness Medical Japan Co, Ltd, Tokyo, Japan) for HIV screening in a point-of-care setting. The pregnant women who were tested signed a consent form, received HIV education materials, and participated in an HIV knowledge survey.

Results: Among the 450 pregnant women accepting HIV screening, 50% were herders who mostly lived in remote areas with poor access to routine medical care. Among those tested, 69.1% were Kazakhs (the second largest minority group in Xinjiang) and 64.7% were 21–29 years of age. All of the participants tested negative for HIV infection. These women correctly answered 50.7% of the questions on the survey, which consisted of 13 questions about the transmission and prevention of HIV.

Conclusions: HIV infection has not become a significant problem among the pregnant women in this remote area of Xinjiang. Education is still necessary to prevent future increases in HIV infection. Training local midlevel medical staff to administer a rapid HIV test can be an efficient way to provide HIV screening for people living in remote areas. (The College of American Pathologists Foundation Humanitarian Grants Program sponsored this project.)

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PULMONARY INFANTILE HEMANGIOMA: A RARE PRESENTATION OF A COMMON PEDIATRIC TUMOR

Poster No. 3

Rebecca J. Varley, MD (tjivarley@gmail.com); Thomas A. Sporn, MD, Department of Pathology, Duke University, Durham, North Carolina.

Infantile hemangiomata are the most common tumor of infancy; however, pulmonary infantile hemangiomata are extremely uncommon. Pulmonary hemangiomata can arise in the bronchus, trachea, diaphragm, pericardium, or the lung parenchyma. We present a case of a 5-month-old girl with multiple cutaneous hemangiomata and a large pulmonary hemangiomata. The patient was born at 30 weeks’ gestation from a multiple pregnancy that was complicated by preeclampsia. She was kept in the neonatal intensive care unit and did not require intubation. A chest x-ray showed a shadow of unknown significance in the left upper lobe. A chest computed tomography angiogram revealed a 2.1 × 1.8-cm rounded mass in the left upper lobe with air bronchograms and suggestion of vascular supply. An ultrasonography of the chest showed a systemic blood supply to the mass coming from the left subclavian artery as well as the aorta. Venous return was unclear. It was felt that the mass was consistent with sequestration or a vascular malformation. The patient underwent an uncomplicated left upper lobectomy. Gross examination revealed an ill-defined, 3.2 × 2.5 × 2.0-cm, firm tan lesion with unremarkable surrounding parenchyma. Histologically, the lesion showed diffuse, benign-appearing capillary proliferations within alveolar septae and areas of hemorrhage. The lesion stained strongly positive for GLUT-1, confirming the diagnosis of infantile hemangiomata. Pulmonary infantile hemangiomata are rare and should be included in the differential diagnosis of pediatric lung tumors. The significance of the multiple cutaneous hemangiomata occurring with the lung hemangiomata remains unknown.

MYOEPITHELIAL CARCINOMA OF THE PLEURA

Poster No. 4

Adnan Khan, MD (akhnan@ummschool.edu); Joel Pinczewski, MD, PhD; John Papadimitriou, MD, PhD; Seble Chekol, MD, Department of Pathology, University of Maryland, Baltimore.

Myoepithelial carcinomas (malignant myoepitheliomas) are rare mesenchymal tumors that are typically associated with the salivary glands. Rarely, they may occur outside of the salivary glands. Myoepithelial carcinomas have recently been added to the World Health Organization’s list of soft tissue tumors. Therefore, they are also recognized as a very rare tumor of soft tissue, occurring principally in the soft tissue of the extremities. Here we present a primary myoepithelial carcinoma occurring in the pleura, a site not previously reported in the literature. The patient was a 56-year-old man with a medical history of diabetes type 2, hypertension, and hyperlipidemia. He also had a long history of smoking. He presented to the University of Maryland with complaints of shortness of breath and weight loss. Imaging revealed a 6.5-cm, parietal, pleural mass with pleural effusions. Biopsy revealed the presence of a high-grade neoplasm, which was composed of loosely adherent spindled to epithelioid cells in both a loose and trabecular arrangement within a loose chondromyxoid stroma. The cells stained positively with S100 and actin and focally with glial fibrillary acidic protein. One year after initial diagnosis, the disease had progressed despite aggressive chemotherapeutic treatment. There has been some recent response to carboplatin and taxol. This case expands...
the range of known pleural tumors, and thus, represents an important addition to the differential diagnosis of malignant pleural tumors.

Cigarette Smoke Directly Contributes to Platelet-Activating Factor Production and Neutrophil Adherence to Pulmonary Microvascular Endothelial Cells (Poster No. 5)

Prerna Rastogi, MD, PhD; Jane McHowat, PhD (mchowaj@slu.edu). Department of Pathology, Saint Louis University School of Medicine, St Louis, Missouri.

Context: Cigarette smoke exacerbates lung injury leading to emphysema and bronchitis, which are characterized by airway inflammation and structural changes. To recruit inflammatory cells to the airways, cells must move from circulation across the capillary endothelial and airway epithelial cell barriers. Platelet-activating factor (PAF), a membrane phospholipid-derived inflammatory metabolite, is involved in transendothelial migration of inflammatory cells. PAF acetylhydrolase hydrolyzes and inactivates PAF. We hypothesized that an increase in PAF production and cell recruitment may exacerbate obstructive pulmonary disease in smokers.

Design: We incubated human lung microvascular endothelial cells with cigarette smoke extract and measured PAF and PAF acetylhydrolase levels. We treated freshly isolated neutrophils with the PAF receptor antagonist CV3988 and measured neutrophil adherence.

Results: PAF production increased in cigarette smoke-extract-treated (20 μg/mL) lung endothelial cells (535 ± 60 to 1580 ± 241 dpm, n = 6, P < .001). Cigarette smoke extract significantly inhibited PAF acetylhydrolase activity after 12 hours of cigarette smoke extract incubation (2.1 ± 0.1 to 0.7 ± 0.1 nmol/mg protein/min, n = 6, P = .001). Neutrophil adherence to endothelial cells also increased (14 ± 3 to 47 ± 3, n = 4, P = .002). Pretreatment of neutrophils with PAF receptor antagonist CV3988 (10 μM for 10 min) resulted in complete inhibition of neutrophil adherence (0.4 ± 0.1, n = 4, P < .001).

Conclusions: In the lung, neutrophil accumulation facilitated by the PAF-PAF receptor interaction is the initial step in inflammation and emphysema. This study demonstrates that PAF plays a central role in the recruitment of inflammatory cells to the small airways of cigarette smokers via inactivation of PAF acetylhydrolase. This process can exacerbate pulmonary inflammation.

Pulmonary Epithelioid Hemangioendothelioma: Case of Multifocal Disease Clinically Mimicking Metastatic Adenocarcinoma (Poster No. 6)

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Pulmonary epithelioid hemangioendothelioma is a rare neoplasm of vascular origin previously referred to as an intravascular bronchioloalveolar tumor. We report a case of pulmonary epithelioid hemangioendothelioma clinically mimicking metastatic adenocarcinoma. A 52-year-old man presented with a large hemithorax. Imaging showed a right-lung hilar mass with scattered, pulmonary bilateral nodules, findings which were suggestive of metastatic adenocarcinoma. Microscopic examination of the wedge biopsy showed multiple hyalinized nodules with a central hypocellular zone and cellular periphery. The cellular areas contained epithelioid cells embedded in the hyalinized matrix. Intracytoplasmic vacuoles were occasionally present in the tumor cells. Immunohistochemical staining showed positivity for CD31 and CD34 in tumor cells. Pulmonary epithelioid hemangioendothelioma is a low to intermediate grade neoplasm of endothelial origin. It usually occurs in middle-aged adults, and most patients are asymptomatic. A characteristic radiographic finding is multiple, bilateral lung nodules that are suggestive of metastatic disease or disseminated infection. Histologically, the tumor nodules demonstrate an abundant myxohyaline matrix in the center, which can be sclerotic or calcified. Tumor cells are present on the periphery of the nodules. They are usually small, with abundant eosinophilic cytoplasm and occasional intracytoplasmic vacuoles that may contain red blood cells. The tumor cells are positive for vascular markers, CD31, CD34, and factor VIII and for vimentin. Ultrastructurally, tumor cells demonstrate tight junctions, cytoplasmic filaments, and Weibel-Palade bodies. Pulmonary epithelioid hemangioendothelioma is a slow-growing neoplasm with a 5-year survival rate of 47% to 71%. Metastatic spread is rare. Surgical removal is the best treatment, while chemotherapy has not proven to be beneficial.

Endobronchial Metastatic Breast Cancer With Pagetoid Histology Mimicking Bronchial Pagetoid Squamous Cell Carcinoma In Situ (Poster No. 7)

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A 56-year-old woman presented with endobronchial breast cancer metastasis of unusual histology. The patient was diagnosed with T1N0 invasive ductal adenocarcinoma of the left breast in 1994. She underwent a modified radical mastectomy and did well until 2003 when she developed a metastatic lung nodule. The nodule was resected, but the patient subsequently developed a soft tissue mass near the resection site and new pulmonary nodules. In February 2008, the patient underwent bronchoscopic examination, which was remarkable for a white lesion in the left mainstem bronchus. Biopsy of the lesion showed extensive squamous metaplasia of bronchial epithelium. Percolating throughout the squamous epithelium were large, atypical cells with abundant eosinophilic cytoplasm and prominent retraction from adjacent cells (pagetoid intraepithelial spread, Figure 65). Atypical cells did not exhibit mucin production. Pagetoid squamous cell carcinoma in situ is a well-recognized diagnostic entity that is most commonly noted in cutaneous pathology. Conversely, pagetoid bronchial spread of breast carcinoma within metaplastic bronchial squamous epithelium has, to our knowledge, never been documented in the literature. Lack of suspicion for this pattern of metastatic disease led to an initial misdiagnosis of bronchial squamous cell carcinoma in situ. We reviewed the case: evaluation with immunohistochemical stains showed the atypical cells to be positive for estrogen/progesterone receptors and HER2 (formerly HER2 or HER2/new), findings consistent with a diagnosis of metastatic breast adenocarcinoma with pagetoid spread. Additional stains, including TTF-1, 34βE12, CAM 5.2, and BRST2, were also consistent with this interpretation. This case raises awareness of this uncommon histologic manifestation of metastatic breast cancer.

A Case of Endobronchial Leiomyoma With Hyaline Globules (Poster No. 8)

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Hyaline globules have been described in a variety of neoplastic and normal tissues. Leiomyomas, particularly those of the gastrointestinal tract, are among the neoplasms containing these globules. We report the microscopic finding of multiple hyaline globules within an endobronchial leiomyoma in a 42-year-old woman. The patient had an endobronchial mass arising from the right mainstem bronchus that was seen radiographically and confirmed endoscopically. She underwent a right thoracotomy with partial resection of the right mainstem bronchus and a right upper lobectomy. Grossly, a polypoid mass protruding into the right mainstem bronchus and arising from the bronchial wall was identified. Microscopically, the lesion was composed.
of uniform, cytologically bland spindle cells, which were arranged in fascicles. The cells had pink fibrillar cytoplasm and elongated blunted nuclei. These findings were consistent with smooth muscle differentiation. The diagnosis of leiomyoma was further supported by strong smooth muscle actin and focal desmin positivity. Immunohistochemical stains were negative for S100, CD34, HMB-45, and Epstein-Barr-encoded RNA. There were numerous intracellular, round to oval globules of pale amphophilic material present within the tumor. The globules were periodic acid–Schiff positive and diastase resistant. They also stained with smooth muscle actin. Ultrastructural studies revealed that the globules were round and had no defined shell or surrounding membrane. The presence of hyaline globules has been described in many entities. It is hypothesized that they are related to degenerative processes. They have been identified in leiomyomas in various locations. We believe that this is the first report of their presence in a leiomyoma of the respiratory tract.

**Neuroendocrine Neoplasms of the Thymus: An Aggressive Mediastinal Tumor**

(Poster No. 9)

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**Context:** Thymic neuroendocrine neoplasms are rarely encountered in routine practice, and the types of neoplasms seen are variant. Neuroendocrine neoplasms (NE) may be misdiagnosed as variants of thymoma, especially in the absence of a paraneoplastic syndrome. It is imperative to correlate clinical history, histologic/cytologic features, and immunohistochemical data to identify NE and to distinguish them from other entities.

**Design:** We reviewed the files of the surgical and cytologic sections of our institution for the last 30 years for mediastinal NEs. We correlated clinical, radiographic, and pathologic findings, including immunohistochemistry (IHC) or ultrastructural studies, were correlated.

**Results:** Four cases were identified as NE of the thymus or anterior mediastinum. All of the cases were high-grade NEs, and 3 presented with metastatic disease. The patients were 36 to 65 years of age with a male to female ratio of 3:1. Specimen types included 2 surgical biopsies, 2 fine-needle aspirations, and 1 resection. Immunohistochemistry (keratin, chromogranin A, synaptophysin, CD56, and TTF-1) performed on 3 cases and electron microscopy performed on 2 cases confirmed the diagnosis of NE.

**Conclusions:** NEs of the thymus are uncommon and behave in a very aggressive manner. Correlating clinical and radiographic information with the pathologic features is needed to exclude thymoma or metastatic NE. Histologically, the tumors form rosettes and trabeculae. They stain strongly with neuroendocrine markers and pancytokeratin but are negative for CK7 and TTF-1. NEN of the thymus should be considered in aggressive anterior mediastinal masses.

**True Thymic Hyperplasia in a 29-Year-Old Woman**

(Poster No. 10)

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True thymic hyperplasia is a very rare pathology that presents clinically as a mass, and it is often difficult to differentiate from other causes of mediastinal mass. We report true thymic hyperplasia in a 29-year-old woman. She presented with a history of a motor vehicle accident, which had resulted in multiple lacerations to the spleen, liver, and esophagus and the complex fracture of multiple ribs. Repeated imaging revealed a relatively enlarged thymic gland that was suggestive of thymoma. She had no history of myasthenia gravis, other autoimmune diseases, radiation therapy, or chemotherapy. She had a history of bipolar disorder, and she occasionally also had generalized tonicclonic seizures. She had undergone thymectomy the previous year. The specimen was received fresh as an anterior mediastinal mass with a volume of 70 cm³. Mean volume of the thymus gland for ages 25 to 29 years is 5.7 cm³. The specimen consisted of a fragment of 10 × 7 × 1 cm, pink-tan, somewhat lobulated, fleshy soft tissue with a weight of 38 g. Mean weight of thymus gland for ages 25 to 29 years is 23 g. The mass appeared as a diffuse symmetric enlargement of the thymic gland. Microscopic examination revealed well-preserved thymic architecture with well-defined thymic lobes and medullae with multiple Hassall corpuscles. No lymphoid follicles or germinal centers were present. Flow cytometry analysis showed immature T cells, a finding consistent with thymic lymphocytes. The histomorphologic features and immunophenotypic findings supported the diagnosis of the enlarged gland as true thymic hyperplasia. It is very rare for a patient to exhibit this pathology. Severe systemic stress experienced by this patient owing to bipolar disorder and generalized tonicclonic seizures may be associated with rare true thymic hyperplasia.

**Retrospective Study of Small Cell Lung Carcinoma at Danbury Hospital: Incidence of Expression of 4 Immunohistochemical Markers**

(Poster No. 11)

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**Context:** In small biopsies, the diagnosis of small cell lung carcinoma (SCLC) becomes difficult because of the common occurrence of crush artifact. The use of immunohistochemical markers can be beneficial for diagnosing SCLC.

**Design:** We searched surgical pathology records from 2006 to 2010 for a biopsy diagnosis of SCLC and found 23 patients. The paraffin blocks were retrieved and cut. They were stained for the following immunohistochemical stains: CAM 5.2, TTF-1, chromogranin, and p63.

**Results:** Most of the 25 cases of SCLC were diagnosed in bronchial or lung biopsies (11) or liver biopsies (10). The remaining cases were diagnosed in 2 lymph node biopsies, 1 sacral bone biopsy, and 1 parotid gland biopsy. The most consistently positive and sensitive marker was low-molecular-weight cytokeratin 5.2, which stained 24 of 25 cases (96%) in a cytoplasmic distribution. The second most sensitive marker was TTF-1, which was positive in 18 of 25 cases (72%), with generally strong nuclear expression. The neuroendocrine marker chromogranin stained only 11 of 25 cases (44%), mostly with a weak cytoplasmic expression. Weak or patchy staining of tumor cell nuclei for p63 was found in 14 of 25 cases (56%). Of interest, only 9 of 25 cases (36%) expressed cytokeratin CAM 5.2, chromogranin, and TTF-1 antigens (ie, all 3 stains positive).

**Conclusions:** Strong nuclear TTF-1 expression and absent or weak p63 nuclear antigen expression can support the morphologic diagnosis and help to exclude small cell lung carcinoma. Chromogranin as a neuroendocrine marker should be considered relatively insensitive for small cell carcinoma.

**An Immunohistochemical Scoring Algorithm for Selecting Patients With Anaplastic Lymphoma Kinase Gene Rearrangement (ALK+) in Adenocarcinoma of the Lung: Preliminary Findings on Immunohistochemical and Fluorescence In Situ Hybridization Correlation**

(Poster No. 12)

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**Context:** Screening for anaplastic lymphoma kinase gene rearrangement (ALK+) in non–small cell lung cancer may be important in targeting therapies for maximum clinical benefit. We hypothesized that immunohistochemistry (IHC) could be used to screen for ALK+ with confirmatory fluorescence in situ hybridization (FISH) based upon IHC scoring. We characterized signet ring cell (SRC) morphology by IHC score, as it has previously been linked with ALK+ tumors.

**Design:** We retrospectively identified patients for this study using the Mayo Clinic Lung Cancer Cohort. Inclusion criteria included adenocarcinoma, nonsmoker status, minimum 1 year of follow-up medical records, and banked tissue samples. Samples were randomly selected from approximately 600 adenocarcinoma cases among never-smokers. IHC was performed using ALK1 monoclonal antibody (Dako, Carpinteria, California) and FISH with dual-color break-apart probe (Vysis, Des Plaines, Illinois) on formalin-fixed, paraffin-embedded tissue for both tests. SRC assessment was conducted on hematoxylin-eosin–stained sections.

**Results:** IHC score distribution for 101 screened samples is shown in Table 1. IHC scores were as follows: score 3 (7.9%); score 2 (33.7%); score 1 (20.8%); and score 0 (68.3%). All 8 IHC score-3 samples were also FISH positive. SRC was more prevalent in cases with an IHC score of 1 or higher (P < .001) versus a score of 0.
Conclusions: Given our results to date, we hypothesize that IHC score 3 samples are likely to be FISH+ and that IHC scores 1 and 2 will require confirmatory FISH. Our ongoing screening will confirm or refute this hypothesis. In previous work, we showed negative FISH in IHC score 0, which could be confirmed upon completion of this ongoing study. SRC morphology may be an indicator for ALK screening.

<table>
<thead>
<tr>
<th>Correlation of IHC Score and Status of FISH and SRC</th>
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<tr>
<td>IHC Score 3 (Intense/Granular Cytoplasmic Staining in ≥10% of Cells)</td>
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<tr>
<td>FISH+ (n = 10)</td>
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<tr>
<td>FISH– (n = 91)</td>
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<tr>
<td>SRC ≥ 10% (n = 22)</td>
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<tr>
<td>SRC &lt; 10% (n = 79)</td>
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<td>IHC total (n = 101)</td>
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Abbreviations: FISH, fluorescence in situ hybridization; IHC, immunohistochemistry; SRC, signet ring cell.

Microcystic Spindle Cell Thymoma: A Clinicopathologic Study of 20 Cases
(Poster No. 13)

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Context: We describe 20 cases of an unusual variant of spindle cell thymoma.

Design: Twenty cases of microcystic spindle cell thymoma were identified from our archives and from the authors’ personal consultation files. We reviewed histologic slides and immunohistochemical studies and obtained clinical information including presentation, treatment, and follow-up.

Results: The patients included 13 males and 7 females between 7 and 82 years of age (mean age, 55 years). Clinically, the patients presented with chest pain and shortness of breath. Radiographic evaluation demonstrated an anterior mediastinal mass, and all patients were treated surgically. Macroscopically, none of the tumors were described as cystic. Histologically, the tumors were characterized by numerous microcystic structures of variable sizes, which in some areas were filled with acellular exudate or fresh blood. These microcystic structures were lined by fusiform epithelial cells focally mimicking signet ring cells in the smallest microcysts. No cellular atypia or mitotic activity was identified in any of the tumors. Seven of these tumors were invasive, and 13 were encapsulated. Immunohistochemical studies showed positive staining for pancytokeratin, while S100, desmin, and smooth muscle actin were negative. Follow-up information was available for 17 patients and showed that all were still alive 12 to 96 months following diagnosis (average period, 54 months).

Conclusions: The cases presented here highlight an unusual growth pattern of spindle cell thymoma that, in our experience, is present almost exclusively in this type of thymoma. This type of thymoma can be easily mistaken for other neoplasms because of the microcystic growth pattern.

MUC4 Expression in Non–Small Cell Lung Carcinoma Does Not Correlate with Radiologic Chemoresponse
(Poster No. 14)

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Context: Increased expression of MUC4, a transmembrane mucin ligand for receptor tyrosine kinase ErbB2, has been reported in non–small cell lung carcinoma (NSCLC). MUC4 overexpression is associated with chemoresistance in pancreatic cancers. However, correlation between MUC4 overexpression and prognosis is unclear in NSCLC.

This study attempts to correlate MUC4 overexpression with radiologic chemoresponse in patients diagnosed with and treated for unresectable NSCLC.

Design: We identified 211 patients from our institution with a pathologic diagnosis of NSCLC between 1999 and 2005. Of these, 140 were classified as stage 3A or higher and were thus eligible for the study. Only 26 met all eligibility criteria, and of these, 16 had adequate tissue for analysis. Archival tissue was retrieved from the pathology files, stained with MUC4, and scored independently by 2 separate pathologists who were blinded to the chemoresponse outcome. A final score of positive or negative was assigned. Response to chemotherapy was measured using the “Response Evaluation Criteria in Solid Tumors” guidelines. Responders were patients with partial response or complete response. Nonresponders were those with stable disease or disease progression. The measurements were done by a pulmonologist and a radiologist blinded to MUC4 status.

Results: There were 7 responders, of which 1 was positive for MUC4 expression. Of the 9 nonresponders, 2 were positive for MUC4 expression. Multivariate analysis showed no relationship between MUC4 expression and chemoresponse (Fisher exact test, $p = .99$).

Conclusions: The results suggest that MUC4 may not be a suitable marker for predicting chemoresponse in NSCLC, although larger studies might be more informative.

Pulmonary Neuroendocrine Cell Hyperplasia Associated With Bronchiectasis: A Rare Preneoplastic Condition
(Poster No. 15)

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Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia is gaining attention in the literature. It is a known precursor to carcinoid tumors, which are designated as such when neuroendocrine cell proliferation extends beyond bronchial basement membrane and nodules are small (2 to 5 mm or less) in size. Carcinoid tumor is designated when lesions are larger than 5 mm. A 47-year-old woman presented with bronchiectasis since childhood and bouts of recurrent pneumonia. Chest imaging revealed severe bronchiectasis without distinct nodules. She underwent lungeulectomy to alleviate symptoms that were refractory to medicines. Microscopy showed prominent bronchial and bronchiolar dilatation with fibrosis and patches of organizing inflammation. Additionally, there were foci of neuroendocrine cell hyperplasia along occasional bronchi and small clusters of neuroendocrine cells within the lung parenchyma (Figure 66). These cells (tumorlets) were highlighted by chromogranin and synaptophysin. Six peribronchial lymph nodes were submitted, none of which had evidence of metastatic tumor. Nor was there evidence of carcinoid tumor elsewhere in the abdominal viscera. Such pulmonary lesions have been incidentally discovered in patients with bronchiectasis and are now classified as preneoplastic by the World Health Organization. Cytokines...
released by the neuroendocrine cells tend to provoke pulmonary fibrosis. Tumors and carcinoid tumors are usually indolent; however, a recent series reported a high prevalence of lymph node involvement by carcinoid tumors, suggesting a potentially more aggressive course. A rare instance of coexisting pulmonary adenocarcinoma has been noted. Although a rare occurrence, the sole presence of pulmonary carcinoid tumors can incite incidental or carcinoid syndrome. Resolution occurs with complete excision of tumors.

**Adenomatous Polypoid Coli Promoter and Ras Association Domain Family 1 Hypermethylation in Pulmonary Hamartomas With Coincident Carcinoma**

(Poster No. 16)

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**Context:** Benign pulmonary hamartoma (PH) may coincide with carcinoma with aberrant gene promoter methylation. To investigate epigenetic factors in PH coincident with non–small cell lung cancer (NSCLC), we quantified promoter methylation of selected tumor suppressor genes reported to be hypermethylated in NSCLC.

**Design:** We evaluated DAPK, LET7, CDH1, APC, BAX, MGMT, RASSF1, RASSF5, PTEN, SHP1, and p16 promoter methylation in patients diagnosed with PH and/or NSCLC between 1995 and 2009. Promoter methylation was analyzed in 7 PH/tumor pairs, 13 PHs without associated NSCLC, and 160 tumors without an associated PH. Percentage of promoter methylation in APC was higher in PHs with associated tumor than those without (P = .02, Fisher exact test). Five of 7 PHs with coincident tumors were hypermethylated at APC in comparison to only 2 of 14 PHs without coincident carcinoma (χ2 test, P = .02). Methylation levels were found to be significantly different (P = .02) between the 2 groups. Although percentage of RASSF1 promoter methylation in PHs with, versus without, associated tumor was marginal (P = .06), 3 of 7 PHs with carcinoma were hypermethylated in comparison to 1 of 13 PHs without carcinoma (P = .05).

**Conclusions:** Promoter methylation of APC and RASSF1 may contribute to a general loss of cell cycle arrest, providing a background for tumor development from aberrations in other cell functions. Further study is warranted to investigate the possible role of PHs in NSCLC. This is the first study to compare molecular characteristics of PHs in patients with and without primary lung carcinomas.

**Endobronchial Schwannoma: Report of a Rare Case**

(Poster No. 17)

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Schwannomas (neurilemmas) are benign neurogenic tumors that arise in peripheral nerve sheaths. Primary neurogenic tumors of the lung are uncommon lesions estimated to account for 0.2% of all pulmonary neoplasms. Bronchial wall schwannoma, first described in 1969 by Feldhaus, is an exceedingly rare entity with only scattered case reports in the English literature. Although endobronchial schwannomas are typically benign, they have been associated with symptomatic airway obstruction and massive hemoptysis. We report a diagnostically challenging case of this unusual entity in a 38-year-old woman who presented with airway obstruction and a left lower lobe endobronchial mass. Initial endobronchial biopsies did not show typical histomorphologic features of schwannoma and were nondiagnostic. Subtle clues in repeated endobronchial biopsies prompted the use of S100 immunostain, which demonstrated uniformly intense staining in spindled tumor cells, a finding that was indicative of schwannian differentiation. Conservative endobronchial resection with combined electrocautery and argon plasma coagulation was performed. The endobronchial resection showed an encapsulated spindle cell tumor with alternating Antoni A and B areas and ectatic blood vessels characteristic of schwannoma. The S100 immunostain showed intense uniform staining. Surveillance bronchoscopy at 6 months revealed patent airways, and the patient reported continued relief from her respiratory symptoms. To our knowledge, this is the first case of successful treatment of endobronchial schwannoma using combined argon plasma coagulation and endobronchial electrocautery. Although endobronchial schwannomas are rare, pathologists should be aware of this entity, since recognition can obviate more radical lobectomy or pneumonectomy.

**Epithelioid Angiosarcoma of Mediastinum**

(Poster No. 18)

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Epithelioid angiosarcoma is a rare vascular neoplasm arising from the endothelial cells of the vessels. It has been associated with poor outcome. To our knowledge, very few cases have been reported in the literature. A 78-year-old woman presented with a history of progressive dyspnea for 3 to 4 days without chest pain, palpitations, or diaphoresis. She had a medical history of breast carcinoma. Computed tomography scan revealed a mediastinal mass extending inferiorly to involve the right hilum and markedly displacing the trachea and esophagus. Based on these findings, we favored high-grade adenocarcinoma. Fine-needle aspiration of the mass showed a metastatic high-grade non–small cell carcinoma of the lymph node, suggesting adenocarcinoma. On microscopic examination, the biopsy revealed a fragment of high-grade malignant neoplasm arranged in anastomosing vascular channels lined by highly atypical tumor cells. The tumor cells were highly pleomorphic in morphology from spindle to polygonal in shape. There was an associated extracellular hemosiderin deposition and extensive necrosis. No glandular or squamous differentiation was identified. Immunoperoxidase stains demonstrated strong diffuse immunoreactivity of the tumor cells for factor VIII–related antigen, CD31, CD34, cytokeratin 7, and CAM 5.2 (Figure 67). Immunostains for TTF-1, carcinoembryonic antigen, polyclonal, and calretinin were negative. Based on the immunohistochemical and morphologic features, a diagnosis of epithelioid angiosarcoma was made. To our knowledge, this is the first reported case of primary mediastinal epithelioid angiosarcoma. Epithelioid angiosarcoma is a rare, malignant, vascular tumor that is usually observed in middle-aged and elderly men. We present a case of an epithelioid angiosarcoma in an unusual location.

**Ciliated Adenocarcinoma of the Lung Associated With Bronchiolar Columnar Cell Dysplasia: A Case Report and Review of the Literature**

(Poster No. 19)

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The loss of cilia on bronchial epithelium is a distinctive change seen in the progression to malignancy. Therefore, the presence of cilia has been used as a marker of benignity. However, rudimentary cilia and cilia-associated structures have been identified ultrastructurally in pulmonary carcinomas. We report a case of a lung adenocarcinoma showing well-developed cilia. A 68-year-old man with a 10 pack-year history of smoking underwent wedge resection of 2 right lower lobe nodules 19 months after having undergone right upper lobectomy and chemotherapy for T3 N0 nonciliated adenocarcinoma. Grossly, we saw 2 tan-white lesions, measuring 4.6 cm and 1.4 cm, respectively.
Microscopically, the lesions were both moderately differentiated adenocarcinoma arising in association with bronchiolar columnar cell dysplasia. In both cases, some of the tumor cells showed well-defined cilia within the areas of bronchial dysplasia as well as within the frankly invasive and cribriform areas. In contrast to the absent staining seen in adenocarcinoma cells, immunostaining for p16 was observed in the dysplastic cells, suggesting the presence of a predysplastic lesion. The overgrown tumor cells showed diffuse cytoplasmic decoration with p16 and >25% nuclear staining with Ki-67 and cyclin D1, results which were strongly supportive of neoplastic change. Nuclear reactivity of p53 antigen was restricted to the nonciliated adenocarcinoma cells and was taken to represent a late component event in pulmonary carcinogenesis. To the best of our knowledge, this is the first reported case of a ciliated adenocarcinoma arising from bronchiolar columnar cell dysplasia.

Benign Metastasizing Leiomyomatous of the Lung That Are Histologically Similar to Lymphangioleiomyomatosis and Have Bilateral Pneumothoraces and Bone Involvement (Poster No. 20)

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Benign metastasizing leiomyomatosis (BML) is a rare condition characterized by uterine leiomyomatosis with small cytologic atypia and distal metastasizes in reproductively active women. The segregation of pulmonary BML from lymphangioleiomyomatosis is not always straightforward, as when BML is located in the subpleural areas with marked cystic changes in a limited biopsy specimen. We present a case of BML in a 35-year-old woman who presented with a retroperitoneal mass and a right upper lobe lung mass. Right middle lobectomy and partial resection of the uterus were performed, showing strong positivity in both the solid tumor nodules and in the areas of lepidic growth. This case illustrates the heterogeneity of the histologic patterns that may be seen in metastatic melanoma, as well as the importance of a broad differential diagnosis in poorly differentiated lung neoplasms.

Pulmonary Sarcomas: A Review (Poster No. 21)

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Context: Pulmonary sarcomas are rarely diagnosed. This retrospective study was undertaken to identify pulmonary sarcomas seen in pathology practice at a university medical center.

Design: The clinicopathologic data of 124 patients diagnosed with sarcoma involving the lung between 1986 and 2008 were reviewed.

Results: Ninety-nine cases (80%) were metastatic and 25 (20%) were primary. Computer tomography showed multiple small nodules in the bilateral lungs and multiple small sclerotic and lytic lesions in bones. Lung wedge biopsies showed multiple small lesions composed of spindle cells with marked cystic changes, morphologically mimicking lymphangioleiomyomatosis. The spindle cells were bland with no mitosis and cytologically identical to those of uterine leiomyomatosis. They were positive for smooth muscle actin, estrogen receptor, and progesterone receptor and negative for S100, HMB-45, and CD34. A diagnosis of BML of uterine origin was rendered. When a young female presents with pneumothoraces and with a biopsy showing cystic spindle cell proliferation, BML and lymphangioleiomyomatosis should be considered in the differential diagnosis. Careful correlation of the histologic findings with a clinical history and imaging studies is critical to reach the definite diagnosis.

Primary Mucinous Cystadenoma of the Lung (Poster No. 23)

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Mucinous cystadenoma is a very rare, benign pulmonary tumor with only 15 reported cases to date. A mucinous cystadenoma is commonly found in the pancreas, ovary, or appendix; it is rarely found in the lung. The differential diagnoses include mucinous cystic carcinoma, metastatic and lymphangioleiomyomatosis should be considered in the differential diagnosis. Careful correlation of the histologic findings with a clinical history and imaging studies is critical to reach the definite diagnosis.

Abstracts 1345

Pulmonary Sarcomas: A Review

Poster No. 21

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Context: Pulmonary sarcomas are rarely diagnosed. This retrospective study was undertaken to identify pulmonary sarcomas seen in pathology practice at a university medical center.

Design: The clinicopathologic data of 124 patients diagnosed with sarcoma involving the lung between 1986 and 2008 were reviewed.

Results: Ninety-nine cases (80%) were metastatic and 25 (20%) were primary. Computer tomography showed multiple small nodules in the bilateral lungs and multiple small sclerotic and lytic lesions in bones. Lung wedge biopsies showed multiple small lesions composed of spindle cells with marked cystic changes, morphologically mimicking lymphangioleiomyomatosis. The spindle cells were bland with no mitosis and cytologically identical to those of uterine leiomyomatosis. They were positive for smooth muscle actin, estrogen receptor, and progesterone receptor and negative for S100, HMB-45, and CD34. A diagnosis of BML of uterine origin was rendered. When a young female presents with pneumothoraces and with a biopsy showing cystic spindle cell proliferation, BML and lymphangioleiomyomatosis should be considered in the differential diagnosis. Careful correlation of the histologic findings with a clinical history and imaging studies is critical to reach the definite diagnosis.

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Poster No. 23

Muhammad A. Syed, MD 1 (muhammadasim.syed@danbhsosp.org); Salman Ayub, MD; John H. DeFrance, MD; Hani El-Fanek, MD. 1 Departments of 1 Pathology and 1 Surgery, Danbury Hospital, Danbury, Connecticut.

Mucinous cystadenoma is a very rare, benign pulmonary tumor with only 15 reported cases to date. A mucinous cystadenoma is commonly found in the pancreas, ovary, or appendix; it is rarely found in the lung. The differential diagnoses include mucinous cystic carcinoma, mucinous cystic tumors of borderline malignancy, mucinous bronchoalveolar carcinoma, and metastatic lesions. We report a case of a primary mucinous cystadenoma of the lung in an 85-year-old man who presented with a right upper lobe lung mass. Right middle lobectomy and partial right upper lobectomy were performed. Analysis of a frozen section revealed a mucin-filled cavitary lesion and associated organizing bronchopneumonia with reactive pneumocytes. The tumor was hemorrhagic, necrotic, and cavitory in nature, containing mucoid gelatinous substance and measuring 8.4 cm in greatest dimension. Pathologic examination showed a mucinous neoplasm lined by tall columnar mucinous epithelium with no cytologic atypia, dysplasia, or invasion. The underlying supporting stroma demonstrated chronic inflammation and patchy areas of fibrosis (Figure 69). Adjacent sections showed osteosarcoma (17 cases) was the most common to metastasize to the lung. The most common primary pulmonary sarcoma was high-grade sarcoma (7 cases). The average age of patients with metastases was younger than that of patients with primary pulmonary sarcomas (P < .01). Ancillary studies, such as immunohistochemistry, cytogenetics, and molecular techniques, are useful in selected cases to differentiate metastatic sarcomas from primary epithelial/mesothelial neoplasms.
chronic organizing bronchopneumonia, suggesting the possibility of secondary obstructive bronchopneumonia. The patient has remained free from recurrence for 1 year postoperatively. Mucinous cystadenoma of the lung appears to be a rare benign neoplasm with an indolent clinical course that should be differentiated from its malignant counterpart, mucinous bronchioloalveolar carcinoma and metastasis.

An Interesting Case of Chondromatous Hamartoma of the Chest Wall (Poster No. 24)

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A 3-month-old Caucasian female infant presented with respiratory distress. A computed tomography scan showed a 5 × 5 × 8-cm intraparenchymal pulmonary mass with calcifications. Multiple ribs on the right side showed disraphic changes as well. A right thoracotomy was performed with resection of tumor and chest wall. A pleural teratoma was suspected. Gross examination of the specimen revealed an 88-g, firm and bossed edges, mass, measuring 6 × 5.5 × 5.5 cm. The surface was white and shiny, and a cut section revealed cysts of varying sizes and shapes. Some cysts contained yellow, thick material, while others contained brown to red fluid. Punctate calcifications were seen throughout the specimen. Microscopic examination demonstrated a mass that appeared to arise from the rib and consisted of multiple cysts lined by bland-appearing stromal cells accompanied by osteoclast-like giant cells. These findings led to a diagnosis of chondromatous hamartoma of the chest wall. Chondromatous hamartoma of the chest wall is a benign primary bone tumor that typically presents at birth or early infancy. It arises in the rib cage and can present as a palpable local mass or with respiratory distress. This tumor consists of a predominance of cartilage, which often exhibits endochondral ossification. This relatively late clinical presentation of a chondromatous hamartoma of the chest wall was histologically distinguished by its cartilaginous degeneration. These rare tumors should be included in the differential diagnosis of respiratory distress in infancy.

Prognostic Factors for Patients With Ewing Sarcoma/Primitive Neuroectodermal Tumor Treated With Multidisciplinary Therapy (Poster No. 25)

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Context: Ewing sarcoma/primitive neuroectodermal tumor (EWS/PNET) is the second most common malignant bone tumor in children. There are approximately 225 to 250 new cases per year in the United States. With multidisciplinary therapy, an overall survival rate can reach up to 72% for patients with localized disease. However, the survival rate for patients who already have metastatic conditions and/or recurrent disease remains low.

Design: We conducted a retrospective study to evaluate clinical characteristics and prognostic factors in 166 cases of EWS/PNET from the Cincinnati Children’s Hospital EWS/PNET Tumor Registry and the files of the Lauren V. Ackerman Laboratory of Surgical Pathology from 1978 to 2009.

Results: There were 51% male and 49% female patients. The median age at primary diagnosis was 12.4 years (65%, 10 to 17 years; 35%, <10 years; and 5%, >18 years). Cases consisted of 69% intrathoracic EWS/PNET and 31% extraabdominal EWS/PNET. The most common extraabdominal sites were extremity (50%), pelvic (29%), rib (9%), skull (3%), clavicle (3%), multiple locations (3%), scapula (2%), and vertebrae (1%). The most common extraabdominal EWS/PNET sites were chest wall (33%), extremity (20%), paraspinal (18%), head (18%), neck (6%), retroperitoneum (4%), and trachea (2%) (Table). The most common first metastatic sites were bone marrow (12%) and lung (10%). In this series, 66% of patients with local diseases only were still alive; 50% of patients with metastatic diseases were still alive; and fewer than 33% of patients with recurrent disease were still alive.

Conclusions: EWS/PNET survivors have poor outcomes with metastatic diseases, especially with recurrent diseases, even after multidisciplinary therapies.

Desmoplastic Small Round Cell Neoplasm: Case Report and Review of the Literature (Poster No. 26)

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Desmoplastic small round cell tumor (DSRCT) is a highly malignant, relatively rare neoplasm that is characterized by small round tumor cells scattered among an abundant desmoplastic stroma. We report a case of a 20-year-old man who presented with complaints of increasing shortness of breath, fever, night sweats, abdominal discomfort, hematuria, and weight loss. Imaging revealed significant right-sided pleural effusion, massive abdominal pelvic ascites, and multiple large soft tissue densities within the abdomen. The soft tissue densities were biopsied and were received for pathologic evaluation. Microscopic analysis revealed infiltrating nests of poorly differentiated small round cytologically malignant cells in a prominent desmoplastic stroma. The immunohistochemical staining pattern and the genetic studies suggested the diagnosis of DSRCT. DSRCT usually arises in the abdominal cavity, although rarely, cases are seen in extra-abdominal sites. The symptoms are specific for location but not for the disease, which makes the diagnosis without histologic confirmation difficult. The chromosomal abnormality t(11;22)(p13;q12) is a unique feature of DSRCT. The tumor cells express immunohistochemical epithelial, neuroendocrine, and muscle markers and are positive for EWSR1-WT1 fusion. It is important to promptly diagnose DSRCT because of its aggressive clinical course. As it is rare with no unique histopathologic features or clinical cues, this diagnosis requires a high level of suspicion by the pathologist.

Diminished Expression of Metastasis Suppressor KAI1/CD82 in Malignant Neuroblastic Tumors (Poster No. 27)

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Context: The metastasis suppressor KAI1 or CD82 is a member of the tetraspanin superfamily. It has many roles, including cell adhesion, migration, intracellular signaling, and trafficking. Diminished KAI1 expression causes reorganization of cellular networks, leading to metastasis. Little is known regarding the role of KAI1 expression in neoplasms other than Kaposi sarcoma.

Design: We retrieved 41 neuroblastosomas (NBs), 15 ganglioneuroblastomas (GNBs), and 9 ganglioneuromas from hospital archives (1989–2009). Median age was 46.2 months (age range, 0.25 to 240 months). Immunohistochemistry was done using anti-KAI1 polyclonal antibody (Santa Cruz Biotechnology, Santa Cruz, California) and was scored with a semiquantitative 3-tiered scale (negative, weak, strong). Tumors were considered positive if there was staining in more than 50% of the cells. Staining patterns were compared to tumor diagnosis and histology. Histology was rated as either favorable or unfavorable.

Results: KAI1 expression was found in the neurupl, cytoplasm of ganglion cells and neuroblasts, and/or Schwannian stroma. All gangliovemomas were positive (strong 55%, weak 45%, negative 0%). GNBs showed overall diminished staining (strong 25%, weak 50%, negative 25%). NBs also showed overall diminished staining (strong 13%, weak 65%, negative 25%). Among NBs and GNBs, 29% of those with unfavorable histology and 12% of those with favorable histology stained negatively.

Conclusions: KAI1 expression was down-regulated in GNBs and NBs in contrast to results for ganglionuromas. In GNBs and NBs, KAI1 expression varied according to cell type, cellular location, reactivity, and intensity, suggesting multiple mechanisms may be responsible for KAI1 dysregulation. In contrast to ganglionuromas, GNBs and NBs showed diminished KAI1 expression, indicating that KAI1 may play a role in neuroblastic tumor biology.

Solitary Fibrous Tumor of the Anterior Abdominal Wall

(Poster No. 28)

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Solitary fibrous tumor is a rare spindle cell tumor of mesenchymal origin. Originally thought to occur primarily in the pleura, solitary fibrous tumors have since been documented in a variety of locations and should be included in the differential diagnosis of any soft tissue lesion, regardless of anatomic locale. We present an unusual case of a solitary fibrous tumor in the anterior abdominal wall of a 35-year-old man who presented with right-sided groin pain. The tumor was completely excised, and histopathologic examination and immunohistochemical profile were consistent with a solitary fibrous tumor.

Characterization of p16 Immunohistochemistry Staining in Benign and Malignant Lipomatous Neoplasms

(Poster No. 29)

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Context: Malignant lipomatous tumors are distinguished from benign lipomatous lesions by their abnormal architecture and the presence of lipoblasts. Discriminating benign deep-seated lipoma and atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDLs) may be difficult owing to infrequent lipoblasts separated by a significant amount of mature adipose tissue. We hypothesized that the diagnostic utility of p16 immunohistochemistry, which resulted in positive staining in ALT/WDLs but not in lipoma. We examined p16 expression in ALT/WDLs, lipomas, and previously uncharacterized categories of lipomatous neoplasms. We hypothesized that p16 staining would be observed in benign but not in malignant tumors, and/ or angiolipoma.

Design: We stained formalin-fixed, paraffin-embedded tissue from ALT/WDLs, dedifferentiated and myxoid liposarcomas, chondroid lipoma, spindle cell lipoma, hibernoma, angiomylipoma, angiolipoma, and conventional lipoma with p16 antibody. Four pathologists scored p16 positivity on a 4-point grading scale (0 to 3+). Average scores of 2 or greater were reported as positive, and lower average scores were reported as negative.

Results: Immunohistochemistry for p16 was positive in 10 of 12 ALT/WDLs (83%), 2 of 2 dedifferentiated (100%) liposarcomas, and 2 of 2 myxoid liposarcomas (100%). Immunohistochemistry for p16 was negative in conventional lipoma (0 of 5), hibernoma (0 of 1), and angiomylipoma (0 of 4). Mixed results were seen in chordoid lipomas and angiolipomas. In the former, immunohistochemistry for p16 was positive in 2 of 3 cases (67%). In the latter, there was positivity in 2 of 5 cases (40%).

Conclusions: Our hypothesis was confirmed, with positive p16 staining in malignant lipomatous lesions. Benign lesions were p16 negative, with the exception of variable expression in chordoid lipomas and angiolipomas. The current study further characterizes the potential diagnostic utility of p16 immunohistochemistry in lipomatous neoplasms.

Aggressive Angiomyxoma Presenting as Bladder Discomfort and Urinary Incontinence

(Poster No. 30)

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Aggressive angiomyxoma is a rare tumor of mesenchymal origin that most commonly arises in the vulvovaginal region, perineum, and pelvis of postmenopausal women. Although traditionally thought to be of gestational origin, the term aggressive emphasizes the often ill-defined, infiltrative nature of the tumor and the high association with local recurrence. We report a case of an otherwise healthy 42-year-old woman who presented with a 6-month history of bladder discomfort and urinary incontinence. Ultimately, a computed tomography scan revealed a 14-cm, multilobulated, peripherally enhancing mass partially encasing the anorectal canal and extending posteriorly to the sacrum and subcutaneous soft tissue of the right buttock. Initial clinical and radiographic differential diagnoses included chordoma, gastrointestinal stromal tumor, melanoma, carcinoma, and a multilocular abscess. The patient underwent abdominopерineal resection, and gross examination revealed a tan-pink, myxoid tumor within the mesorectal soft tissue. Histologic examination revealed a hypcellular neoplasm consisting of bland spindle cells in a myxoid background without significant nuclear atypia or mitotic activity. Prominent vascular spaces, some surrounded by a ring of hyalinized stroma, were also identified. The histologic findings were diagnostic of aggressive angiomyxoma. Immunohistochemistry was positive for estrogen and progesterone receptors, which was consistent with prior reports and with the presumed origin of this neoplasm from hormonally responsive perineal cells. The patient has been followed closely with serial radiographic imaging, and to date there has been no evidence of recurrence. This case illustrates how aggressive angiomyxoma can present with nonspecific symptomatology and is often unsuspected in the differential diagnosis at initial presentation.

Dedifferentiated Paratesticular Liposarcoma Mimicking High-Grade Extraskeletal Osteosarcoma: Role of Immunohistochemistry in Diagnosis

(Poster No. 31)

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Dedifferentiated liposarcoma (DDL) of the paratesticular region with osteosarcomatous differentiation is a rare malignancy. Only a few cases have been described in the English literature. We describe a case of DDL, resembling extraskeletal osteosarcoma. A 79-year-old man presented with an enlarging scrotum. Ultrasonography demonstrated a complex mass adherent to the right testicle. Radical orchectomy showed a 4.5 × 3.0 × 3.0-cm, gray-white, firm mass completely replacing the epididymis. The transmucosal cord and epididymis were adherent. Microscopically, the tumor was composed of fascicles of spindle-shaped cells with oval nuclei, granular unevenly distributed chromatin, and inconspicuous nucleoli. Large pleomorphic and multinucleated tumor cells were seen with atypical mitotic figures. In multiple areas, neoplastic cells formed multilocular abscess. The patient underwent abdominoperineal resection, and histologic examination revealed a tan-pink, myxoid tumor within the mesorectal soft tissue. Histologic examination revealed a hypcellular neoplasm consisting of bland spindle cells in a myxoid background without significant nuclear atypia or mitotic activity. Prominent vascular spaces, some surrounded by a ring of hyalinized stroma, were also identified. The histologic findings were diagnostic of aggressive angiomyxoma. Immunohistochemistry was positive for estrogen and progesterone receptors, which was consistent with prior reports and with the presumed origin of this neoplasm from hormonally responsive perineal cells. The patient has been followed closely with serial radiographic imaging, and to date there has been no evidence of recurrence. This case illustrates how aggressive angiomyxoma can present with nonspecific symptomatology and is often unsuspected in the differential diagnosis at initial presentation.
MDM2 showed nuclear positivity, indicating 12q13-15 gene amplification and confirming the diagnosis of DDL. A minor component of well-differentiated liposarcoma was not appreciated on first viewing. Extensive de novo dedifferentiation obscured the minor component of well-differentiated liposarcoma and led to an erroneous interpretation in this case. Paratesticular tissue represents an extension of retroperitoneal adipose tissue, and sarcoma in this location should always arouse suspicion of DDL. Our case illustrates that immunohistochemistry to detect amplification of MDM2 and CDK4 genes can establish the diagnosis of DDL.

**Soft Tissue Angiosarcoma With Abundant Metaplastic Bone Formation Mimicking Osteosarcoma**

(Poster No. 32)

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Angiosarcomas represent fewer than 1% of soft tissue sarcomas and most commonly occur in cutaneous tissue. Fewer than 25% of angiosarcomas occur in the deep soft tissue and then most commonly in the deep muscles of the lower extremities. Typically, angiosarcomas consist predominantly of epithelioid cells with abundant eosinophilic cytoplasm and large vesicular nuclei arranged in sheets, nests, cords, or rudimentary, freely anastomosing vascular channels with dilated vascular spaces. Metaplastic bone formation within angiosarcoma has not been reported in the literature and is a very unusual characteristic of this case. We describe a case of soft tissue angiosarcoma with metaplastic bone formation that was originally diagnosed as extraskeletal osteosarcoma by biopsy at an outside facility. The patient was a 57-year-old man who was performing heavy labor when he noted a “pop” in his right thigh, which was followed by mild to severe, sharp, burning pain. An x-ray of the right lower extremity showed a large soft tissue mass. A biopsy was performed and showed abundant osteoid bordered by small, flat osteoblasts admixed with neoplastic cells that formed nests and irregular vascular spaces with a hobnail appearance (Figure 70). The neoplastic cells had abundant eosinophilic cytoplasm, irregular nuclear membranes, and hyperchromatic nuclei. The initial diagnosis was extraskeletal osteosarcoma. Review of the pathology at the University of California Davis Medical Center revealed that the neoplastic cells expressed vascular immunohistochemical markers CD31 and CD34. We determined the osteoblasts to be reactive in nature. A diagnosis of soft tissue angiosarcoma with abundant metaplastic bone formation was made.

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Desmoplastic Fibroma of Rib: Case Report and Literature Review

(Poster No. 34)

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Desmoplastic fibroma is a very rare tumor of the bone that accounts for 0.1% to 0.3% of all bone tumors. Rib involvement by desmoplastic fibroma is extremely rare with only 9 cases reported in the literature. We present a case of desmoplastic fibroma in a 54-year-old man who presented with a history of trauma to the chest after a surfing incident. History was also significant for rib fractures. A chest x-ray showed a 6.3 × 2.5-cm, expansile, lytic lesion of the left posterior seventh rib, which was indeterminate in nature. This lesion had a lytic/bubbly appearance. The patient underwent left seventh rib resection. A segment of rib was received, measuring 9.3 × 3.5 × 2.1 cm. The cut section showed a tan-gray lesion expanding toward the cortex (Figure 72, top left). Microscopic examination revealed benign proliferation of spindle cells separated by abundant collagen fibers (Figure, top right). The nuclei of spindle cells were uniformly hyperchromatic, varied from ovoid to elongated, and were without atypia. Nucleoli and mitotic figures were absent (Figure, bottom). Scattered blood-filled cysts were also present. Desmoplastic fibroma was first described by Jaffe et al in 1958. The maximal incidence is in the second and third decades of life, with a slight male preponderance. The tumor does not metastasize, but it is locally aggressive. Pathologic fractures occur in 10% to 15% of cases. Radiographically, a desmoplastic fibroma is a purely lytic lesion that often widens the bone. Cortical thinning and internal trabeculations are

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Melanotic Neuroectodermal Tumor of Infancy: An Unusual Location

(Poster No. 33)

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Melanotic neuroectodermal tumor of infancy is a rare benign neoplasm of neural origin that affects infants. More than 90% of these tumors involve the head and neck region. A literature search yielded only 7 of approximately 350 case reports involving the subcutaneous tissue. Although this tumor has been widely reported in the English literature, there is only a rare mention of it being present in the upper limb. A 7-month-old female infant presented with a palpable, subcutaneous mass in the upper arm. On ultrasonography, the lesion was a rounded, avascular, heterogeneously lobulated, and echoic mass located superficially to the bicep muscle in the subcutaneous plane. A frozen section of the mass revealed a morphologically biphasic tumor composed of nests of small round blue cells resembling neuroblasts and larger nests and cords of epithelioid cells with melanin pigment set in a dense fibroblastic stroma (Figure 71). Immunohistochemistry showed polyphenotypic differentiation with the small cell population strongly immunoreactive for neuroendocrine markers, synaptophysin, and neuron-specific enolase, whereas the large epithelioid cells were strongly positive for epithelial marker AE13 and melanocytic marker HMB-45. These results confirmed the diagnosis of melanotic neuroectodermal tumor of infancy. This tumor is extremely rare in subcutaneous tissue and should be kept in mind as a differential in pediatric cases involving pigmented soft tissue lesions or round blue cells on frozen section examination.
often present, giving the appearance of “soap bubbles.” The treatment options reported in the literature are wide or marginal resection of the tumor and aggressive curettage.

A Rare Case of Giant Cell Tumor in the Thumb of an 82-Year-Old Woman

(Poster No. 35)

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Giant cell tumor of the bone is a benign tumor that commonly occurs in skeletally mature women with a peak incidence between 20 and 45 years of age. Although this tumor can occur anywhere in the skeleton, it occurs most commonly in the distal femur, proximal tibia, distal radius, and sacrum. We present a case of a giant cell tumor occurring in the proximal phalanx of the thumb in an 82-year-old woman with a history of breast cancer. Imaging studies showed an expansile lytic lesion with cortical disruption of the proximal phalanx of the thumb. There was a soft tissue prominence, suggesting an associated soft tissue mass. The lesion had the typical radiographic appearance of a giant cell tumor. Given the patient’s age and history of breast cancer, the differential diagnosis consisted of a tumor metastasis followed by a giant cell tumor. An excisional biopsy was performed and demonstrated a proliferation of round to oval and elongated mononuclear cells mixed with numerous osteoclast-like giant cells. This histology was characteristic for both giant cell tumor and brown tumor. Because the patient’s calcium levels were in the reference range, a brown tumor was excluded. We found 27 articles reporting on giant cell tumors in the carpals, metacarpals, or phalanges of the hand. There were only 6 cases of giant cell tumor in the thumb: 1 in the distal phalanx, 1 in the proximal phalanx, and 4 in the first metacarpal. Of these 6 cases, only 1 patient was older than 45 years (Table).

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Pleomorphic Malignant Fibrous Histiocytoma or Undifferentiated High-Grade Pleomorphic Sarcoma of the Scrotum in a Patient Presenting With Fournier Gangrene

(Poster No. 36)

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Pleomorphic malignant fibrous histiocytoma or undifferentiated high-grade pleomorphic sarcoma, according to the latest World Health Organization classification, is a diagnosis of exclusion and is extremely rare in the adult scrotal/paratesticular region. Scrotal/paratesticular pleomorphic malignant fibrous histiocytoma usually presents clinically as painless and gradual scrotal swelling. We report a case of scrotal malignant fibrous histiocytoma in a 63-year-old man who presented with Fournier gangrene following 10 months of painful scrotal swelling and multiple procedures. The specimen of emergent debridement was submitted for pathologic and bacteriologic evaluation. Grossly, the specimen consisted of multiple fragments of tan-white soft tissue with large areas of necrosis and hemorrhage. Microscopically, the lesion had marked architectural and cytologic pleomorphism. The tumor growth pattern varied from fascicles to storiform to patternless pattern. Hemangiopericytoma-like vascular feature was focally prominent. The neoplastic cells varied from spindled to epithelioid to giant cells with nuclear pleomorphism, marked mitotic activity, and atypical mitoses. The neoplastic cells were positive for vimentin but negative for all lineage-specific markers. Fluorescence in situ hybridization showed multiple copies of chromosome 12q13 and 16p11 that were consistent with a complex aneusplid karyotype. Neither rearrangement of the CHOP gene, a hallmark of myxoid/rond cell liposarcoma, nor amplification of 12q13-15 regions, which is commonly seen in atypical lipomatous tumors/well-differentiated liposarcoma and dedifferentiated liposarcoma, were evident. Bacterial cultures of the specimen showed extensive growth of virulent polymicrobes. We diagnosed scrotal/paratesticular pleomorphic malignant fibrous histiocytoma with concurrent Fournier gangrene. Thoracic computed tomography scan showed bilateral multiple pulmonary nodules. The patient died 1 month later.

Sclerosing Rhabdomyosarcoma in an Adult Patient’s Right Knee: Case Report and Literature Review

(Poster No. 37)

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Sclerosing rhabdomyosarcoma is a variant of rhabdomyosarcoma that has so far not been accepted as an entity in the World Health Organization’s book. Thus, we report a rare case of sclerosing rhabdomyosarcoma that occurred in the right knee of a 54-year-old man. Histologically, the tumor was characterized by abundant extracellular hyaline matrix with primitive small round cells displaying various growth patterns and focally resembling osteosarcoma. Typical features of embryonal or alveolar rhabdomyosarcoma were not identified. Immunohistochemically, this case displayed positivity for desmin and myo-D1, focal positivity for myogenin, and negativity for pancytokeratin, S100 protein, CD117, CD31, and HMB-45. The karyotype for this tumor was: 3(q21.31-p14.3), 3q13.3-3q13.3, 7(q11.23-q21.11), 8q13.3, 10p15.3, 10q22.2-22.3, 15q12, 15q12, 17q12, 19q13.3. The patient underwent surgery combined with adjuvant radiation and chemotherapy. Recurrence or metastasis was not found 1 year postoperatively. We report this case of an adult patient with a right knee sclerosing rhabdomyosarcoma to increase exposure of this rare entity and to help develop a greater understanding of the diagnostic criteria and behavior of this tumor. Distinguishing sclerosing rhabdomyosarcoma from other entities is of value to both clinicians and pathologists so that they may deliver optimal care to patients. Future genetic studies of additional cases will assist in classification and prognosis of this rare soft tissue neoplasm.

Malignant Peripheral Nerve Sheath Tumor With Lymph Node Metastasis in the Absence of Widespread Disease: A Rare Finding

(Poster No. 38)

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Malignant peripheral nerve sheath tumor (MPNST) is a rare soft tissue neoplasm that accounts for fewer than 10% of all soft tissue sarcomas. This tumor can arise spontaneously in otherwise healthy individuals or in association with a neurofibroma in patients with neurofibromatosis type I. Lymph node metastasis from MPNST is rarely seen and has been reported only in the setting of widespread metastasis. Therefore, regional lymph node
diseases are not routinely performed in the management of MPNST. To our knowledge, this is the first reported case of cutaneous MPNST that is metastatic to a regional lymph node in the absence of widespread disease. We report the case of a 49-year-old man with a history of neurofibromatosis type I and a MPNST involving only the right elbow from which it was excised with clear margins. Five years later, he presented with an isolated right axillary mass that was completely excised. Microscopic examination of the tumor revealed metastatic MPNST with lymph node involvement (Figure 73). Although isolated lymph node metastasis from MPNST is rare, this case expands our knowledge of the clinical behavior of MPNST.

A CD117+ and CD34+ Sarcoma Masquerading as Gastrointestinal Stromal Tumor: Case Report, Literature Review, and Diagnostic Pitfalls of Ancillary Studies in Sarcoma
(Poster No. 39)

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The immunohistochemical hallmarks of gastrointestinal stromal tumor (GIST) are positivity for CD117 (c-kit) and CD34; however, CD117 is not specific for GIST, and the list of CD117 tumors/tissue is increasing. We report on a spindle cell sarcoma arising in the mediastinum that morphologically and immunohistochemically mimicked GIST, to illustrate the diagnostic pitfalls of ancillary studies in sarcoma. A 75-year-old woman with a history of well-differentiated liposarcoma of the pelvis/inguinal region from 5 years ago developed a 5.5-cm heterogeneous enhancing mediastinal mass by computed tomography. Fine-needle aspiration biopsy revealed spindle cells with moderate pleomorphism; they were also immunohistochemically reactive to CD117 and CD34. These findings were consistent with GIST (Figure 74, A–C). The clinical picture, however, was unusual for GIST. Mutational analysis for c-kit and platelet-derived growth factor receptor were negative, and therefore, ruled out GIST. Analysis of MDM2 copy number by fluorescence in situ hybridization revealed amplification, suggesting this neoplasm represented a dedifferentiated liposarcoma versus spindle cell sarcoma, NOS (Figure, D). It is important to realize that CD117+/CD34+ sarcoma is not diagnostic for GIST and MDM2 sarcoma is not diagnostic for liposarcoma. MDM2 is almost always positive in well-differentiated liposarcoma, which is useful in differentiating benign from atypical/well-differentiated lipomatous tumor. However, MDM2 should not be used in differentiating liposarcoma from other sarcomas. Here we report a sarcoma that is positive for CD117/CD34/MDM2 and that presents a diagnostic challenge to illustrate the importance of being aware of the potential diagnostic pitfalls of ancillary studies and to use them appropriately in conjunction with clinical content.

Osteosarcoma Presenting With Associated Osteoma Cutis: A Previously Unreported Disease Entity
(Poster No. 40)

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Osteoma cutis refers to the presence of bone within the skin without evidence of any preexisting lesion. It is usually differentiated from cutaneous ossification, which occurs secondarily to previous inflammatory, traumatic, or neoplastic processes. Patients typically present with areas of hard tissue within their skin that may cause pain and/or disfigurement. Treatment is typically simple excision. Histologically, osteoma cutis shows mature bone formation within the dermis that may extend into the subcutaneous tissues. This bone may enclose areas of mature adipose in an attempt to form a medullary cavity, but bone marrow elements are rarely identified. We present a case of a 64-year-old man who presented with a left arm nodule and no previous history of malignancy. The lesion was excised and diagnosed as osteosarcoma presenting in association with osteoma cutis. Microscopically, a benign area of mature bone formation was seen within the dermis in association with cells that showed severe pleomorphism with increased mitotic activity and malignant bone matrix formation (Figure 75). An immunohistochemical stain for Melan-A was performed with the atypical osteosarcoma cells showing lack of immunoreactivity. A thorough literature search revealed no previously identified cases of osteosarcoma developing in association with osteoma cutis. This case may have clinical impact as osteoma cutis has been previously recognized as a benign lesion with no potential for malignant transformation. This is a unique presentation that may have treatment and prognostic implications.
Utility of Fluorescence In Situ Hybridization in Subclassifying Unclassified High-Grade Sarcomas: A Study of 38 Cases Using Probes to EWSR, FOXO1, SYT, and DDIT3 Gene Break-Aparts
(Poster No. 41)
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Context: EWSR1, FOXO1A, SYT, and DDIT3 gene break-aparts are associated with chromosomal translocations and are widely used as specific molecular markers in diagnosing the Ewing tumor family, alveolar rhabdomyosarcoma, synovial sarcoma, and myxoid liposarcoma, respectively. However, the utility of these markers in evaluating unclassified high-grade sarcomas has not been studied.

Design: We identified 38 sarcomas from 2003 to 2009 that exhibited a high-grade spindle or epithelioid morphology and that remained unclassified after routine immunohistochemistry using neural, smooth muscle, skeletal muscle, melanocytic, epithelial, fibrohistiocytic, and vascular markers. All showed marked nuclear pleomorphism, including bizarre forms, increased mitotic rate, areas of necrosis, and no discernible evidence of differentiation. Thirty-three cases were resection specimens, and the remaining 5 were needle-core biopsies. Fluorescence in situ hybridization was applied to formalin-fixed, paraffin-embedded tissue using probes for EWSR1, FOXO1A, SYT, and DDIT3 gene break-aparts. In positive cases, reverse transcriptase polymerase chain reaction was performed to detect specific gene fusions associated with translocations.

Results: One of 38 cases (2.6%) was positive for the DDIT3 gene break-apart. Subsequent reverse transcriptase polymerase chain reaction showed a TLS-DDIT3 fusion, indicating a myxoid liposarcoma that had likely undergone dedifferentiation. Another case was positive for the FOXO1 gene break-apart, as occurs in rhabdomyosarcoma. However, subsequent reverse transcriptase polymerase chain reaction failed to reveal the PAX3/FOXO1 gene fusion.

Conclusions: Our findings indicate that fluorescence in situ hybridization using a variety of probes can provide precise information in a few otherwise unclassified high-grade sarcomas. The findings further affirm the utility of fluorescence in situ hybridization in formalin-fixed, paraffin-embedded tissue specimens, including small core biopsies.

Blastozyomicosis: Unusual Presentation in a 13-Year-Old Boy
(Poster No. 42)
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Blastomyozomicosis, a chronic granulomatous disease, is generally caused by inhalation of Blastomyozocites dermatitidis following exposure to contaminated soil. Primary infection often involves the lungs. Other body sites or organs can be affected by secondary dissemination or primary inoculation of skin. Inoculation following an occupational or sporting injury is therefore a risk factor. We report on a 13-year-old African American adolescent boy who first presented at an outside facility with a swollen right ring finger. He was diagnosed with bacterial osteomyelitis and was treated with intravenous and oral antibiotics. He showed no improvement after 3 weeks. Examination showed a blister. Lytic bone lesion with soft tissue swelling was seen on x-ray and magnetic resonance imaging. These findings confirmed osteomyelitis. Further questioning revealed that he had a productive cough with brownish sputum. Chest x-ray showed opacity of the upper portion of the right middle lobe with right hilar and paratracheal lymphadenopathy. No clinical evidence of immunosuppression was identified. Microscopy of finger tissue debridement revealed extensive necrosis with supplicative granulomatous inflammation and underlying bone destruction. Refractile thick-walled fungal spores, morphologically consistent with Blastomyozos, were readily detectable on hematoxylin-eosin sections. Figure 76 shows yeast forms with double-walled contour and stained with periodic acid–Schiff and Grocott-Gomori methenamine-silver in macrophages and giant cells. Culture confirmed B dermatitidis. These fungal yeast forms are detectable in tissue biopsy in 80% to 90% of culture-confirmed cases. Blastomyozomicosis can be reliably diagnosed morphologically in tissue sections, allowing for prompt treatment. The patient was discharged and prescribed itraconazole for 6 months. This case illustrates that blastomyozomicosis should be considered as a differential diagnosis of osteomyelitis not responding to antibiotic treatment.

Epstein-Barr Virus–Associated Smooth Muscle Tumor of the Liver in a Patient With Human Immunodeficiency Virus
(Poster No. 43)
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Epstein-Barr virus (EBV) infection has been associated with numerous human neoplasms, including Hodgkin and non-Hodgkin lymphomas, nasopharyngeal carcinomas, and gastric carcinomas. More recently, it has been associated with smooth muscle neoplasms in patients with acquired immunodeficiencies, including those with human immunodeficiency virus infection and those receiving immunosuppressive therapies. The rarity and relative novelty of EBV-associated smooth muscle tumors can present a diagnostic quandary for the practicing pathologist because histologically similar lesions, such as angiomylipomas, leiomyosarcomas, and gastrointestinal stromal tumors, are exceedingly more common. We present the case of a 38-year-old African American man with long-standing, poorly controlled human immunodeficiency virus infection who presented with weight loss (20 kg). On workup, he was found to have a 1.8-cm liver mass by computed tomography. Core biopsy of the lesion revealed a cellular proliferation of fairly uniform spindled cells displaying a storiform growth pattern (Figure 77). Mitoses were rare, but Ki-67 immunohistochemical staining showed a 10% proliferative index. Tumor cells were immunoreactive for smooth muscle actin.
and muscle-specific actin (HHF35). They were focally positive for desmin and negative for EBV late membrane protein, CD117, S100, CD34, and HMB-45. Stains for microorganisms, including mycobacteria, were negative. Two years later, the patient developed additional hepatic lesions and an increase in the size of the original one, necessitating another core biopsy that revealed a morphologically and immunohistochemically similar proliferation. In situ hybridization for EBV-encoded RNA on this specimen was positive, supporting the diagnosis of EBV-related smooth muscle tumor. The patient is currently stable on targeted chemotherapy.

Presence of Extravasated Red Blood Cells in Low-Grade Sarcomas Versus Low-Grade Fibroblastic Proliferations

(Poster No. 44)

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Context: Low-grade fibroblastic proliferations are diagnostically challenging. These lesions must be differentiated with confidence from low-grade sarcomas. However, both sets of lesions can appear histologically similar, and immunohistochemistry may not be helpful in making a definitive diagnosis. The presence of extravasated red blood cells (RBCs) in low-grade fibroblastic proliferations versus low-grade sarcomas has not been previously reported.

Design: We evaluated the following low-grade sarcomas for the presence of extravasated RBCs: synovial sarcoma, low-grade fibromyxoid sarcoma, malignant peripheral nerve sheath tumors, low-grade leiomyosarcomas, fibrosarcomas, myofibroblastic sarcomas, dermatofibrosarcoma protuberans, and spindle cell rhabdomyosarcomas. We also evaluated the following pseudosarcomatous lesions for the presence of extravasated RBCs: nodular fasciitis, ischemic fasciitis, hypertrophic scars, desmoid and plantar fibromatosis, and myositis ossificans. The sarcomas evaluated had no previous treatment. Presence of extravasated RBCs was defined as RBCs not within blood vessels and found in greater than 5 consecutive high-power fields in the fibrous portions of the lesion.

Results: A total of 65 cases of low-grade sarcomas and 27 cases of pseudosarcomatous lesions were evaluated. Only 12.3% of low-grade sarcomas (bolded in Table) had extravasated RBCs, while 85.2% of pseudosarcomas had extravasated RBCs (Table).

Conclusions: The presence of extravasated RBCS is almost ubiquitous in pseudosarcomatous lesions. Although we found a few cases of low-grade sarcoma with extravasated RBCs, the percentage was low. Our findings support the utility of evaluating low-grade sarcomas and pseudosarcomatous lesions for extravasated RBCs. In the absence of extravasated RBCs, a diagnosis of pseudosarcomatous lesion (with the exception of fibromatosis) is unlikely.

### Low-Grade Sarcomas and Pseudosarcomatous Lesions (Sarcomas in Bold)

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Total Cases</th>
<th>No. (%) of Cases With Extravasated RBCs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synovial sarcoma</td>
<td>22</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Low-grade fibromyxoid sarcoma</td>
<td>12</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>Malignant peripheral nerve sheath tumor</td>
<td>10</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Low-grade leiomyosarcoma</td>
<td>3</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Myofibroblastic sarcoma</td>
<td>3</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Fibrosarcoma</td>
<td>3</td>
<td>1 (33.3)</td>
</tr>
<tr>
<td>Dermatofibrosarcoma</td>
<td>3</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Protuberans</td>
<td>10</td>
<td>4 (40)</td>
</tr>
<tr>
<td>Spindle cell rhabdomyosarcoma</td>
<td>2</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Nodular fasciitis</td>
<td>7</td>
<td>7 (100)</td>
</tr>
<tr>
<td>Ischemic fasciitis</td>
<td>2</td>
<td>2 (100)</td>
</tr>
<tr>
<td>Hypertrophic scar</td>
<td>3</td>
<td>3 (100)</td>
</tr>
<tr>
<td>Fibromatosi (desmoid and plantar)</td>
<td>12</td>
<td>8 (66.7)</td>
</tr>
<tr>
<td>Myositis ossificans</td>
<td>3</td>
<td>3 (100)</td>
</tr>
</tbody>
</table>

Abbreviation: RBCs, red blood cells.

Ovarian Teratoma With Thoracic Nodal Gliomatosis: Clinicopathologic Study of 2 Cases

(Poster No. 45)

Yvonne S. Noronha, MD (lyrononha@gmail.com); Brian Hutchins, MD; Shobha Castelino-Prabhu, MD; Craig Zuppan, MD. Department of Pathology, Loma Linda University Medical Center, Loma Linda, California.

Nodal gliomatosis is a very rare complication of ovarian teratomas, and to our knowledge, it has only been described involving intra-abdominal lymph nodes. We present clinical and histopathologic features of 2 patients with ovarian teratoma and thoracic nodal gliomatosis. Two adolescent girls, ages 10 and 13 years, presented with large ovarian teratomas. Serum α-fetoprotein levels were moderately elevated. In the first case, surgical resection revealed a 17-cm, grade 1, immature ovarian teratoma with an intact capsule but associated mature glial implants on the ovarian surface and mature gliomatosis peritonei. An intrathoracic juxtapdiaphragmatic mass was also present, and resection revealed it to be consistent with a large lymph node nearly completely replaced by mature glial tissue. No adjuvant therapy was given, and the child was tumor-free at last follow-up. In the second case, a 22-cm, grade 2, immature teratoma of the ovary was resected with associated mature gliomatosis peritonei. Mature glial tissue also focally penetrated the capsule of the ovary. An associated 8.5-cm, cystic, anterior mediastinal mass and smaller pulmonary nodule were also resected, both consisting of mature glial tissue that replaced lymph node capsule. No adjuvant therapy was given initially, but she was later given chemotheraphy following radiographic diagnosis of local pelvic recurrence 6 months after initial resection. She was disease-free 2.5 years after presentation. These cases indicate that mature nodal gliomatosis is a benign process. Therefore, the presence of thoracic nodal gliomatosis should not alter staging or treatment decisions in patients with ovarian teratoma.

Collision Tumor of Malignant Struma Ovarii and Lymphoplasmacytic Lymphoma in an Ovary: Case Report and Review of the Literature

(Poster No. 46)

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The coexistence of malignant struma ovarii and lymphoma is extremely rare, with only 1 case cited in the literature. Struma ovarii is predominantly an expression of thyroid tissue in a monodermoid teratoma of the ovary. Malignant transformation from struma ovarii has been reported, the most common transformation being to papillary thyroid carcinoma. However, to our knowledge, collision tumor of malignant struma ovarii and lymphoplasmacytic lymphoma in the ovary has not been previously reported. A 59-year-old woman presented with abdominal bloating and unexplained weight loss. Examination revealed a palpable left adnexal mass and bilateral inguinal lymphadenopathy. A preoperative computed tomography scan revealed retroperitoneal lymphadenopathy and a 7-cm, left adnexal, complex mass. Gross examination of the left adnexal mass revealed a capsulated but distorted multiloculated cyst filled with brown gelatinous materials. Histologic examination confirmed a 6.5-cm papillary microcarcinoma arising in the struma ovarii and subjacent, dense, monotonous small-cell infiltrate with plasmacytoid appearance. There was extensive involvement in the myometrium and cervix. The left pelvic lymph node was also effaced by similar lymphoid infiltrate, including a well-preserved sinus that was distended owing to hemosiderin-laden macrophages. Flow cytometry on the lymph node revealed x-restricted CD20 B cells and no expression of CD5 or CD10. Immunohistochemical stain was negative for cyclin D1. In summary, synchronous malignancies can be a diagnostic challenge and require careful interpretation from an astute pathologist. Our case represents a treatment challenge with competing risks, one of which is delay in the commencement of treatment for lymphoplasmacytic lymphoma.

Nicotinamide Phosphoribosyltransferase Expression Is Increased in Malignant Ovarian Tumors

(Poster No. 47)

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Context: Nicotinamide phosphoribosyltransferase (Nampt) catalyzes the rate-limiting step of NAD⁺ synthesis. NAD⁺ is required for cell survival and division and for DNA replication. There are few data on Nampt activity in human malignancy, with only 1 study showing increased Nampt mRNA expression in human colon cancer compared to nearby benign tissue. We examined Nampt expression in benign and malignant ovarian tissues.

Design: We used tissue microarray to analyze Nampt expression in benign ovarian tissue and several benign and malignant ovarian tumors. Nampt protein expression was determined in ovarian tissue from 165 different patient samples using the AccuMax Tissue Microarray (Hsi-Chih City, Taiwan) and Protein Biotechnologies (San Diego, California). The array was immunonstained with Nampt murine anti–pan-visfatin monoclonal antibody (AdipoGen, Incheon, South Korea, at 1:1000 dilution), using the avidin-biotin-peroxidase method. A semiquantitative measure of Nampt protein expression was determined as the product of immunostain intensity and percentage of cells stained, with both scored on a 0 to 3 scale, with 3 being maximal.

Results: Nampt expression was very low in benign ovarian Stromal tissue, ovarian fibromas, mucinous cystadenomas, dysgerminomas, yolk sac tumors, and mucinous borderline tumors. Brenner tumors, transitional cell tumors, and serous adenocarcinomas had moderate expression. Clear cell carcinomas, mucinous adenocarcinomas, and endometrioid carcinomas showed the highest staining.

Conclusions: Nampt expression is increased in ovarian cancer, with higher-grade malignancies showing greater Nampt staining. Thus, Nampt expression is likely an important aspect of malignant progression and a paracrine role of S100A4 in triggering a prometastatic cascade in ovarian cancer cells.
Progesterone Receptors A and B in Grade 1 Endometrial Adenocarcinoma and Complex Atypical Hyperplasia Predict Response to Progestin Therapy
(Poster No. 51)

Kristine Penner, MD, MPH; Madhuri Wadehra, PhD; Angela Steinhardt, MD; Claire Hogue; Jonathan Braun, MD, PhD; Oliver Dorigo, MD, PhD. Departments of Obstetrics and Gynecology and Pathology, UCLA Medical Center, Los Angeles, California.

Context: Ten percent of grade 1 endometrial adenocarcinomas (G1EACs) and complex atypical hyperplasias (CAHs) occur in patients younger than age 40. Progestin therapy is an option to preserve fertility, but no biologic markers that predict response are known. We investigated whether progesterone receptor isoforms A (PRA) and B (PRB) at initial endometrial biopsy or first follow-up biopsy postprogestin therapy might predict treatment response.

Design: We retrospectively identified premenopausal patients with CAH or G1EAC who had undergone progestin therapy for more than 8 weeks and for whom there was outcome data and available specimens pretreatment and within the first 9 months posttreatment. Immunohistochemical staining for PRA and PRB was performed on all tissues, tumors, and stroma. Results were evaluated using a histologic scoring system.

Results: We identified 38 subjects (median age, 36 years; age range, 23 to 48 years) who had an initial pathology of G1EAC (55%) or CAH (65%). Of these subjects, 50% had documented resolution to normal histopathology (median time, 7 months). Levels of both PRA and PRB were greater pretreatment versus posttreatment (P < .05); pretreatment expression of both isoforms was greater in tumor versus stroma (P < .01); at first follow-up, there was no difference in expression between tumor tissue and stroma for either isoform; and a higher proportion of PRA (>0.6) to total PR in the initial specimen correlated with a higher likelihood of disease resolution (P = .04).

Conclusions: The ratio of PRA and PRB for young patients with CAH or G1EAC at initial diagnostic biopsy may be a useful guide to individual likelihood of resolution of G1EAC or CAH with progestin therapy.

Melanoma With An Unusual Immunophenotypic Profile
(Poster No. 52)

Xiu Yang, MD, PhD; Emily A. O’Rourke, MD; Claire Hogue; Jonathan Braun, MD, PhD; Oliver Dorigo, MD, PhD. Departments of Obstetrics and Gynecology and Pathology, UCLA Medical Center, Los Angeles, California.

The diagnosis of malignant melanoma can be challenging given the wide variation in morphologic features and immunohistochemical stains that are often used to confirm the diagnosis. Useful immunohistochemical markers include the highly sensitive S100 and more specific markers, including HMB-45, Melan-A, tyrosinase, and microphthalmia-associated transcription factor. We report a case of amelanotic melanoma with unusual immunophenotypic profile. A 43-year-old African American woman complained of having a vaginal mass for 1 month. Histopathologic analysis on an excisional biopsy demonstrated that the mass was composed of neoplastic cells with extensive necrosis. The neoplastic cells were medium-sized to large with abundant eosinophilic cytoplasm and prominent eosinophilic nucleoli. No melanocytic pigments were identified. Immunohistochemistry showed negativity for S100, HMB-45, vimentin, actin, and desmin and showed positivity for cytoplasmic placental alkaline phosphatase and Melan-A. A diagnosis of amelanotic melanoma was rendered. Five months later, a recurrent exophytic mass with infiltration to adjacent vulva was present. A radical vulvectomy was performed, and the pathologic analysis revealed morphologic and immunohistochemical profiles similar to those from the previous biopsy specimen. This case is rare in the concomitant loss of S100, HMB-45, and vimentin and the single expression of Melan-A, albeit Melan-A is more sensitive for amelanotic melanoma. Furthermore, to our knowledge, this is the first reported melanoma case in which a strong cytoplasmic positivity for placental alkaline phosphatase in both primary and recurrent lesions was observed. Awareness of these unusual findings will be helpful in the diagnosis of melanoma with unusual immunophenotypic profiles.

Personalized Treatment of Ovarian Cancer and the Effect of Chemotherapy: A Pilot Study
(Poster No. 53)

Emily A. O’Rourke, MD; Chelsea Hayes, MD; Elvio G. Silva, MD. Department of Pathology and Laboratory Medicine, Cedars-Sinai Medical Center, Los Angeles, California.

Context: When ovarian carcinomas recur after chemotherapy, their hormone receptor status is typically not examined. Instead, the receptor status of the original tumor is relied upon to help direct treatment. Using 3 candidate markers, this study examined the potential need for immunohistochemical evaluation of the metastatic tumor when prescribing targeted treatment for ovarian carcinomas recurring after chemotherapy.

Design: We examined material from 10 cases of primary ovarian carcinoma and corresponding tumor recurrence after chemotherapy for estrogen receptor, progesterone receptor, and epidermal growth factor receptor status by immunohistochemistry. Prechemotherapy and postchemotherapy receptor profiles for each tumor were compared for changes in intensity and quantity of staining. A personalized treatment plan was developed.

<table>
<thead>
<tr>
<th>Case</th>
<th>Tumor Classification</th>
<th>Change in ER</th>
<th>Change in PR</th>
<th>Change in EGFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Papillary serous carcinoma</td>
<td>Increased intensity and quantity</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>Papillary serous carcinoma</td>
<td>Decreased intensity and quantity</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>Endometrioid carcinoma</td>
<td>Increased intensity</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>Müllerian carcinoma</td>
<td>Increased intensity</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>Papillary serous carcinoma</td>
<td>None</td>
<td>None</td>
<td>Increased intensity and quantity</td>
</tr>
<tr>
<td>6</td>
<td>Papillary serous carcinoma</td>
<td>Increased intensity and quantity</td>
<td>Decreased intensity</td>
<td>None</td>
</tr>
<tr>
<td>7</td>
<td>Papillary serous carcinoma</td>
<td>None</td>
<td>None</td>
<td>Increased intensity and quantity</td>
</tr>
<tr>
<td>8</td>
<td>Mixed serous, endometrioid, clear cell carcinoma</td>
<td>None</td>
<td>None</td>
<td>Increased intensity</td>
</tr>
<tr>
<td>9</td>
<td>Papillary serous carcinoma</td>
<td>Decreased intensity and quantity</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>10</td>
<td>Papillary serous carcinoma</td>
<td>None</td>
<td>Decreased intensity and quantity</td>
<td>None</td>
</tr>
</tbody>
</table>

Abbreviations: ER, estrogen receptor; EGFR, epidermal growth factor receptor; PR, progesterone receptor.
difference between prechemotherapy tumor and postchemotherapy tumor was considered present if a change in the percentage of stained cells was greater than 20% or if the intensity of the staining changed by 2 or more points.

Results: Nine of 10 cases demonstrated a change in receptor status in prechemotherapy versus postchemotherapy tumors. The most commonly observed variation was a change in estrogen receptor status, as seen in 5 cases, with no predominance of increased or decreased intensity or quantity of staining. Three cases showed a change in progesterone receptor status, and 4 cases showed variation in epithelial growth factor receptor status (Table).

Conclusions: The variable receptor status observed in ovarian tumors before and after chemotherapy demonstrates the plasticity of tumor antigen expression. The data from this study confirm the need for additional investigation and the importance of obtaining recurrent tumor samples to determine the appropriateness of targeted therapy.

The Expression Patterns of Connexins 43 and 26 in Benign and Dysplastic Ectocervical Epithelium

(Poster No. 54)

Ian S. Hagemann, MD, PhD (ian.hagemann@gmail.com); Teresa L. Pasha, MT; Shelley A. Roberts, MS; Paul J. Zhang, MD. Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia.

Context: Gap junction intercellular communication mediated by connexins (Cxks) permits cell-to-cell communication and has been proposed to have cell signaling and tumor suppressor functions. There are conflicting published data on the expression of Cxks in cervical squamous epithelium, including claims that connexins are absent in dysplasia. We performed a semiquantitative immunohistochemical survey of 2 important connexins (Cx43 and 26) in a series of cervical specimens.

Design: Cervical resections were selected from the surgical pathology archives at our institution and were reviewed to confirm the diagnoses. Sections were stained with monoclonal anti-Cx43 or polyclonal anti-Cx26. Immunoreactivity was assessed semiquantitatively by light microscopy.

Results: The tested samples included 12 benign ectocervices, 29 low-grade squamous intraepithelial lesions (human papillomavirus change or CIN, grade 1), and 10 high-grade squamous intraepithelial lesions (CIN, grades 2-3). In benign ectocervix, there was weak membranous Cx43 staining in the parabasal and intermediate layers (10 of 12, 83%). Cx43 was often increased and restricted to the intermediate layer in low-grade squamous intraepithelial lesions (18 of 29, 62%) and was more prominent in superficial layers in high-grade squamous intraepithelial lesions (9 of 10, 90%) ("reverse polarity" of expression). For Cx26, benign cases showed strong membranous basal staining and weak granular staining of the intermediate layer (10 of 12, 83%). The distinct basal pattern was weakened in 26 of 29 low-grade squamous intraepithelial lesions (90%), with more obvious changes in mildly dysplastic cases (n = 8). All 10 high-grade squamous intraepithelial lesions lost the basal Cx26 pattern. No Cx43 or Cx26 reactivity was seen in normal cervical tissue.

Conclusions: The expression pattern of both Cxks is altered in human papillomavirus-infected or dysplastic epithelium. The disrupted Cx26 basal pattern might be useful for differentiating early dysplastic lesions from benign ectocervical epithelium.

Fetal and Placental Findings in Intrauterine Candida lusitaniae Infection Following In Vitro Fertilization and Embryo Transfer

(Poster No. 55)

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Intrauterine infections with non-albicans Candida species are rare. However, 5 cases of intrauterine Candida glabrata infection associated with in vitro fertilization and embryo transfer have been reported. We report the first case of Candida lusitaniae intrauterine infection associated with in vitro fertilization and embryo transfer and identified in the placenta. A 33-year-old healthy woman who was pregnant with triplets by in vitro fertilization and embryo transfer presented with preterm premature rupture of membranes at 16 weeks' gestation. She subse-
Expression of Glypican-3 in Placental Site Trophoblastic Tumor
(Poster No. 57)

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Context: Glypican-3 (GPC3) is a membrane-bound heparan sulfate proteoglycan that functions in embryonic cell growth and differentiation and is highly expressed in the placenta. Although GPC3 expression has been studied in nonneoplastic placental tissue, its presence in gestational trophoblastic diseases has not been explored. We investigated the immunohistochemical expression of GPC3 in placental site trophoblastic tumor (PSTT), a gestational trophoblastic neoplasm that may be morphologically confused with nonneoplastic tumors, to assess its utility as a diagnostic marker.

Design: Sections from 15 cases of PSTT and samples from endometrial adenocarcinoma, leiomyosarcoma, and leiomyoma were stained with GPC3. Cytoplasmic and membranous immunoreactivity was semiquantitatively evaluated as negative (0, <5% of cells stained), focally positive (1+, 5% to 10% of cells stained), positive (2+, 11% to 50% of cells stained), or diffusely positive (3+, >50% of cells stained). Staining intensity for each subtype was graded from 0 to 3 and a mean intensity was calculated.

Results: Twelve of 15 PSTT samples (80%) were immunoreactive for GPC3 (0, 20%; 1+, 20%; 2+, 40%; and 3+, 20%). Stronger, predominately cytoplasmic staining with focal membranous expression was seen in larger multinucleated and mononucleated cells. Smaller mononucleated cells demonstrated weak, muddy, cytoplasmic staining. Endometrial adenocarcinoma (n = 11), leiomyosarcoma (n = 1), leiomyoma (n = 1), and nonneoplastic myometrium, endometrium, and cervix were negative for GPC3.

Conclusions: GPC3 was expressed in most PSTT cases. Therefore, GPC3 may be a useful immunohistochemical marker in differentiating PSTT from nonneoplastic tumors. Further studies must be done to investigate the expression of GPC3 in other gestational trophoblastic tumors.

Keywords: Glypican-3, Placental Site Trophoblastic Tumor

Polymorphic Deletion Probe Fluorescence In Situ Hybridization: Novel Molecular Diagnostic Technique in the Evaluation of Hydatidiform Moles
(Poster No. 58)

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Context: Subclassification of hydatidiform moles is challenging, often requiring ancillary studies. Because products of conception contain maternal and villous tissue, genetic polymorphisms can be used to discern maternal and paternal chromosomal contribution and aid in diagnosing moles. Polymorphic deletion probes (PDPs), recently developed fluorescence in situ hybridization (FISH) probes based on copy number variants, are highly polymorphic and allow in situ determination of genetic identity. Using 3 PDPS from chromosomes 2p, 4q, and 8p, we compared maternal and villous genotypes to subclassify moles.

Design: PDP FISH was performed on 13 nonmolar abortions, 13 complete moles, and 13 partial moles. PDP FISH and p57 immunofluorescence were performed on a suspected partial mole.

Results: PDP FISH was successful in all cases with genotypes identified for maternal and villous tissue. A definitive diagnosis of complete mole was permitted in 5 of 13 cases for which maternal and villous genotypes were mutually exclusive (Figure 80). A low rate of homozygosity in nonmolar portions allowed for a test specificity of 98.4% in diagnosing complete moles in cases in which villous genotypes were homozygous for all probes. Triploidy was shown in all partial moles, including 6 of 13 cases in which PDP FISH confirmed diandric triploidy. In the suspected partial mole, 8p PDP FISH and immunofluorescence showed p57 expression in heterozygous cytotrophoblasts and no expression in homozygous villous stromal cells, confirming placentorial mosaicism.

Conclusions: PDP FISH is an accurate, cost-effective, and practical molecular ancillary technique for classifying moles and evaluating unusual products of conception, including mosaic and chimeric conceptions.

Keywords: Hydatidiform Mole, Polymorphic Deletion Probe Fluorescence In Situ Hybridization

Constitutive pSTAT-3 Activation and Associated FoxP3 Cell Infiltration in Cervical High-Grade Squamous Intraepithelial Lesions: Pathogenetic and Therapeutic Implications
(Poster No. 59)

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Context: The forkhead box P3 (FoxP3) gene is involved in the regulation of the immune system by upregulating T-regulatory cells (Tregs). Tregs block the host’s immune response against malignant tumors and are important regulators of tumor immunity. In this study, we investigated the association between pSTAT-3 and Tregs (FoxP3) activation in high-grade squamous intraepithelial lesions (HGSILs) and cervical cancer.

Design: A tissue microarray composed of benign cervix, HGSIL, and invasive squamous carcinoma was assembled. Immunohistochemical probes using monoclonal antibodies to CD8, Fox P3, and pSTAT-3 were applied. Results for the CD8 and Fox P3 were recorded, and the ratio of CD8+ to Fox P3 was documented by counting individual positive cells per high-power field (>40). Results for pSTAT-3 were graded according to intensity of staining (scale of 0 to 3+) and percentage of cells (0% to 100%) stained. A composite score (0 to 3, the lowest number being little or no staining) was obtained by taking both variables into account.

Results: See Table.

Conclusions: Our results show that there is activation of pSTAT-3 in HGSIL and invasive squamous cell carcinoma of the cervix, leading to activation of FoxP3 and Tregs through IL-23. Tregs produce IL-10, down-regulating cytotoxic CD8+ cells and upregulating the E7 oncoprotein of human papillomavirus. This leads to the progression of HGSIL into frank invasive carcinoma. The receptor tyrosine kinase inhibitor, sunitinib, can inhibit both pSTAT-3 and Tregs, potentially halting the progression from HGSIL to invasive squamous carcinoma of the cervix.

<table>
<thead>
<tr>
<th>Staining Results</th>
<th>Percentage (n)</th>
<th>pSTAT-3 Score</th>
<th>CD8: Fox P3</th>
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<tbody>
<tr>
<td>High-grade squamous intraepithelial lesions</td>
<td>58 (7)</td>
<td>3</td>
<td>1.3</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>72 (8)</td>
<td>3</td>
<td>1.7</td>
</tr>
<tr>
<td>Benign cervical tissue</td>
<td>28 (3)</td>
<td>2</td>
<td>No Fox P3 staining</td>
</tr>
</tbody>
</table>

Testicular Hamartomata in Complete Androgen Insensitivity Syndrome
(Poster No. 60)

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Complete androgen insensitivity syndrome (CAIS) is a rare X-linked disorder characterized by 46,XY karyotype. Individuals with CAIS ordinarily have normal breast development, pubertal feminization, bilateral testes, female external genitalia, blind-ended vagina, and no müllerian derivatives. Benign tumors such as hamartoma, Sertoli cell adenoma, and Leydig cell tumor in association with CAIS. A 21-year-old woman presented with primary amenorrhea since 16 years of age. The physical examination showed normal breast development, pubic hair, and external genitalia. The pelvic examination revealed a blind-ended vagina and the absence of cervix. Pelvic ultrasonography and computed tomography studies showed the absence of adnexa and müllerian structures. Two testicular masses were seen in the areas where ovaries are expected. The cytogenetic analysis revealed a 46,XY karyotype. Laboratory studies demonstrated low estradiol and high testosterone levels. Laparoscopic bilateral gonadectomy was performed. The resected bilateral testes showed multiple sharply demarcated, firm, yellow-white nodules (0.3–1.2 cm) located beneath the tunica albuginea. Microscopic examination showed these nodules to be composed of numerous tightly packed immature tubules filled with Sertoli cells. Scattered or solid sheets of Leydig cells were present among the immature tubules. These nodules were separated from the surrounding parenchyma by thin fibrovascular capsules. Testicular hamartoma is an uncommon, testicular, benign lesion, particularly seen in patients with CAIS. It has no malignant potential. The differential diagnosis includes Sertoli cell adenoma and malignant germ cell tumor or malignant sex-cord tumor. CAIS should be considered in cases of primary amenorrhea. Gonadectomy eliminates the risk of gonadal malignancy.

**Expression of Cell Cycle Regulatory Proteins in High-Grade Endometrioid and Serous Endometrial Adenocarcinomas**  
(Poster No. 61)

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**Context:** Alterations of the p16-Rb cell cycle regulatory pathway play an important role in the pathogenesis of many cancer types, including endometrial adenocarcinomas. p16 is overexpressed in most serous carcinomas (SCs), and it may be a helpful marker in differentiating them from high-grade endometrioid adenocarcinomas (HGEmCas). The aim of our study was to further analyze and compare the expression patterns of cell cycle markers in these 2 distinct subtypes of endometrial tumors.

**Design:** We retrieved 20 cases of endometrial adenocarcinoma (10 HGEmCas and 10 SCs) from our departmental archives. All available slides were reviewed, and immunohistochemical stains were performed. Stains included Rb as follows: 3 different antibodies marking the total amount (Rb) and the active (actRb) and inactive (inactRb) forms of retinoblastoma protein. Other stains included p16, cyclin D1, p53, and p14. Normal endometria were used as controls.

**Results:** All cases showed intense, diffuse staining for p14 and Rb. However, only 2 SCs reacted strongly with actRb and 3 SCs with inactRb. p16 stained all but 1 SC and 7 HGEmCas. Cyclin D1 was negative or only weakly/focally positive in SCs. Two of the HGEmCas had strong positive immunoreaction with cyclin D1. Among SCs, 5 cases were p53 positive, and 2 cases showed total absence of staining, suggesting null mutation. Only 2 HGEmCas stained intensely with p53.

**Conclusions:** The expression pattern of cell cycle regulatory proteins is different between SC and HGEmCa. Expression of p16 and cyclin D1 was negative or only weakly/focally positive in SCs. Two of the HGEmCas had strong positive immunoreaction with cyclin D1. Among SCs, 5 cases were p53 positive, and 2 cases showed total absence of staining, suggesting null mutation. Only 2 HGEmCas stained intensely with p53.

**Anaplastic Spindle Cell Carcinoma Arising in a Background of Ovarian Mucinous Cystic Tumor: Case Report and Review of the Literature**  
(Poster No. 62)

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Anaplastic carcinoma of spindle cell type is an exceedingly rare and malignant ovarian neoplasm. This neoplasm was first thought to carry an invariably unfavorable prognosis; however, recent data indicate that this does not necessarily apply to stage Ia tumors. The distinction of anaplastic carcinoma from true sarcomas is important because the latter tumors have a worse prognosis in comparison to the quite favorable behavior of anaplastic carcinoma. To date, there have been fewer than 10 cases of anaplastic spindle cell carcinoma reported in the medical literature. Furthermore, our case is the first in which this tumor has been described as malignant spindle cells merging with epithelioid-appearing carcinoma cells and subsequently merging, to a limited degree, with conventional high-grade adenocarcinoma (Figure 81) in a 40-year-old woman. The differential diagnosis of spindle cell proliferation in the ovary will be discussed, and a distinction will be made using a panel of immunohistochemical stains. This report demonstrates that malignant spindle cell proliferation admixed with conventional adenocarcinoma does not necessarily imply a diagnosis of carcinosarcoma. However, when anaplastic carcinoma is admixed with carcinoma cells, a careful sampling is necessary to accurately distinguish anaplastic carcinoma and carcinosarcoma. This distinction is critical for planning further management and ultimately to predict prognosis.
Immunohistochemical staining showed positivity for pancytokeratin, inhibin, and synaptophysin focally. The lesion was thus consistent with a poorly differentiated Sertoli-Leydig cell tumor with heterologous elements. One month after her unilateral salpingo-oophorectomy, the patient is without complaints and is progressing well. There is currently no evidence of disease recurrence. Sertoli-Leydig cell tumors represent only 0.1% to 0.5% of ovarian neoplasms. They are predominantly benign and unilateral. Patients may experience virilizing symptoms secondary to tumor androgen production. Prognosis is related most strongly to differentiation, with better differentiation having less risk of malignant behavior.

The Prognostic Value of MicroRNAs in Low-Risk Endometrial Carcinomas

(Poster No. 64)

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Context: MicroRNAs (miRNAs, miRs) are small noncoding RNAs that negatively regulate gene expression at the posttranscriptional level. MicroRNAs are dysregulated in cancer and may play essential roles in tumorigenesis through regulation of cell proliferation, apoptosis, invasion, metastasis, and angiogenesis. Additionally, miRNAs have been shown to have prognostic and diagnostic value in certain types of cancer. Endometrial carcinoma is clinically classified as low, intermediate, or high risk, based on pathologic staging criteria. Low-risk endometrial carcinomas are treated with surgery, and adjuvant treatments are generally not offered since the risk of recurrence is considered low. We aimed to determine whether miRNA expression differs among low-risk tumors that have recurred compared to those that have not.

Design: We compared the expression profiles of 723 miRNAs from low-risk endometrial carcinomas with recurrence (n = 5) and without recurrence (n = 3; mean follow-up interval was 63 months), using Agilent Human miRNA arrays (Agilent Technologies, Santa Clara, California) following RNA extraction from formalin-fixed, paraffin-embedded tissues. Differentially expressed miRNAs were identified using GeneSpring GX software (version 11.0) (Agilent Technologies).

Results: We identified 2 miRNAs that could distinguish between the tumors with recurrence and those without recurrence (P < .05). MicroRNA-429 and miR-200a showed an average 5.2-fold and 4.0-fold increase in the tumors with recurrence and controls, respectively.

Conclusions: These preliminary results show that miRNA expression differs among low-risk endometrial carcinomas and can be used to distinguish an aggressive subgroup. This information, once validated, could be used to identify patients who are at increased risk of recurrence and would therefore benefit from adjuvant treatment.

Fine-Needle Aspiration Biopsy of an Osteoclast-Rich Undifferentiated Urothelial Carcinoma: A Cytology Case Report

(Poster No. 65)

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We report the first cytology case of metastatic osteoclast-rich undifferentiated carcinoma of the urinary bladder (ORUCUB) that was diagnosed by fine-needle aspiration biopsy. ORUCUB is an extremely rare variant of high-grade urothelial carcinoma that has aggressive behavior and poor outcome. Recognizing its cytomorphic features can be helpful in making an accurate diagnosis. The differential diagnoses included giant cell carcinoma, foreign body/granulomatous reaction, trophoblastic carcinoma, sarcomatoid carcinoma, and giant cell tumor of bone. A 74-year-old man with a history of high-grade urothelial carcinoma and prostatic cancer came to the genitourinary clinic complaining of a painful left groin lump for 2 weeks. Fine-needle aspiration biopsy of the groin mass was performed by the cytopathologist. The histology of a prior surgical specimen was reviewed. The literature was also reviewed. The specimen was hypercellular and consisted of 2 distinct cell populations. They were predominantly smaller, highly pleomorphic, dyscohesive, spindle, ovoid to polygonal mononuclear cells in the background of abundant, large, benign-appearing, osteoclast-like multinucleated giant cells (Figure 83). The mononuclear cells were malignant and immunohistochemically positive for vimentin, cytokeratin, Ki-67, and p53. Osteoclast-like multinucleated giant cells were scattered and morphologically similar to osteoclasts, which were positive for CD68 and vimentin. The 2 specimens resulted in similar histology findings. A final diagnosis of metastatic ORUCUB was rendered. ORUCUB is a rare but specific diagnosis that can be recognized by fine-needle aspiration cytology. This study demonstrates the cytologic, histologic, and immunohistochemical features of ORUCUB.

Immunolocalization of the von Hippel-Lindau Gene Product in Cell Block Preparations Is a Useful Adjunct in Distinguishing Salivary Oncocytoma From Acinic Cell Carcinoma

(Poster No. 66)

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Context: Cytologic distinction of oncocytic neoplasm from acinic cell carcinoma can be diagnostically challenging. Loss of or reduced expression of von Hippel-Lindau gene product (pVHL) has been demonstrated in malignant salivary gland epithelial neoplasms in a small number of cases in our previous study. In this study, we further investigated the utility of pVHL immunostaining on cell blocks in distinguishing true oncocytic neoplasm from acinic cell carcinoma.

Design: Immunostaining for pVHL was performed on 22 cell blocks in 3 diagnostic groups: 9 oncocytes (G1); 6 oncocytic neoplasms, cannot exclude acinic cell carcinoma (G2); and 7 acinic cell carcinomas (G3). Tissue follow-up was available in all cases and confirmed the diagnoses in G1 and G2; immunostain for pVHL was also performed on 6 oncocytes and 3 acinic cell carcinomas.

Results: In group G1, pVHL was positive in 7 and negative in 2 cases. In both of the negative cases, cell blocks were hypocellular. In group G2, 5 of 6 cases were negative and 1 case was positive for pVHL. Subsequent biopsies in these cases revealed acinic cell carcinoma in 5 cases and oncocytoma in 1 case. In group G3, all 7 cases were negative for pVHL. All 6 cases of oncocytoma on surgical specimens were positive for pVHL, including the 2 cases that were negative for pVHL on cell blocks. The 3 surgical acinic cell carcinoma specimens were negative for pVHL.

Conclusions: Our findings suggest that pVHL is a useful marker in distinguishing salivary acinic cell carcinoma from oncocytoma on fine-needle aspiration specimens in cell blocks.

Adenocarcinoma In Situ Performance in Liquid-Based and Conventional Preparations

(Poster No. 67)

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tal, Houston, Texas; 5College of American Pathologists, Northfield, Illinois; and 6Department of Pathology, Massachusetts General Hospital, Boston.

Context: Between 2000 and 2009, the College of American Pathologists’ Interlaboratory Comparison Program in Gynecologic Cytopathology received 10,031 individual responses from 229 slide challenges of endocervical adenocarcinoma in situ (AIS).

Design: False-negative responses (negative or unsatisfactory responses) and variation in response rate by preparation type and participant type were analyzed by Fisher exact test at the .01 level of significance.

Results: Of the 10,031 responses, 852 (8.5%) incorrectly classified AIS as negative or unsatisfactory. There was a significant difference in the response rate for AIS, based upon the specimen preparation and participant types (Table).

Conclusions: In the College of American Pathologists’ PAP educational program, there is a false-negative rate of 8.5% for slides with the reference diagnosis of AIS. Pathologists have a significantly higher false-negative rate for AIS than cytopathologists. Liquid-based preparations have higher rates of false-negative interpretations than conventional Papanicolaou tests. SurePath slides have the highest false-negative rate. For comparison, the false-negative rate for high-grade squamous intraepithelial lesions was previously reported as 4.6%. The Papanicolaou test is primarily a screening tool for squamous lesions of the cervix, but AIS is an important diagnosis that can be made. It, however, represents a significant source of false-negative results in an educational glass slide interlaboratory comparison program. These findings have implications for the ability to identify AIS in the clinical setting.

### False-Negative Rate by Preparation Type

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<th>SurePath</th>
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<tr>
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<td>6.7</td>
<td>8304</td>
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### False-Negative Rate by Participant Type

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<tr>
<td>N Rate, %</td>
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<td>7.8</td>
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<tr>
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Satisfactory Rates of Ultrasound-Guided Fine-Needle Aspiration of Thyroid Nodules Without Immediate Adequacy Assessment at a Teaching Institution

(Poster No. 68)

Angelo G. Lapus, MD, MPH (lapusag@yahoo.com); Jing Liu, MD, PhD. Department of Pathology and Laboratory Medicine, University of Texas, Houston Medical School, Houston.

Context: Ultrasound-guided fine-needle aspiration of thyroid nodules is increasingly used as a screening modality. Immediate cytologic adequacy assessments may not be available in some circumstances. It therefore becomes incumbent on the clinicians to obtain sufficient material. To define the optimal number of passes required to achieve sufficient material without immediate adequacy assessment, we retrospectively analyzed the adequacy of each pass of thyroid ultrasound-guided fine-needle aspirations performed by clinical resident physicians under the supervision of experienced attending physicians at our teaching institution.

Design: We retrieved 73 archival cases for a 9-month period. The slides were reviewed to determine the adequacy of each pass. An “adequate” pass was defined as at least 6 clusters of follicular cells on 1 slide from each of 2 passes for a solid nodule or on 1 slide from 1 pass for a cystic nodule.

Results: Adequacy rates were as follows: 61 of 73 cases (83.6%) with combined passes 1 to 3; 63 of 73 cases (86.3%) with 4 passes; 64 of 73 cases (87.7%) with 5 passes; and 67 of 73 cases (91.8%) when including cytopsin. The sixth pass was available in 8 cases but did not further increase the adequacy rate.

Conclusions: The results show that 3 passes are minimal and that 5 passes appear to be appropriate for the thyroid fine-needle aspiration performed by the clinical resident physicians under the supervision of experienced attending physicians without immediate adequacy assess-

Carcinoma Metastatic to the Thyroid Detected by Fine-Needle Aspiration

(Poster No. 69)

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Thyroid fine-needle aspiration has become the best test to order in the evaluation of patients for whom there is a clinical suspicion of thyroid tumors. The tumors that are often diagnosed by thyroid fine-needle aspiration are papillary carcinomas and thyroid metastatic carcinomas. Although metastatic tumors to the thyroid are rare, the incidence is rising owing to the increased use of thyroid fine-needle aspiration. The frequent primary sites include kidney, lung, breast, stomach, esophagus, melanoma, and lymphoma. The differential diagnosis may be challenging to the cytopathologist. Immunohistochemical staining on the cell block plays a valuable role. The patient with tumor metastatic to the thyroid is usually older, with a history of malignancy and multiple thyroid lesions. A 57-year-old woman with no previous history of malignancy presented with dyspnea and hoarseness. Thyroid fine-needle aspiration smear showed groups of tumor cells with pleomorphic nuclei and prominent nucleoli. Mitotic figures were easily found. Many cells had intracytoplasmic vacuoles. The cell block of the aspirate showed pleomorphic cells forming glandular structures. The tumor cells had diffuse positivity for CK7, focal positivity for gross cystic disease fluid protein-15, and negativity for thyroglobulin and TTF-1. The immunohistochemical staining profile and the morphology suggested a metastatic adenocarcinoma, probably of mammary origin.

The Importance of Fine-Needle Aspiration in Conjunction With Radiologic Examination in the Evaluation of Granular Cell Tumor Presenting as a Thyroid Mass

(Poster No. 70)

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Granular cell tumors (GCTs) may resemble other common thyroid tumors and may arise from extra thyroid gland tissues. Because of the rarity of a GCT presenting as a thyroid mass, its accurate evaluation has not been well addressed. We present the findings from a 27-year-old woman with a 6-year history of a right thyroid mass. A fine-needle aspiration of the mass showed large polygonal cells with relatively small pyknotic and irregular nuclei, abundant coarsely granular cytoplasm, and ill-defined cell borders. The cells were arranged singly or in clusters. The clusters of tumor cells had a syncytial appearance. The differential diagnosis included GCT and Hurthle cell neoplasm. Immunostaining revealed that the cells were positive for S100 and CD68 and negative for TTF-1. These findings were consistent with GCT. Subsequently, computed tomography–guided needle core biopsy of the neck mass confirmed the diagnosis of GCT. Because of the extensiveness and multifocality of the tumor, a malignant nature or metastasis was suspected. Thus, we recommended that the patient have chemotherapy before surgical resection of the tumors. This case demonstrates that the accurate evaluation of a GCT presenting as a thyroid mass is important for management and requires both pathologic and radiographic examinations.

Fine-Needle Aspiration of Soft Tissue Giant Cell Tumor of Low Malignant Potential: Case Report and Review of the Literature

(Poster No. 71)

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Soft tissue giant cell tumor of low malignant potential is a rare neoplasm with approximately 100 cases identified in the literature.
Peripheral T-Cell Lymphoma Presenting as Ascites
(Poster No. 72)

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We report a case of a 42-year-old man who presented with a 2-week history of vague abdominal pain. His symptoms included night sweats, nausea, vomiting, and a 15-pound weight loss. On physical examination, we noted hyperactive bowel sounds, diffuse abdominal tenderness, and ascites. A 57-year-old woman presented with abdominal pain, abdominal distention, and ascites. Serum-ascites albumin gradient was 1, and there were no destructive bone lesions. Ascitic fluid cytology revealed numerous pleomorphic, atypical plasma cells with prominent nucleoli (Figure 84, A). Most of the plasma cells demonstrated a light chain restriction by immunohistochemistry (Figure 84, B). Features were consistent with myelomatous ascites. The patient’s clinical status worsened despite chemotherapy, and she subsequently died. Myelomatous ascites, a rare feature of multiple myeloma, is defined as malignant myeloma in which plasma cells and/or monoclonal immunoglobulin can be demonstrated in ascitic fluid. Myelomatous ascites heralds a poor prognosis and is usually aggressive and rapidly fatal. It has a median survival rate of only 1.5 to 2 months after the development of ascites. It is speculated that postsinusoidal portal hypertension due to plasma cell infiltrate represents the underlying pathology of the myelomatous ascites. To date, only a few cases of myelomatous ascites have been reported. A disproportionately high percentage of those rare cases included IgA paraprotein, as in our patient. The triad of myelomatous ascites, IgA paraprotein, and absence of bone lesions may represent a distinct clinicopathologic syndrome. This entity is rare; therefore, more clinical follow-up, autopsy studies, and basic research are required to understand it.
Hepatocellular Carcinoma Presenting as Parotid Gland Swelling: Fine-Needle Aspiration as a Useful Diagnostic Tool
(Poster No. 75)

Tanya Varma, MD (tvarma@lsuhsc.edu); Joel Thibodeaux, MD; Jaiyeola O. Thomas, MBBS, FRCPath. Department of Pathology, Louisiana State University Health Sciences Center, Shreveport.

A 57-year-old, white man presented to the outpatient clinic with complaint of swelling in the right parotid region for 2 months. He was otherwise in his usual state of health. On examination, a 1 × 1-cm ulcer was seen on the right cheek in the area overlying the parotid gland. An incisional biopsy was performed that showed ulceration and granulation tissue with acute and chronic inflammation. Ten days later, a fine-needle aspiration was attempted. Papanicolaou and Diff-Quik-stained smears and cell block preparations were done. Microscopically, the smears were cellular and showed numerous naked nuclei of varying sizes with prominent macronucleoli that were interspersed with benign salivary gland tissue. Occasional cells showed green bile pigment in the cytoplasm (Figure 85). A diagnosis of metastatic hepatocellular carcinoma was made, and additional clinical workup was suggested. Further evaluation revealed cirrhosis and a liver mass with an 1109.2 mg/mL serum α-fetoprotein level, confirming the fine-needle aspiration diagnosis. Morphologic recognition is the key to diagnosis because the salivary glands are the site of numerous benign and malignant neoplasms. The characteristic cell morphology and presence of bile in the cytoplasm were key diagnostic features in this case. Fine-needle aspiration is an important clinical tool in identifying benign and metastatic lesions of the salivary glands. In experienced hands, this technique can reach high levels of accuracy and is an indispensable tool for evaluation of swellings in the parotid region.

Correlation of Papanicolaou Tests That Are Positive and Suspicious for Malignancy With Follow-up Histopathologic Findings
(Poster No. 76)

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Context: The Papanicolaou (PAP) test is a screening tool, which may occasionally include highly significant, interpretive, diagnostic clinical information, indicating the possible presence of an invasive malignant neoplasm. Under recently revised laboratory accreditation standards, such reports can be classified by laboratories as “significant and unexpected findings,” requiring telephone notification of the clinician. Limited published information is available on the positive predictive value of these rare PAP reports.

Design: We electronically retrieved PAP reports from between 2005 and 2009 with cytologic interpretations of “positive” or “suspicious” for malignancy. Histopathologic follow-up, including biopsies, excisional procedures, and hysterectomies, were documented and correlated with the PAP interpretations.

Results: We identified 224 positive or suspicious for malignancy PAP reports. Twenty-three cases were excluded because of the absence of available histopathologic follow-up. The mean age of patients was 61 years (age range, 21 to 96 years). There were 162 (72.6%) patients who had a previously recorded diagnosis of malignancy and 55 patients (27.4%) who had a malignant diagnosis on a companion histopathologic specimen. The average period between the PAP report and the follow-up histopathologic procedure was 1.3 months. Malignant endometrial neoplasms (99 cases) were the most commonly diagnosed malignancy, accounting for 38% and 61% of the suspicious and positive PAP reports, respectively. Fifty-eight of 100 suspicious PAPs (58%) and 94 and 101 positive PAPs (93.1%; P < .001) were confirmed by follow-up histopathologic diagnosis.

Conclusions: PAP interpretations of positive or suspicious for malignancy had high positive predictive values for malignant histopathologic diagnoses and may represent significant and unexpected findings warranting telephone notification by the laboratory.

Sebaceous Carcinoma of the Parotid Gland
(Poster No. 77)

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A 58-year-old man presented with a history of a prior stroke and a 1.5-year history of right facial swelling. He had a 6-pack-year smoking history and reported occasional pain with the mass. A computed tomography scan revealed a right-sided parotid mass without significant deep or extraparotid extension. The lesion appeared relatively well circumscribed. He had no history of any prior tumors. A fine-needle aspiration was performed that demonstrated neoplastic cells of uncertain etiology. The most of the cells were basaloid, the differential diagnosis included mucopidermoid carcinoma, basal cell adenocarcinoma, myoepithelial carcinoma, basal cell adenoma, the solid variant of ademoid cystic carcinoma, pleomorphic adenoma, and nonsalivary gland neoplasms. The mass was resected, and grossly, it was relatively well circumscribed, yellow-tan, and lobulated. Histologic sections demonstrated a 4.5-cm infiltrating neoplasm with a mixture of vacuolated cells and atypical basaloid cells with prominent mitoses and pleomorphism. A mucicarmine stain was negative in the vacuolated cells, which supported their sebaceous differentiation. A diagnosis was rendered of sebaceous carcinoma, which was completely excised with 16 benign lymph nodes. No perineural invasion was identified. Sebaceous glands have been reported in the parotid gland of 28% of autopsy specimens and 24% of surgical specimens; but both benign and malignant sebaceous salivary gland tumors are extremely rare, making up less than 0.2% of all major salivary gland neoplasms. This case demonstrates the importance of keeping this rare neoplasm in the differential at the time of both fine-needle aspiration and resection.

Pancreatic Plasmacytoma in a Patient With Multiple Myeloma
(Poster No. 78)

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Plasma cell neoplasms can present as multiple myeloma, solitary plasmacytoma of bone, extra-osseous plasmacytoma, or monoclonal gammopathy of undetermined significance. Multiple myeloma affects mainly bone, but any organ can be affected. However, pancreatic involvement has rarely been reported. Plasmacytoma is defined as a monoclonal proliferation of plasma cells without evidence of systemic disease. In the gastrointestinal tract, the small bowel is most often affected. The clinical and radiographic findings of pancreatic plasmacytoma are nonspecific. Because the treatment of plasmacytoma is radically different from that for other, more common neoplasms involving the pancreas, preoperative diagnosis is crucial for patient care. Here, we present the case of an 84-year-old man with a previous history of multiple myeloma (previously diagnosed on bone marrow biopsy) who presented with jaundice. Abdominal ultrasound and computed tomography scan demonstrated an 8.5-cm pancreatic head and body mass. Endoscopic ultrasound-guided fine-needle aspiration of the mass revealed numerous plasma cells (CD138+), including immature forms. Subsequent protein electrophoresis revealed a monoclonal immunoglobulin Gκ gammopathy (2.2 g/dL). Our case demonstrates the potential of...
multiple myeloma to involve any organ and the utility of endoscopic fine-needle aspiration in rendering a diagnosis.

**Cell Clusters With Atypical Cytologic Features Are A Frequent Finding in Postrenal Transplant Urine Cytology**

(Poster No. 79)

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**Context:** Urine cytology is primarily used for screening and follow-up of urothelial carcinoma; however, in certain cases, urine cytology is used following renal transplant to screen for polyoma virus infection. There is limited literature on the cytologic findings in postrenal transplant urine, and in our anecdotal experience, the findings have distinctive features that pose diagnostic challenges.

**Design:** The voided urine cytology for 100 patients with renal transplants and 100 control cases were reviewed. The presence of atypical cell clusters and cytologic features and the date of transplant were recorded. Immunohistochemical staining was performed in select cases, and select patients were followed during the course of several repeat urine cytologies to assess the consistency of findings over time.

**Results:** Fifteen patients (15%) in the renal transplant group and zero control patients (0%) exhibited atypical cell clusters. Cytologic features of the tightly cohesive atypical clusters included increased nuclear to cytoplasmic ratio; enlarged, round, hyperchromatic, eccentric nuclei with a single, prominent central nucleolus; and granular or vacuolated cytoplasm (Figure 86). Immunohistochemical staining showed renal cell carcinoma positivity, strongly suggesting a renal tubular origin. The atypical cell clusters were not consistently found on repeat urine cytologies.

**Conclusions:** Clusters of atypical cells, most likely of renal tubular origin, were seen in voided urine cytology in a significant minority of patients with renal transplants. These clusters, which are believed to be benign, may indicate renal cell carcinoma, prostatic adenocarcinoma, or in some cases, urothelial carcinoma. This is of concern when not considered by cytologists. Further studies of the clinical significance of renal tubular cell clusters in urine within this population are underway.

**Comparative Staining for Basal-Type Breast Carcinoma Markers in Cytologic and Histologic Material**

(Poster No. 80)

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**Context:** Immunohistochemistry has been shown to be a promising alternative to DNA analysis for identifying basal-type breast cancer, particularly when using the triple-negative phenotype with basal markers and other markers, such as epidermal growth factor receptor (EGFR). The use of these markers in cell blocks derived from cytology specimens has not been investigated, to our knowledge.

**Design:** We reviewed recent cases of breast fine-needle aspirations and pleural fluids, which had both generated cell blocks containing atypical or malignant cells and corresponding histologic specimens positive for breast carcinoma. The cell blocks and corresponding histologic material were stained for CK5 and EGFR.

**Results:** Twenty of 26 cell blocks (77%) used in this study displayed immunohistochemical staining results for CK5 that matched the corresponding histologic specimen, and 23 of 26 of the cell blocks (88%) had matching EGFR staining results. Six of 26 cases were triple-negative phenotype cancers. Of the 8 cell blocks associated with these 6 cases, 7 (88%) had CK5 staining results that matched the corresponding histologic specimen, and 8 of 8 (100%) had matching EGFR staining results. Seven of 8 (88%) had both matching CK5 and EGFR staining results.

**Conclusions:** In this study, staining for CK5 and EGFR in cell blocks was comparable to staining in the corresponding histologic specimen for those tumors with the triple-negative phenotype. Although further study is necessary, our results suggest that staining for basal-type breast cancer in cell block material may predictably reflect basal-type staining in the surgical resection specimen, potentially allowing for recognition of this subtype of breast cancer before resection.

**Clinical, Histopathologic, and Cytologic Diagnosis of Mucosal Leishmaniasis and Literature Review**

(Poster No. 81)

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**Context:** Leishmaniasis is endemic in Iran. Mucosal leishmaniasis is rare. Clinical analysis, histology, and cytology may help in the diagnosis of mucosal leishmaniasis.

**Design:** Review of our files showed 11 patients diagnosed with mucosal leishmaniasis. Of these, 7 patients (64%) had oral lesions. One was a known case of oral leishmaniasis with recurrence of oral lesions, 2 had laryngeal lesions, and 3 had nasal lesions. One case of laryngeal leishmaniasis was a recurrence of a prior oral lesion. Cytologic smears were prepared by scraping the lesions using scalpel or cytobrush. Histology biopsy was performed on the 7 patients. In 2 patients with nasal lesions, exfoliative cytology was achieved by washing the nasal cavity. Smears were air-dried, fixed in alcohol, and stained with Wright stain.

**Results:** Cytologic findings showed free Leishman bodies, intrahistiocytic Leishman bodies, granuloma, acute and chronic inflammatory cells, histiocytes, multinucleated giant cells, mast cells, immunoblastic histiocytes (Reed-Sternberg-like cells), and plasma cells. In 6 of the patients, a biopsy was inconclusive, but in subsequent cytology, the organism was detected. In 3 cases, findings from clinical and cytologic examinations were suggestive of leishmaniasis; however, the diagnosis was confirmed by response to treatment. In 5 patients, either clinically or histologically, a malignant tumor was suspected, but cytology helped to diagnose leishmaniasis.

**Conclusions:** Mucosal leishmaniasis can be clinically or histologically mistaken for benign and malignant lesions. Scraping or exfoliative cytology is easy, reliable, and a cost-effective method for diagnosing mucosal leishmaniasis. Thus, clinical, histologic, and cytologic features may together help in mucosal leishmaniasis diagnosis.

**Squamous Intraepithelial Lesions of the Anogenital Region in African American Women With Breast Cancer**

(Poster No. 82)

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**Context:** Human papillomavirus is the most important factor in cervical oncogenesis. African American (AA) women are twice as likely to develop this disease as white women are. AA women also have a
higher breast cancer mortality rate, and the disease manifests itself earlier in life and is more aggressive. Breast cancer immunosuppression may affect human papillomavirus clearance. The purpose of this study was to determine whether AA women with breast cancer have a higher incidence of human papillomavirus–related abnormalities.

**Design:** We conducted a computer search for AA patients with breast cancer and a corresponding Papanicolaou test (PAP) within 3 years of cancer diagnosis. Pathologic and prognostic tumor variables, clinical data, and PAP results were recorded. The control group was an age, race, and socioeconomic matched population whose members had routine PAPs.

**Results:** We identified 252 AA women with breast cancer. Of these, 103 had PAPs (41%); 94 of the 103 patients (91%) had normal findings, and results from 9 patients (9%) showed abnormalities. Of these 9 cases, there were 5 atypical squamous cells, 2 low-grade squamous intraepithelial lesions, 2 high-grade squamous intraepithelial lesions, and 1 atypical glandular cell. The difference in prevalence of abnormal PAP results between the cancer group (8.7%) and controls (n = 1673; 4.2%) was statistically significant (P < .046). The rate of high-grade squamous intraepithelial lesions was significantly higher (P < .048) in the AA cancer population (1.9%) than in the control group (0.24%). There was no significant association between PAP results and tumor stage, type, or other variables.

**Conclusions:** In our group of AA women with breast cancer, the rate of abnormal PAP findings, including high-grade squamous intraepithelial lesions, was higher than in the control group. Although the study was small, preliminary data suggest AA women with breast cancer may be at a higher risk of squamous intraepithelial lesions of the anogenital region and may require closer gynecologic follow-up.

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**Recurrent Respiratory Papillomatosis: Cytohistologic Correlation of a Difficult Case** (Poster No. 83)

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Recurrent respiratory papillomatosis is characterized by recurrences of squamous papillomas that are caused by infection with human papillomavirus (HPV) types 6 and 11. Most lesions involve the larynx, but spread throughout the respiratory tract can occur. These lesions rarely involve the lung parenchyma. Airway obstruction with resultant atelectasis, bronchiectasis, and pneumonia may result in significant morbidity or death. Malignant transformation is rare and has been associated more frequently with HPV-11. We present a case of a 56-year-old man with recurrent respiratory papillomatosis who underwent fine-needle aspiration and core biopsies of the enlarging right and left pulmonary nodules. The presence of necrosis and discohesive keratinized cells present on fine-needle aspiration of the right lung were suspicious for squamous cell carcinoma. Correlation with the core biopsy, which was interpreted as a squamous papilloma arising in the setting of respiratory tract papillomatosis, and consideration of the clinical history were necessary to arrive at the correct diagnosis of benign papilloma. Making the cytologic distinction between malignant transformation and squamous papillomas displaying atypia can be challenging and is rarely noted in the literature. This case illustrates the need for extreme caution before rendering a diagnosis of malignancy. Given the diverse cytologic spectrum of squamous papillomas, cytomorphologic correlation is recommended before a definitive diagnosis of malignant transformation is provided. In addition, given the emerging evidence of HPV-11 in most papillomas that undergo malignant transformation, testing for HPV type is recommended in equivocal cases.

**Granular Tumors of the Central Nervous System: Two Case Studies and Review of Current Literature** (Poster No. 84)

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Granular cell tumors of the central nervous system are very rare. To date, 7 cases arising from cranial nerves have been reported. They have also been found arising from the neurohypophysis of the pituitary gland and its stalk. Because of their rarity and histologic similarity to other tumors, they may cause a diagnostic dilemma. The differential diagnosis includes astrocytoma with granular features, which carries a much worse prognosis. We report 2 cases of granular cell lesions in the central nervous system. The first case was a 54-year-old woman with a history of recurrent numbness in a third trigeminal branch pattern, which was thought to be Bell palsy. Further workup revealed a middle-fossa mass. Craniotomy revealed a tumor with prominent granular cytoplasm (Figure 87). Immunohistochemical staining for S100, chromogranin, and most pituitary hormones was negative. Prolactin was positive. Morphology and immunophenotype were consistent with a prolactinoma with prominent granular differentiation. Both of these lesions represent a rare finding that could be confused with a granular cell astrocytoma. Granular cell tumor and its variants, although uncommon, must be included in the differential diagnosis of central nervous system lesions.

**Astrocytic Tumor With Mixed Components of Pilocytic Astrocytoma and Pilomyxoid Astrocytoma** (Poster No. 85)

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Pilomyxoid astrocytoma is currently regarded as a variant of pilocytic astrocytoma. It has a distinctive histology, which often exists in its pure form. We report a case with components resembling both pilomyxoid astrocytoma and pilocytic astrocytoma. The patient was a 2-year-old girl with an enhancing mass involving the cerebellum. Imaging workup revealed a mass in the lateral portion of the fourth ventricle with hypointensity on T1 weighted images and hyperintensity on T2 weighted images with heterogeneous enhancement. On histologic sections, there were areas with classic features of pilomyxoid astrocytoma demonstrated by a mucoid tumor with perivascular arrangement of tumor cells. Separate areas showed features resembling a pilocytic astrocytoma, displaying Rosenthal fibers and vascular glomeruli. Pilomyxoid astrocytoma is a World Health Organization grade II tumor and was recently recognized as a variant of pilocytic astrocytoma, which is a World Health Organization grade I tumor. Pilomyxoid astrocytomas tend to be more aggressive in biologic behavior, and they have an increased tendency to disseminate through the cerebral spinal fluid. The tumor cells typically show perivascular arrangement resembling pseudorosettes as seen in ependymomas. Rosenthal bodies and eosinophilic granular bodies are rare. It is important to distinguish pilomyxoid astrocytoma from pilocytic astrocytoma because of the more aggressive behavior of the former.

**Immunohistochemical p75NTR Expression Pattern in Low-Grade Glioneuronal Tumors** (Poster No. 86)

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**Context:** Gangliogliomas comprise a spectrum of central nervous system lesions having neoplastic glial and neuronal components.
Although these tumors rarely behave aggressively, malignant transformation can occur, typically in the glial component following radiation therapy. The biology of this transformation is not fully understood. Although there is growing evidence that P75 neurotrophin receptor (p75NTR), which plays a critical role in the growth and development of the nervous system, is important in the malignant progression of medulloblastomas and glial tumors, its expression in glioneuronal tumors has not been characterized.

**Design:** We retrieved 28 gangliogliomas from 23 patients from Children’s Memorial Hospital (2004–2009). Primary tumors from 22 patients (12 ganglioglioma NOCS, 5 DNT-like, 1 desmoplastic infantile, 4 with desmoplasia, 3 anaplastic/malignant) were obtained; only a recurrent tumor was available for one patient. There were 5 recurrent tumors. The patients ranged from 4 to 19 years. Immunohistochemistry was done using anti-p75NTR (United States Biological, Swampscott, Massachusetts). Tumors were scored according to location (astrocytic processes, desmoplastic processes, cytolytic, nuclear, membranous), distribution (single cell, focal, multifocal, diffuse), and intensity (negative, weak, strong).

**Results:** The main patterns of staining included negative (6 of 14 ganglioglioma/DNT-like), astrocytic processes (5 of 14 ganglioglioma/DNT-like), desmoplastic processes (3 of 4 with desmoplasia), and perivascular staining (3 of 5 recurrent tumors).

**Conclusions:** Expression patterns of p75NTR were variable and complex and did not correlate with tumor diagnosis or prognosis in most cases. Perivascular staining pattern was seen in 3 of 5 recurrent cases having a higher mitotic index/high-grade glial component. Further studies are indicated to understand the role of p75NTR in glioneuronal tumor progression.

**Simultaneous Central Nervous System and Cutaneous Tuberculosis: A Rare Presentation of Systemic Tuberculosis**

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Cutaneous tuberculosis is seen in less than 2% of all tuberculosis cases. Central nervous system involvement by tuberculosis occurs in approximately 1% of all cases and carries high rates of morbidity and mortality. We report a rare case of simultaneous central nervous system and cutaneous tuberculosis presenting with acute mental status change. A 22-year-old woman presented with sudden altered mental status. She was clinically unresponsive. She had a 1.5-cm skin ulcer on her right lower leg and diffuse ronchi in the lungs. Magnetic resonance imaging of the brain showed foci of meningeal and cortical enhancement that were consistent with meningitis and developing encephalitis. A punch biopsy from the ulcer showed diffuse granulomatous inflammation. A brain biopsy showed foci of acute inflammation and neuronal necrosis. Ziehl-Neelsen staining was positive for acid-fast organisms compatible with Mycobacterium tuberculosis. Polymerase chain reaction study of bronchial washings further confirmed the diagnosis of Mycobacterium tuberculosis. A literature review suggested that cerebrospinal fluid culture with dermato-specific staining for acid-fast bacilli is the test most frequently used to confirm the diagnosis of tuberculosis. This case illustrates the importance of clinical presentation. A literature review suggested that cerebrospinal fluid culture with dermato-specific staining for acid-fast bacilli is the test most frequently used to confirm the diagnosis of tuberculosis. This case illustrates the importance of clinical presentation.
Vertigo and headaches was admitted to a tertiary university hospital for evaluation to determine further treatment options. Magnetic resonance imaging showed a heterogeneously enhancing mass with cystic and calcific components in the anterior horn of the left lateral ventricle measuring 2.5 × 2.2 × 1.6 cm. The patient underwent tumor resection through a left frontal craniotomy with transfrontal approach to the left ventricle and excision of the intraventricular mass. Histologically, the hematoxylin-eosin sections showed a low-grade glial neoplasm, which, in most areas, was composed of fibrillated spindle cells that demonstrated a fascicular pattern of growth. Some areas were more cellular and showed nuclear pleomorphism, whereas others were hypocellular and composed mainly of fibrillated cell processes. Subtle perivascular rosetting was seen only rarely around a vessel. Some of the hypocellular areas merged into foci with a microcystic appearance that was characteristic of subependymoma. There were also collections of large pleomorphic glial cells resembling those seen in subependymal giant cell astrocytoma. The Ki-67 immunostain showed low proliferative activity. The synaptophysin immunostain showed focal entrapment of preexisting axons, but there was not much diffuse infiltration of preexisting parenchyma. The tumor was strongly immunoreactive for glial fibrillary acidic protein but showed no immunoreactivity for epithelial membrane antigen. We consider the present case to be an unusual example of tanyctytic ependymoma. The occurrence of subependymal giant cell astrocytoma-like pleomorphic cells was another unusual feature.

A Case of Brain Leiomyoma
(Poster No. 91)

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Intracranial mesenchymal tumors are rare. Documented cases include tumors of fibrous tissue, adipose tissue, blood vessels, cartilage-forming and bone-forming tissue, muscle, and fibrohistiocytic tumors. There have been only a few cases reported during the past decades, and among them, the smooth muscle tumor has been extremely uncommon. Here, we present a case of primary intracranial leiomyoma. A 43-year-old African American man reported diplopia for some time. Physical examination revealed fairly dense sixth nerve palsies on the right-hand side. Magnetic resonance imaging demonstrated a large, intensely enhancing mass (1.5 cm at greatest diameter) on the right middle cranial fossa adjacent to the cavernous sinus. A presumptive diagnosis of meningioma was made based on the radiologic impression. Alternatively, schwannoma appeared to be a differential diagnosis. Grossly, the biopsy specimen from the operation revealed pink-tan soft tissue. Microscopic examination showed that the mass was a spindle cell lesion organized in a fascicular pattern. The cytoplasm was eosinophilic. The nuclei were oval to elongated. The chromatin was granular, and some nuclei showed small nucleoli. Rare mitosis was identified. However, tumor necrosis was not seen.

Nuclear hyperchromasia or polymorphism was not observed. To further classify the tumor, immunohistochemistry was used to stain for the epithelial membrane antigen, glial fibrillary acidic protein, S100, CD31, CD34, and smooth muscle actin. The results showed tumor cells to be positive only for smooth muscle actin (Figure 88) and negative for the rest of the markers. The characteristics of histology and intracranial localization of the tumor were consistent with the diagnosis of brain leiomyoma.

Ganglioneurocytoma: Case Report and Review of the Literature
(Poster No. 92)

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Ganglioneurocytoma, a variant of central neurocytoma, is a rare tumor that is recognized as a distinct clinicopathologic entity among brain tumors. We report a case of ganglioneurocytoma in a 14-year-old adolescent boy who presented with a short history of persistent headaches and blurry vision. Magnetic resonance imaging studies revealed an abnormal third ventricular mass with a small central area of enhancement involving the septum pellucidum with calcifications and obstructive hydrocephalus. On intraoperative consultation, touch preparations showed large tumor cells with vesicular nucleus and prominent nucleoli in a fibrillary background with psammoma bodies. Frozen tissue section showed a predominance of large tumor cells with focal clustering and psammoma bodies in a fibrillary background. Tumor cells showed moderate to abundant amounts of amphophilic cytoplasm, large vesicular nuclei, and prominent nucleoli. On permanent sections, the tumor showed a predominance of synaptophysin-positive ganglionic cells, focal intranuclear inclusions, binucleate and multinucleate ganglionic cells, a few scattered mitosis, psammoma bodies, and clustering of tumor cells around the neurons. Few small, round neurocytes were identified. This case, including frozen section, touch preparation, and complete workup findings, enhances our understanding in the diagnosis of this rare entity.

Secondary Tumors in Meningiomas: Pitfalls in Diagnosis
(Poster No. 93)

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Meningiomas are benign tumors; they arise from the arachnoid stromal cells that are found along the cerebral convexity attached to the dura or less frequently within the ventricular system. We present 2 patients with preexisting meningiomas who developed secondary tumors as a consequence of tumor to tumor metastasis and radiation induced dedifferentiation. Case 1 was a 77-year-old man with a medical history of recurrent prostate cancer that was treated with chemotherapy. He presented with sudden onset of left hand weakness. Magnetic resonance imaging revealed a 2.7-cm cystic meningioma in the posterior right frontal lobe. Intraoperative histologic examination confirmed a meningioma. Examination of the entire surgical specimen, however, demonstrated the presence of metastatic prostate cancer within the meningioma. Case 2 was a 62-year-old who was diagnosed with a right frontal meningioma (3.1 cm), which was treated by γ knife surgery 10 months earlier. She later presented with headache and psychomotor slowing. Magnetic resonance imaging revealed an increase in the size of the meningioma (3.5 cm) and necrosis. Histologic examination revealed foci of a nested growth of cells with a prominent chicken-wirelike vascular pattern, which was compatible with hemangioblastoma within the necrotic meningioma. Hematoxylin-eosin–stained, formalin-fixed, paraffin-embedded tissue sections were examined by light microscopy. Immunohistochemical stains were performed on selected tissue sections using the streptavidin–horseradish peroxidase method. In conclusion, secondary tumors can develop within meningiomas due to metastasis or radiation-induced transformation. Histologically benign meningiomas can present diagnostic dilemmas because they serve as homing sites for metastatic cancers or as a nidus for development of secondary, aggressive tumors. Hence, a careful examination is warranted in the presence of relevant history.
Primary Neuroectodermal Tumor of the Spinal Cord in an Adult
(Poster No. 94)

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Central nervous system primitive neuroectodermal tumor (PNET) is an embryonal tumor composed of predominantly undifferentiated neuroectodermal cells. Most neuroectodermal tumors occur predominantly in children and adolescents. PNET is typically metastatic to the spinal cord. However, primary PNET is very rare in the spinal cord. We report a case of primary PNET in the spinal cord of a 46-year-old man. Findings from the radiologic examination of the thorax, abdomen, and other parts of the central nervous system were normal. The tumor relapsed 3 times in the spinal cord. Histopathology showed a highly cellular infiltrative tumor that was composed of small, round cells with little cytoplasm. Mitotic figures and apoptosis were abundant. Immunohistochemistry demonstrated neuron-specific enolase, synaptophysin, chromogranin, and focal membranous CD99 positivity. Gial fibrillary acidic protein, S100, vimentin, Melan-A, HMB-45, pancytokeratin, epithelial membrane antigen, desmin, actin, CD45, CD138, CD34, and myeloperoxidase were all negative. Ki-67 proliferation index was high. Although PNETs are relatively common in children and are mainly located intracranially, they may occur in the spinal cord of adult patients and may arise in the different segments of the spinal cord with intradural or extradural involvement.

Epstein-Barr Virus–Associated Primary Nervous System Lymphoma Involving the Conus Medullaris in a Patient on Long-Term Azathioprine Therapy for Psoriasis
(Poster No. 95)

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Primary nervous system lymphoma associated with Epstein-Barr virus often occurs in patients with acquired immunodeficiency syndrome or following organ transplantation. We performed clinical and pathologic examinations of a 47-year-old, white man who had psoriasis treated with azathioprine for more than 10 years and who presented with progressive motor and sensory problems. He experienced perianal numbness, erectile dysfunction, and difficulty urinating and walking. The physical examination showed motor and sensory abnormalities in the proximal and distal right leg. The magnetic resonance imaging scan showed a homogenously enhancing mass lesion within the conus medullaris and several nerve roots of the cauda equina. These findings were initially thought to be consistent with myxopapillary ependymoma. However, gross findings were inconsistent with a solid mass, and microscopic examination showed polymorphous cellular infiltrate composed of small lymphocytes and scattered epithelioid cells that were positive for CD45 and CD20. These findings were consistent with diffuse large B-cell lymphoma. An immunoglobulin gene rearrangement study showed clonal rearrangement of the heavy chain gene. Histopathology showed a highly cellular infiltrative tumor that was composed of small, round cells with little cytoplasm. Mitotic figures and apoptosis were abundant. Immunohistochemistry demonstrated neuron-specific enolase, synaptophysin, chromogranin, and focal membranous CD99 positivity. Gial fibrillary acidic protein, S100, vimentin, Melan-A, HMB-45, pancytokeratin, epithelial membrane antigen, desmin, actin, CD45, CD138, CD34, and myeloperoxidase were all negative. Ki-67 proliferation index was high. Although PNETs are relatively common in children and are mainly located intracranially, they may occur in the spinal cord of adult patients and may arise in the different segments of the spinal cord with intradural or extradural involvement.

Familial Hypokalemic Periodic Paralysis
(Poster No. 96)

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Familial hypokalemic periodic paralysis is the most common form of primary periodic paralyses. Inheritance is autosomal dominant with most cases caused by a mutation of the L-type calcium channel. We present a 43-year-old man who started having episodes of intermittent paralysis every 2 weeks from age 13 to 18 years. He became asymptomatic until he was around 41 years, at which time, he started experiencing 6 episodes per month with symptoms of periodic weakness and paralysis predominantly affecting his lower extremities. The patient also had a family history of similar weakness in his father, brother, and one of his father’s cousins. Prebiopsy investigations demonstrated elevated total creatinine phosphokinase (moderately elevated, 403 U/L), CK-MB, and aldolase with a low potassium of 3.2 mmol/L. A muscle biopsy was performed. Histologic sections demonstrated numerous solitary, empty, round to oval vacuoles at the center of the fibers that occupied up to 80% of the volume of the fibers. Type I and Type II fibers were both affected. No fiber-type dominance was present. The vacuoles were not completely empty under histochemical stains, and some glycogen was present in many of the vacuoles. Vacuoles can be seen in many different neuromuscular diseases and can vary in size, shape, and number per cell. Neither the presence of vacuoles nor their morphology is specific for any one disease. Clinical correlation is critical in establishing the diagnosis. Given the patient’s clinical manifestations, laboratory findings, and family history, the biopsy features are most consistent with a periodic paralytic myopathy.

Intracranial Mesenchymal Choristoma
(Poster No. 97)

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Choristomas, which are defined as mass lesions consisting of normal tissue in an abnormal location, are rarely found in the central nervous system. Reports of choristomas in the central nervous system have described heterotopic tissue of squamous epithelial, adipose, skeletal muscle, and pancreatic differentiation. Cartilaginous choristomas have been reported in the oral cavity, including the tongue, lip, tonsil, and gingiva, but not yet, to our knowledge, within the central nervous system. Here, we describe an intracranial choristoma. A 16-year-old adolescent girl suffered minor head trauma while playing volleyball. About a week later, she noticed vertical binocular diplopia and discomfort in her right leg as well as mild papilledema. Magnetic resonance imaging of the brain revealed a large left frontoparietal mass lesion. She underwent a craniotomy and gross total tumor resection. Intraoperatively, the tumor was found to be a subdural, well-circumscribed mass compressing the underlying parietal cortex. Pathologic analysis showed a 9-cm tumor surrounded by a firm, granular capsule. The tissue displayed a homogenous, pearly white, cut surface. Histologically, the tumor was primarily composed of mature cartilage with areas of cystic degeneration. There were focci of ossification and dense fibrous bands reminiscent of tendon. No histologically immature elements were identified. The differential diagnosis of mature cartilage in the central nervous system includes teratoma and chordoma. Among possible etiologic factors, intracranial mesenchymal choristoma are metaplasia and congenital heterotopic rest. A developmentally derived rest of the heterotopic mesenchymal stem cells is a more likely etiologic possibility. These have been reported in the neck and are thought to be derived from branchial arch remnants.

Pediatric Malignant Neoplasms: A Comparative Analysis
(Poster No. 98)

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Context: Pediatric malignant neoplasms (PMNs) continue to be a significant cause of death among children. We evaluated the pattern and frequency of PMNs at our hospital and compared the results with those reported from other parts of the United States and world.

Design: We reviewed 131 PMNs from our pathology database (2000–2008). We evaluated the pattern and frequency of these tumors and their histologic features and compared these to reports from other parts of the world and with a cohort of 101 PMNs from an academic hospital in India.

Results: The male to female ratio was 1.19 to 1 (mean age, 4.7 years). The male to female ratio for nervous system tumors was 2:1 compared with 1:1.9 in the Surveillance, Epidemiology and End Results (SEER) database. Lymphomas were more common in the 5- to 12-year-old group. The top 5 sites included central nervous system (35%), neuroblastomas and peripheral nervous system (14%), soft tissue tumors

Microcystic Meningioma Presenting as a Cystic Lesion With an Enhancing Mural Nodule in Elderly Women: Report of 2 Cases With Review of Literature
(Poster No. 99)

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We report 2 rare and unique cases of microcystic meningioma in elderly women. One patient was age 72 (case 1), and the other was age 76 (case 2). In case 1, the patient presented with a 3-year history of vertigo and a history of carotid artery stenosis, hypertension, and hypothyroidism. Magnetic resonance imaging showed a right frontal lobe, peripheral cystic mass with an enhancing mural nodule. Radiologic differential diagnosis included astrocytoma, hemangioblastoma, and pleomorphic xanthoastrocytoma. In case 2, the patient presented with an acute episode of weakness in her legs. Magnetic resonance imaging showed a 4.4 x 4.2 x 3.3-cm, right frontoparietal lesion with a mural enhancing nodule. Intraoperative consultation, permanent paraffin sections and immunohistochemistry in both cases showed World Health Organization grade I meningioma with microcystic formations. The tumors were strongly and diffusely immunopositive for epithelial membrane antigen and progesterone receptor, weakly positive for inhibin, and negative for glial fibrillary acidic protein and S100. Ki-67 index was less than 1%. Cystic meningiomas with an enhancing mural nodule are rare and can present as a radiologic and clinical dilemma with wide differential diagnoses. This pattern is commonly seen in hemangioblastoma, pilocytic astrocytoma, ganglioglioma, and pleomorphic xanthoastrocytoma. Case reports are mainly of fibrous meningioma with a cystic lesion with a mural nodule. Male predominance and young age are most commonly reported. Our cases are unique because of the rare and unusual clinical-radiologic presentation of World Health Organization grade I microcystic meningioma in elderly women.

Granular Cell Astrocytoma: Case Report and Review of Literature
(Poster No. 100)

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Granular cell astrocytoma (GCA) is a rare type of infiltrating malignant brain tumor that was first reported in 1973. A 75-year-old man presented with progressive, expressive aphasia. Magnetic resonance imaging showed a 4.4 x 4.2 x 3.3-cm, right frontoparietal lesion with a mural enhancing nodule. Intraoperative consultation, permanent paraffin sections and immunohistochemistry in both cases showed World Health Organization grade I meningioma with microcystic formations. The tumors were strongly and diffusely immunopositive for epithelial membrane antigen and progesterone receptor, weakly positive for inhibin, and negative for glial fibrillary acidic protein and S100. Ki-67 index was less than 1%. Cystic meningiomas with an enhancing mural nodule are rare and can present as a radiologic and clinical dilemma with wide differential diagnoses. This pattern is commonly seen in hemangioblastoma, pilocytic astrocytoma, ganglioglioma, and pleomorphic xanthoastrocytoma. Case reports are mainly of fibrous meningioma with a cystic lesion with a mural nodule. Male predominance and young age are most commonly reported. Our cases are unique because of the rare and unusual clinical-radiologic presentation of World Health Organization grade I microcystic meningioma in elderly women.

Gliomatosis Cerebri: An Unusual Cause of Late Fetal Immobilism
(Poster No. 102)

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Gliomatosis cerebri is a rare, primary, aggressive brain tumor characterized by an infiltration of neoplastic glial cells involving at least 2 lobes of the brain, according to the World Health Organization classification of brain tumors. The lesion occurs in adults and intracranial pressure. Most occur in the cerebral hemispheres. The differential diagnosis includes progressive multifocal leukoencephalopathy, cerebral infarction, and multiple sclerosis. Electron microscopic studies reveal increases in intracytoplasmic lysosomes. Cytogenetic analysis shows a loss of 9p or 10q in most cases. Surgical excision with chemotherapy or radiotherapy is the treatment of choice.
occasionally in children. The most common causes of late pregnancy fetal immobility are neuromuscular disorders. We report a case of gliomatosis cerebri as a cause. A cesarean section was performed on a 29-year-old woman (gravida 1, para 0), who presented with nonreassuring fetal monitoring and breech presentation at 38 weeks' gestation. At birth, the baby benefited from assisted ventilation because of pulmonary distress and asphyxia from major hypotonia. Magnetic resonance imaging revealed thickening of the cervical spinal cord (hyperintense on T2-weighted, without contrast enhancement). In addition, a centrally located, noncontrasted enhancing lesion was observed in the lower part of the spinal cord. The baby died on day 11, and an autopsy was performed. Gross examination of the brain did not reveal any supratentorial macroscopic lesions. The pons appeared enlarged and was surrounded by mucoid material. Spinal cord leptomeninges were white and thickened. A cross section of the thoracic spinal cord demonstrated a centrally located, yellowish parenchyma. Histologic examination revealed the presence of a diffuse infiltration of tumoral astrocytes in both cerebral hemispheres, the brain stem, cerebellum, spinal cord, and spinal nerves. Immunohistochemistry showed overexpression of both Ki-67 and p53. To our knowledge, this is the first case of late fetal immobility caused by this kind of lesion extending to the spinal cord.

Nonfunctioning Prolactinoma Presenting With Proptosis and Widespread Local Extension in a 56-Year-Old Woman: Case Report and Review of Literature

(Poster No. 103)

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We describe the histopathology and neuroradiology of an unusual pattern of local extension in a nonfunctioning pituitary adenoma. A 56-year-old woman presented with increasing proptosis, pain, and decreasing vision in the left eye. There were no symptoms of hyperprolactinemia. Magnetic resonance imaging showed a mildly heterogeneous, T1 and T2 isointense, enhancing mass, measuring 2.9 cm, with suprasellar extension. A similar-appearing, enhancing fusiform mass measuring 2.3 cm was identified within the left orbit and surrounding the optic nerve. This represented an intraorbital extension via the left optic canal with narrowing of the left optic nerve sheath complex. The pituitary gland was not identifiable. The mass invaded the left cavernous sinus and bilateral sphenoid sinuses and surrounded the left cavernous carotid artery. The sphenoid portion of the tumor appeared enlarged and was surrounded by mucoid material. Spinal cord leptomeninges were white and thickened. A cross section of the thoracic spinal cord demonstrated a centrally located, yellowish parenchyma. Histologic examination revealed the presence of a diffuse infiltration of tumoral astrocytes in both cerebral hemispheres, the brain stem, cerebellum, spinal cord, and spinal nerves. Immunohistochemistry showed overexpression of both Ki-67 and p53. To our knowledge, this is the first case of late fetal immobility caused by this kind of lesion extending to the spinal cord.

Amplification of ERBB2 Gene Using Fluorescent In Situ Hybridization in Breast Carcinoma That Showed 1+ ERBB2 Positivity by Immunohistochemistry: A Danbury Hospital Experience

(Poster No. 2)

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Context: Immunohistochemistry (IHC) and fluorescent in situ hybridization (FISH) are the techniques widely used to detect human epidermal growth factor receptor ERBB2 (formerly HER2 or HER2/neu) status in patients with invasive breast carcinoma. We aimed to correlate the results of IHC and FISH and to detect specific clinicopathologic features that may predict the amplification of ERBB2 gene in our population with negative (1+) findings to justify the use of FISH on those patients.

Design: A retrospective analysis was made of 77 cases referred for FISH confirmation during 2007–2010. The IHC was performed using Dako (Carpinteria, California) Hercept test and FISH was performed using PathVysion (Vysis, Downers Grove, Illinois) on cases with missing data elements in 7 of 48 cancer resection surgical pathology reports resulted in the identification of missing data elements in 7 of 48 cancer resection surgical pathology reports (14.6%). We made pathologists aware of these issues and issued addendum reports.

Conclusions: Pathologists play a central role in their hospitals' regulatory compliance and quality improvement initiatives. Enhancing pathologists' awareness, monitoring surgical pathology reports, and working with cancer registrars promotes compliance with standards and successful accreditation.
testing with FISH were those that showed the worse prognostic indicators, including high tumor grade and positive lymph node metastasis.

**Downregulation of the Cell Adhesion Molecule CD44 in Metaplastic Breast Carcinoma With Chondroid Differentiation**

(Poster No. 3)

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**Context:** CD44 is a cell-surface adhesion molecule functioning in cell to cell and matrix interactions, such as aggregation, migration, hyaluronate degradation, lymphocyte activation, and angiogenesis. In mammary carcinoma, loss of CD44 is thought to play an important role in mediating tumor invasion and metastasis via interaction with the extracellular matrix. Breast carcinomas with chondroid differentiation are a subtype of metaplastic breast carcinomas (MBCs) and are associated with high metastatic potential and aggressive clinical behavior. We hypothesized that MBC might show downregulation of CD44.

**Design:** We included 10 cases of MBCs, as defined by the 2003 World Health Organization classifications. Of these, 6 of 10 were lymph node-negative. Archival, paraffin-embedded material from all 10 breast lesions and 2 available axillary lymph node metastases were examined by immunohistochemistry for expression and localization of CD44.

**Results:** Four of 6 (67%) MBCs with positive axillary lymph node findings and both axillary node metastases (2 of 2) revealed loss of CD44 expression. Three of 4 (75%) lymph node-negative MBCs expressed CD44. No difference in CD44 expression was noted between the epithelial and the mesenchymal components.

**Conclusions:** Loss of CD44 expression was more frequently seen in patients with positive lymph nodes, whereas CD44 immunoreactivity strongly correlated with node negativity. Downregulation of CD44 expression has been observed in invasive micropapillary breast carcinomas, and in our study, was associated with a higher incidence of lymph-vascular permeation and positive axillary nodes. Similar findings are reported in endometrial, colorectal, and prostatic adenocarcinomas. Our results indicate that downregulation of CD44 appears to play a significant role in the high metastatic potential of matrix-producing carcinomas.

**ERBB2 Overexpression by Immunohistochemical Staining in Ductal Intraepithelial Neoplasia: Application of the 2007 American Society of Clinical Oncology/College of American Pathologists Fixation and Scoring Guidelines**

(Poster No. 4)

Gillian H. Levy, MD (gillian.levy@yale.edu); Jeeyon Kim, MD; Alexander Finkelstein, MD, DO; Fattaneh Tavassoli, MD, Department of Pathology, Yale University and Yale New Haven Hospital, New Haven, Connecticut.

**Context:** ERBB2 (formerly HER2 or HER2/neu) overexpression occurs in approximately 25% of invasive carcinomas and is considered an adverse prognostic factor. ERBB2 overexpression may also play an important role in the development and progression of ductal intraepithelial neoplasia (DIN). We investigated the incidence of ERBB2 overexpression in cases of DIN, using the 2007 American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) scoring guidelines.

**Design:** Ninety-one cases (167 lesions) of DIN, with or without carcinoma, were evaluated. In 40 cases of invasive ductal carcinomas, the scores were 10 versus 22 of 57 versus 9 of 40). Among the morphologic subtypes of DIN, apocrine, solid, and comedo showed the highest rate of HER2 overexpression, with all DIN 2 and 3 apocrine cases demonstrating 2+ or 3+ staining. Cases with a periductal lymphocytic infiltrate had a higher incidence of ERBB2 overexpression (7 of 11).

**ERBB2 Score 3+ Cases Based on Ductal Intraepithelial Neoplasia (DIN) Grade and Morphologic Subtype**

<table>
<thead>
<tr>
<th>Grade/Subtype</th>
<th>Other</th>
<th>Apocrine</th>
<th>Solid</th>
<th>Comedo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-risk DIN</td>
<td>0/10</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>(usual intraductal hyperplasia)</td>
<td>0/14</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>DIN 1 flat</td>
<td>0/14</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>DIN 1 (atypical intraductal hyperplasia)</td>
<td>1/2</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>DIN 1 (DCIS grade 1)</td>
<td>0/14</td>
<td>0/2</td>
<td>0/3</td>
<td>NA</td>
</tr>
<tr>
<td>DIN 2 (DCIS grade 2)</td>
<td>3/34</td>
<td>2/8</td>
<td>6/25</td>
<td>NA</td>
</tr>
<tr>
<td>DIN 3 (DCIS grade 3)</td>
<td>6/16</td>
<td>1/1</td>
<td>5/17</td>
<td>10/23</td>
</tr>
</tbody>
</table>

Abbreviations: DCIS, ductal carcinoma in situ; NA, not applicable.

**Adenoid Cystic Carcinoma of the Breast in Reduction Mammaplasty: Case Report and Review of the Literature**

(Poster No. 5)

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Adenoid cystic carcinoma of the breast is a very rare neoplasm that constitutes less than 1% of all mammary carcinomas. We report a case of incidental breast adenoid cystic carcinoma in a reduction mammaplasty specimen. A 54-year-old woman with biopsy-proven invasive lobular carcinoma of the left breast underwent left mastectomy for breast cancer and right-sided reduction mammaplasty given significant symptomatic hypertrophy. Before the surgery, right breast magnetic resonance imaging showed Breast Imaging Reporting and Data System category 2 with scattered punctuate enhancement and was interpreted as benign. Gross specimen evaluation was performed and multiple sections from both breasts were submitted for microscopic examination. The incidental adenoid cystic carcinoma was identified in her right breast. Microscopic examination showed infiltrating cribriform islands of neoplastic cells with uniform, dark nuclei and rimming luminal spaces containing a mucinous, ground substance as well as basement membrane-like material. A few neoplastic cells formed tubular ductlike structures. Immunohistochemical stains revealed the tumor cells were positive for p53 and focally positive for smooth muscle actin. Immunohistochemical stains for estrogen receptor, progesterone receptor, and fluorescent in situ hybridization for HER2/neu were all negative in the tumor cells. Occult breast carcinoma has been detected in up to 0.4% of breast reduction specimens. To our knowledge, this is the first reported case of adenoid cystic carcinoma in breast reduction mammaplasty. An adequate sampling of reduction specimen, leading an accurate diagnosis, is vital for optimal clinical management.

**Metastatic Endometrial Carcinoma to the Breast: A Case Report and Review of the Literature**

(Poster No. 6)

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Metastatic endometrial carcinoma to the breast is an exceedingly rare event. Such cases can be mistaken for primary breast carcinoma both clinically and radiologically, even with known histories of endometrial carcinoma. To our knowledge, this is the first reported case of endometrioid endometrial carcinoma metastatic to a breast. We report a case of unilateral breast metastasis from endometrioid adenocarcinoma of the uterus in the absence of widespread disease in a 54-year-old woman who had a total hysterectomy a few months before the development of a right breast mass (Figure 90). An extensive review of
the published literature reveals only one case of metastatic stromal sarcoma to the breast from endometrial primary. This case report is a reminder that, although rare, endometrial carcinoma has the potential to metastasize to breast. Lumpectomy alone may be effective in these patients, so mastectomy, and especially axillary dissection, can be avoided. The histologic appearance of endometrial carcinoma metastatic to the breast may mimic ductal adenocarcinoma of the breast. However, the distinction is important because of differences in management and prognosis.

Metastases of Breast Carcinoma to the Female Genital Tract: A Clinicopathologic Study

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Context: Metastases in the female genital tract from a distant primary are uncommon. Mammary and gastrointestinal carcinomas are the most frequent extragenital carcinomas that metastasize to the genital tract. The most common sites of disseminated breast carcinoma include lungs, bone, and liver. In the genital tract, metastases occur most frequently in the ovaries, followed by the endometrium, and less commonly, the uterine cervix. Metastatic tumors often pose diagnostic problems for both clinicians and pathologists if they present before a primary tumor is evident.

Design: We identified 5 cases of breast carcinoma metastatic to the genital tract. The patients’ clinical and pathological characteristics were reviewed, including the histologic type of breast carcinoma, with estrogen receptor, progesterone receptor, and HER2/neu status; time since breast cancer diagnosis; symptoms; and sites of metastasis.

Results: A total of 5 patients with involvement of the genital tract by breast carcinoma (3 with lobular, 2 with grade 3 ductal) were identified (Table). Metastatic sites included ovary, fallopian tube, endometrium, cervix, and uterine leiomyoma. Four cases had a prior diagnosis of breast cancer. In one case, a diagnosis of breast cancer was made at the time of vaginal mass biopsy.

Conclusions: Metastatic breast cancer to the genital tract usually has a prior diagnosis of breast cancer. The breast carcinoma may be lobular or poorly differentiated ductal. Lobular carcinoma is proportionally more likely to spread to the ovary. Simultaneous involvement of the ovary and omentum may mimic an ovarian primary. Oophorectomy is sometimes performed for hormonal treatment of breast cancers, revealing microscopic evidence of ovarian metastases.

Morphoproteomic Profiling of Triple-Negative Breast Carcinoma Supports Incorporation of Metformin Into Clinical Trials

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Context: Triple-negative breast carcinomas are clinically aggressive tumors that do not express estrogen or progesterone receptors or ERBB2 expression profiling in 3 triple-negative breast cancers. The results of this study support the use of metformin in clinical trials of triple-negative breast cancers.

Conclusions: Morphoproteomic characterization of triple-negative breast carcinoma cases in this pilot study revealed constitutive activation of mTOR and cancer stem cell markers in such tumors. These findings coincide with the putative actions of metformin in blocking the mTOR pathway and its selective targeting of breast cancer stem cells. These findings also support its use in clinical trials of triple-negative breast cancer. An expanded study of triple-negative breast cancer is underway at our laboratory.
Invasive Papillary and Micropapillary Carcinoma of the Breast With Osteoclast-Like Giant Cells
(Poster No. 10)
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Invasive carcinoma with osteoclast-like giant cells (OGCs) is a rare type of mammmary adenocarcinoma that accounts for less than 1% of human breast cancers. Immunocytochemical and ultrastructural studies suggest OGCs originate from stromal histiocytes. We report an unusual case of papillary and micropapillary carcinoma with OGCs. The patient was an 85-year-old woman with no prior history of cancer who was found to have a right breast mass after sustaining trauma to that region. A mammogram and ultrasound identified a mass in the upper, outer quadrant. It appeared as a hypoechoic lesion with associated internal vascularity and was suspicious for malignancy. An ultrasound-guided needle core biopsy revealed invasive adenocarcinoma of the breast. The lesion was strongly positive for estrogen and progesterone receptors and negative for epidermal growth factor receptor and ERBB2 (formerly HER2 or HER2/neu) protein. The patient was treated with a simple mastectomy. Gross examination of the specimen showed a well-circumscribed, 3 × 3 × 3-cm, firm, hemorrhagic mass located in the upper, outer quadrant. Microscopic examination of the tumor showed an invasive adenocarcinoma with papillary and micropapillary differentiation (combined Nottingham grade 2). It was remarkable for a diffusely hemorrhagic stroma with abundant OGCs. An in situ component was absent, but lymphovascular invasion was identified. No axillary lymph nodes were available for evaluation. We have not been able to identify previous reports of this constellation of histopathologic features in the English literature, and thus, we believe this to be the first report of invasive papillary and micropapillary adenocarcinoma of the breast with OGCs.

β-Catenin Expression in Matched Pretreatment and Post Neoadjuvant Chemotherapy Breast Cancers
(Poster No. 11)
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Context: β-catenin is a cell adhesion molecule that is associated with E-cadherin and is a pivotal part of the Wnt signal pathway. We sought to verify that β-catenin immunostaining in residual breast cancer cells, indicating resistance to neoadjuvant chemotherapy, with frequent activation of the Wnt signaling pathway.

Design: Twenty-nine breast carcinomas, with matched pretreatment and posttreatment neoadjuvant chemotherapy, were subjected to immunohistochemical staining with anti–β-catenin antibody. A normal β-catenin stain result was defined as crisp membrane staining in >90% of the tumor cells; aberrant expression was nuclear staining in >5% tumor cells. Reduced membranous staining and cytoplasmic staining were also recorded. Clinicopathologic data, including tumor type, tumor size, tumor necrosis, lymph node status, predictive and prognostic marker studies (estrogen receptor, progesterone receptor, and HER2), and clinical stage, were available.

Results: Normal β-catenin expression was observed in all pretreatment and posttreatment neoadjuvant samples, except in 5 cases of invasive lobular carcinoma, which were negative for β-catenin stain. Mild to moderate, reduced membranous staining was seen in 2 posttreatment samples. Less than 5% cytoplasmic staining was seen in some cases, but there was no difference in pretreatment and posttreatment specimens.

Conclusions: There is no difference in the expression pattern of β-catenin in pretreatment and posttreatment, neoadjuvant chemotheraphy specimens. Lobular carcinoma has a complete absence of β-catenin immunoreactivity. Except for the tumor type, there is no difference in the expression patterns of β-catenin. β-catenin’s role in activating the Wnt signaling pathway and, thereby, possibly conferring neoadjuvant chemotherapy resistance warrants further investigation.

Breast Carcinoma Versus Benign Breast Lesions Diagnosed by Core Biopsies: Types and Risk Factors
(Poster No. 12)
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Context: Most studies on risk factors for breast carcinoma (BCA) compare them to the general population. In this study, we compared BCA risk factors to those for benign breast lesions (BBL).

Design: Core breast biopsies were performed on 610 patients. Histories included number of children, lactation, pill intake, abortions, smoking, menarche age, and age at first pregnancy.

Results: Forty-three percent of cases were BCA, with an average age of 50 years versus 39 years for BBL. Family history was positive for breast cancer in 26% of BCA cases and 30% of BBL cases. In BCA cases, 52% did not lactate versus 20% in BBL cases (P < .005). There was no significant difference between the 2 groups (BCA versus BBL) in number of children (4.2 versus 3.9), the percentage having children (77% versus 74%), menarche age (13.2 years versus 12.9 years), and age at first pregnancy (22.2 years versus 21.5 years). Differences between the 2 groups (BCA versus BBL) were seen in the use of contraceptive pills (29% versus 16%, P < .008), smoking (21% versus 14%, P < .009), and obesity (83 kg versus 74 kg, P < .01). Carcinoma types were ductal (84%), lobular (11%), and in situ (5%).

Conclusions: Lactation is a protective factor. No differences were seen between the 2 groups in number of children, menarche age, and age at first pregnancy. Factors associated with breast carcinoma were smoking, use of hormonal pills, and obesity. Family history of BCA in a first-degree relative is a negative risk factor for breast carcinoma, and history of breast carcinoma in a first-degree relative is a positive risk factor for breast carcinoma.
Significance of Lymphatic and Blood Vascular Density in Intraductal Comedo-Type Carcinoma With Lymphocytic Infiltration and Periductal Fibrosis
(Poster No. 13)

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Context: Intraductal carcinoma with comedonecrosis (ICC) is sometimes associated with surrounding lymphocytic infiltration and periductal fibrosis. Previous studies have shown that ICC without this periductal reaction, when compared with intraductal carcinoma without comedonecrosis, showed an increase in lymphangiogenesis and angiogenesis. We aimed to demonstrate that periductal angiogenesis and lymphangiogenesis, detected by CD31 and D2-40, in invasive ductal carcinoma (IDC) would not differ significantly from cases of ICC with this periductal reaction because these periductal changes may be evidence of invasion or perhaps regression.

Design: Twelve cases of ICC and lymphocytic infiltration and fibrosis, treated by excision, were reviewed and stained with CD31 and D2-40. Three areas with the most periductal, positive staining of microvessels (“hotspots”) were selected by 2 authors independently. The microvessels were counted at ×400 magnification (=0.17 mm²), averages were taken, and discordant cases were recounted. Six cases of healthy breast tissue and 7 cases of IDC were used as controls.

Results: There was no significant difference between ICC and IDC in the number of periductal CD31⁺ and D2-40⁺ microvessels (P = .08 and P = .06). Comparison of ICC with healthy breast tissue controls showed significant differences (P < .05) with CD31 and D2-40. The densities of the mean periductal CD31 and D2-40 microvessels in ICC, IDC, and healthy breast tissue are shown in the Table.

Conclusions: We demonstrated that angiogenesis and lymphangiogenesis in ICC did not differ significantly from that in IDC. Therefore, we speculate that the lymphocytic infiltration and fibrosis seen in ICC indicate either a desmoplastic reaction to early invasion or, more remotely, represent regression.

<table>
<thead>
<tr>
<th>Mean Values of Positively Staining Periductal Microvessels</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD31</td>
</tr>
<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>Intraductal carcinoma with comedonecrosis</td>
</tr>
<tr>
<td>Invasive ductal carcinoma</td>
</tr>
<tr>
<td>Healthy breast tissue</td>
</tr>
</tbody>
</table>

Heterotopic Epithelial Inclusions With Micrometastatic Mammary Carcinoma in Sentinel Lymph Nodes: Report of 2 Cases
(Poster No. 14)

Soma G. Karak, MD (somakarak@yahoo.com); Andrew Ricci, Jr., MD. Department of Pathology, Hartford Hospital, Hartford, Connecticut.

Cellular inclusions in axillary lymph nodes are unusual. They include breast ectopias, melanocytic nevi, and heterotopic elements (squamous or Mullerian). We report 2 cases of nodal heterotopic epithelial inclusions with concomitant metastatic carcinoma (Figure 91; cases 1 and 2). In case 1, a 66-year-old woman diagnosed with right-sided duct carcinoma had 2 types of cytokeratin-positive epithelial cells in a sentinel lymph node. The first type showed tubule formation resembling the primary lesion. The second type showed squamous metaplasia/cyst formation that merged into structures resembling terminal acini. Myoepithelial cells (calponin-positive) were present around the ectopia but absent in the metastasis. In case 2, a 61-year-old woman diagnosed with left-sided duct carcinoma showed 2 types of cytokeratin-positive epithelial cells in a sentinel lymph node. The first type showed lumen formation consistent with her primary lesion. The second type showed dilated duct structures with “tubal” cytology and no myoepithelial cells. The WT1 immunostain was positive, which is consistent with a Mullerian inclusion. Heterotopic epithelial inclusions are rare. It is essential to recognize them to avoid overtreatment. Our cases show benign inclusions and metastatic carcinoma. There are 3 categories of epithelial inclusions: cystic squamous inclusions, tubular/ductal inclusions, and terminal lobules. Resetkova et al (Arch Pathol Lab Med, 2003) suggested that inability to demonstrate myoepithelium in squamous inclusions suggests derivation from a dermal anlage rather than mammary or skin adnexae. The transition from terminal acini to squamous cysts in case 1 argues instead for a metaplastic alteration in breast inclusions. Some previously reported “ductal-type” inclusions may have actually represented Mullerian ectopias as in case 2.

Pseudoangiomatous Stromal Hyperplasia of the Breast in a 10-Year-Old Girl
(Poster No. 15)

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Pseudoangiomatous stromal hyperplasia (PASH) of the breast is a benign breast lesion of myofibroblastic origin susceptible to hormonal influence. It is characterized by dense proliferation of mesenchymal stromal cells with irregular slitlike formations resembling angiomatous structures. PASH lesions are most commonly seen in women of childbearing age and elderly women with estrogen replacement therapy. PASH lesions in teenage girls are rare. Currently, the youngest patients with PASH reported in the literature, to our knowledge, are 12 years. Here, we report a 10-year-old girl who presented with a tender, mobile, solitary mass under her left breast adjacent to healthy breast tissue. She had onset of thelarche ( Tanner stage 2 ) 5 months before this presentation. Incisional biopsy revealed a soft, white nodule. Histologic examination showed interlobular stromal expansion with interanastomosing, slitlike, empty channels separated by dense, acellular collagenous stromata. The spaces were lined by attenuated spindle myofibroblasts. Immunohistochemistry study revealed that these stromal myofibroblastic cells were positive for CD34 and BC12, but negative for CD31 and desmin, which supported the diagnosis of PASH. Because of the benign nature of this lesion, the mass was not removed at the time of diagnosis to minimize the deformity of the growing breast. The patient was scheduled for a follow-up visit 2 years later when her healthy breast tissue would be in good working order in later life.

The Status of Vitamin D in the Geriatric Population
(Poster No. 16)

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Context: Vitamin D is not only a predictor of bone health, but it is also an independent predictor of risk for cancer and other chronic diseases. Several studies have linked vitamin D levels with different clinical outcomes, like incidence of cancer, diabetes, and autoimmune disorders. In addition, vitamin D may have an important role in keeping the brain in good working order in later life.
Status of Vitamin D in the Geriatric Population

<table>
<thead>
<tr>
<th>Age</th>
<th>Mean Age</th>
<th>≤20 ng/mL</th>
<th>21–29 ng/mL</th>
<th>&gt;30 ng/mL</th>
<th>&gt;150 ng/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>&lt;50</td>
<td>42</td>
<td>41.9</td>
<td>19.6</td>
<td>38.0</td>
<td>0.0</td>
</tr>
<tr>
<td>51–60</td>
<td>56.1</td>
<td>34.7</td>
<td>26.1</td>
<td>38.8</td>
<td>0.4</td>
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<td>61–70</td>
<td>65.8</td>
<td>38.3</td>
<td>26.9</td>
<td>34.8</td>
<td>0.0</td>
</tr>
<tr>
<td>71–80</td>
<td>76.2</td>
<td>36.5</td>
<td>28.9</td>
<td>34.6</td>
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<td>81–90</td>
<td>85.7</td>
<td>30.9</td>
<td>29.3</td>
<td>40.4</td>
<td>0.3</td>
</tr>
<tr>
<td>&gt;90</td>
<td>93.8</td>
<td>25.4</td>
<td>33.2</td>
<td>39.9</td>
<td>0.0</td>
</tr>
</tbody>
</table>

Design: A total of 5417 specimens (27% men, 63% women) collected from residents in long-term care facilities were tested for the quantitative measurement of total vitamin D using Liaison. The results were separated into deficiency (≤20 ng/mL), insufficiency (21–29 ng/mL), sufficient (>30 ng/mL), and possible toxicity (>150 ng/mL). Patients were separated further by gender and age (<50, 51–60, 61–70, 71–80, 81–90, and >90 years).

Results: We found 32.3% of the samples had vitamin D level ≤20; only 38.2% had sufficient levels (Table). There was no difference between men and women except in the <50 years group where deficiency was higher in women.

Conclusions: Our data support the notion that vitamin D insufficiency is more common than was previously believed and increases with age because of the limited exposure to the sun in the elderly because of limited outdoor activity and the decrease in their ability to make vitamin D supplements (and calcium). Although exposure to sunshine is recommended, it is still controversial because of the risk of skin cancer and its limited effectiveness among the elderly.

Most Deviations in Handling Do Not Increase Potassium Concentrations in BD Serum Separator Tubes in Healthy Volunteers

| Potassium Concentration at Baseline and After Specimen Handling Deviation |
|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| Deviation                  | Mean (n = 9), mmol/L | SD (mmol/L) | Change, % | P Value |
| None (baseline)            | 4.49                     | 0.27         | NA         | NA     |
| Vigorously mixed after collection | 4.68                     | 0.20         | 4.2        | .004   |
| Not mixed after collection | 4.53                     | 0.24         | 1.0        | .10    |
| Held horizontal during 30-min wait | 4.49                     | 0.25         | 0.0        | >.99   |
| 15-min wait before spin | 4.39                     | 0.19         | -2.2       | .11    |
| Placed on rocker during 30-min wait | 4.39                     | 0.15         | -2.2       | .16    |
| Heated during 30-min wait | 4.37                     | 0.21         | -2.7       | .03    |
| Collected after EDTA tube | 4.45                     | 0.30         | -0.9       | .24    |
| Respun after initial analysis | 4.51                     | 0.29         | 0.5%       | .35    |

Abbreviations: EDTA, ethylenediaminetetraacetic acid; NA, not applicable.

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Clinical Correlation Between Point-of-Care i-STAT Troponin I and Laboratory Centaur Troponin I Ultra Assays
(Poster No. 19)
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Context: Point-of-care i-STAT (POC) Troponin I (Tnl) assays (Abbott Laboratories, Abbott Park, Illinois) are used in emergencies for triage of patients. Some discordance may exist between POC and the concurrent Centaur Troponin I Ultra (TPIU) assays (Siemens Healthcare Diagnostics Inc, Tarrytown, New York).

Design: Results of POC Tnl and TPIU for the same patient were compared within 60-minutes, and related clinical information was reviewed.

Results: Of 772 paired assays for patients with chest pain, there were 644 normal, 30 borderline, and 18 myocardial infarction (MI) results, as determined by both POC Tnl and TPIU, with a concordance rate of 90%. Of 80 discordant test pairs, 74 had normal POC Tnl results (≤0.09 mg/mL) but borderline TPIU values (0.07–0.77 ng/mL). Three pairs were diagnosed as MI by TPIU (≤0.78 ng/mL), but POC reported borderline values (10.59 ng/mL). Another 3 pairs were borderline by POC but normal by TPIU (≤0.06 ng/mL). Seven of 74 patients (9%) with normal POC Tnl but borderline TPIU eventually developed MI, which was confirmed by serial cardiac marker assays or coronary artery catheterization. Of 3 patients diagnosed with an MI based on TPIU values, only 1 MI was confirmed. Of 3 cases with normal TPIU but borderline POC Tnl, none had an MI. The other common causes of elevated TPIU or POC Tnl testing included cardiovascular disorders and renal failure.

Conclusions: The TPIU assay was more sensitive in diagnosing MI; however, it had a higher false-positive rate. Serial follow-up of Tnl levels in patients with chest pain is critical to facilitate a correct clinical diagnosis.

A Retrospective Review at the University of Alabama, Birmingham, on the Use of QuantiFERON-TB Gold In-Tube in Children
(Poster No. 20)
Virginia Dailey, MD (gin208@uab.edu); Elizabeth Kerr, MD; William Benjamin, PhD. Department of Pathology, University of Alabama at Birmingham.

Context: QuantiFERON-TB Gold In-Tube (QFT) is an interferon-γ release assay recently approved as a screening test for latent tuberculosis infection in immunocompetent adults. Few studies have assessed this assay in children. We evaluated the results of the use of the QFT test in children at our institution.

Design: The clinical and radiologic findings on all patients with QFT tests ordered from the pediatric hospital were reviewed.

Results: We identified 143 QFT tests performed at University of Alabama at Birmingham Hospital, of which 18% (n = 26) were carried out on patients 0.5 to 22 years (mean, 11.4; median, 11) including 14 males and 12 females. A clinical history was available for 24 patients; of those, 3 had suspicious social histories. The most common clinical finding was abnormal chest radiograph (18 of 24), including pneumonia/plural effusion (9 of 18), lymphadenopathy (6 of 18), and suspicious lung “mass” (4 of 18). The remaining 6 patients had nonlung granulomatous disease (3 of 6), immunosuppressant therapy with chronic cough (2 of 6), or positive tuberculin skin test only (1 of 6).

Positive, negative, and indeterminate QFT test results were found in 0, 22, and 4 patients, respectively. Tuberculin skin tests were placed in 14 patients (2 with potential exposure) that were positive in only 4 patients who were all subsequently negative or indeterminate by QFT; of those, 3 were given chemoprophylaxis despite the discordant QFT results.

Conclusions: The QFT test is being used for diagnosing active tuberculosis, rather than as a screening method, in children at our institution. However, 3 of 4 patients were treated based on tuberculin skin tests and clinical histories regardless of the nonpositive QFT results.

Down-Regulation of CD28 Receptor in Lyme-Positive Patients: A Test for Chronic Lyme Disease
(Poster No. 21)
Kilik Keshu, MD; Tatiana Perdomo, MD (tatiana.perdomo@danbhospi.org); Leonel W. Edwards, MD; Beverly Ellis, MT; Martha Woodruff, MT; Ramon N. Kranwinkel, MD. Department of Pathology, Danbury Hospital, Danbury, Connecticut.

Context: Lyme disease is caused by Borrelia burgdorferi. Infected individuals can progress to chronic joint inflammation. The CD28/B7 pathway plays a central role in immune responses against pathogens, autoimmune diseases, and graft rejection. We studied the expression of CD28 in the T cells of patients with Lyme disease during the off-peak season (December 2009–February 2010).

Design: We performed multiparametric analysis consisting of cellular light characteristics and the simultaneous staining for CD45 and CD28 on whole blood. We selected 62 patients for evaluation. Of these, 32 (52%) had a Lyme disease–positive 2-tier test. We used 30 patients with no history of Lyme disease as random controls; however, 6 patients were eliminated from the control group because of evidence of inflammation (see Table and histograms [Figure 93]).

Results: A 2-tailed t test was performed that showed a statistical significance between the means (P value = .005). Because of the low number of patients and not wanting to assume a parametric distribution, we performed a Mann-Whitney test, which also showed a statistically significant difference (P = .006).

Conclusions: A significant down-regulation of the CD28 receptor was observed in patients with a positive Lyme disease 2-tier test compared with controls, suggesting a causative association with decreased CD28 expression and Borrelia burgdorferi infection. The cohort of patients tested during the off-peak Lyme disease season and may be more representative of persistent cases of Lyme disease. The findings need to be validated in a cohort of patients clinically defined or self-defined with chronic Lyme disease to better understand the relationship in humans.

Lyme positive patient
Lyme-negative patient (no history of Lyme disease)

A Computational Analysis of Melanocytic Lesions
(Poster No. 22)
Jayson Miedema, MD1 (jmiedema@unch.unc.edu); James S. Maron, PhD2; Marc Neithammer, PhD2; David Borland, PhD2; John Woosley, MD, PhD2; Nancy Thomas, MD, PhD2. Departments of 1Pathology and Laboratory Medicine, 2Computer Science, Renaissance Computing Institute, and 3Dermatology, University of North Carolina, Chapel Hill.

Context: Melanoma is a significant cause of morbidity and mortality in the Western world. A diagnosis of melanoma is commonly made via histologic examination of clinically suspicious lesions. However, this diagnosis is often challenging given the difficulties in differentiating melanoma from other benign melanocytic lesions.

Design: Twelve slides of a representative, superficial, spreading melanoma were examined along with 11 slides representing conventional nevi. On the slides representing melanoma, 113 groupings of malignant melanocytes were identified, whereas 99 groupings of melanocytes from conventional nevi were identified. Nuclei were automatically segmented from the identified regions, and more than 40 appearance features were extracted (Figure 94). Using statistical analysis of the high-dimensional feature space, we compared the characteristics of these lesions.
Abstracts

Plasmacytoma-Like Posttransplant Lymphoproliferative Disorder Presenting as a Cutaneous Nodule
(Poster No. 24)

Christine S. Lin, MD (clin4@pathology.ufl.edu); Ian M. Bovio, MD; Ann A. Church, MD; Vladimir Vincok, MD. Department of Pathology, University of Florida, Gainesville.

Posttransplant lymphoproliferative disorder (PTLD) is a well-recognized complication following a solid organ or bone marrow transplant. It comprises a spectrum of pathologic patterns, ranging from reactive Epstein-Barr virus–driven lymphocytic/plasmacytic hyperplasia to high-grade malignant lymphomas. PTLD may involve the lymph nodes or extranodal tissue at any site. Here, we present a plasmacytoma-like PTLD, a very rare form of PTLD, with an even less-common initial presentation as a cutaneous nodule. Using morphologic and immunophenotypic approaches, we studied a case of plasmacytoma-like PTLD in a cutaneous nodule that developed in a patient on immunosuppressive therapy following a heart and unilateral kidney transplant. The neoplasm demonstrated a diffuse infiltration of CD138-positive, morphologically atypical, k-restricted plasma cells with a proliferation index of more than 40% (Figure 95). In situ hybridization for Epstein-Barr virus was positive. This case highlights the importance of increasing awareness of this entity in all organ systems, including the skin.

Comparison of CD10 and Procollagen 1 Expression in Select Fibrohistiocytic Tumors
(Poster No. 25)

Adeel Ahmad, MD1 (aahmad@tuftsmedicalcenter.org); Jennifer O’Brien, MD, PhD2; Harty Ashby-Richardson, DO3; Scott Schlauder, MD2; Mandana Mahmoodi, MD. 1Department of Pathology, Tufts Medical Center, Boston, Massachusetts; 2Department of Dermatology, Tufts Medical Center and Caris Cohen Dx, Boston, Massachusetts.

Context: Dermatofibrosarcoma protubersans (DFSP), dermatofibroma (DF), and atypical fibroxanthoma (AFX) are fibrohistiocytic tumors with overlapping morphology. Immunohistochemistry plays an important role in their diagnosis. Procollagen 1 and CD10 are recently recognized, immunohistochemical markers; their expression has been studied in DFSP, DF, and AFX.

Results: The staining pattern of CD10 was membranous, and the percentage of cells staining with a clear histologic pattern. These lesions tend to favor the face, back, and extremities. Histologically, they resemble verruca vulgaris with acanthosis, hypergranulosis, dense keratohyaline granules, and viral cytopathic effect often seen in the stratum corneum. Until now, the findings of prominent dendritic melanocytes and mature sebaceous cells in the cyst lining have not been reported. We do not feel that these findings alter the expected benign nature of this lesion. Instead, we report this case to suggest the possible adnexal embryonic origin of this lesion, given the presence of sebaceous cells and dendritic melanocytes that support this histologic lineage in our specific case.
Malignant Melanoma With Myxoid and Desmoplastic Features
(Poster No. 26)

Stephen Hammond, MD1 (stephen.hammond@bmc.org); Alicia Ogram, MD; Suraj Venna, MD; Deon Wolpowitz, MD. 1Pathology and 2Dermatology, Dermatopathology Section, Boston University Medical Center, Boston, Massachusetts; 3Washington Cancer Institute, The Melanoma Center, Washington, DC.

The histologic morphology and immunohistochemical profiles of malignant melanomas are notably varied. These features, which serve as diagnostic aids, become more relevant when describing rare melanocytic lesions with heterologous components, which may confound pathologists and broaden the differential diagnoses. We present a case of a 77-year-old, white woman, with no family history of melanoma, who presented with an amelanotic lesion on the acral surface of the right hallux. Routine hematoxylin-eosin staining of an incisional punch biopsy revealed a sparse junctional proliferation of atypical melanocytes with a biphasic dermal component, composed predominantly of scattered, moderate to severe, atypical melanocytes within a markedly myxoid stroma, as well as focal areas of spindle cells within a more fibrotic stroma. Immunoperoxidase staining showed the junctional and dermal lesional cells to be strongly and diffusely positive for S100 protein and focally and intermittently positive for MART-1/Melan-A. The dermal component was diffusely positive for p75NGFR-Rc and rarely positive for HMB-45. Negative staining for CD1a and cytokeratins excluded Langerhans and epithelial cellular proliferations, respectively. In evaluating cutaneous myxoid lesions, our report highlights both the utility of including neural crest-lineage markers (S100 protein and p75NGFR-Rc) in the immunohistochemical evaluation and the importance of considering rare melanoma variants in the differential diagnosis. Moreover, the coexpression of p75NGFR-Rc and S100 protein, in both the myxoid and spindle cell components of this tumor, provides support for the assertion that myxoid melanomas represent a desmoplastic melanoma variant.

Cytokeratin OSCAR: An Excellent Adjuvant or Alternative Immunostain for Carcinomas of Different Origins
(Poster No. 27)

Byung K. Kim, MD (freudkim@gmail.com); Plamen Kossev, MD. Department of Pathology, Monmouth Medical Center, Long Branch, New Jersey.

Context: The AE1/AE3 cocktail has been used to identify carcinomas as well as their metastases. However, variable sensitivity of AE1/AE3 in certain carcinomas emphasizes another cytokeratin stain is needed to improve the detection rate of carcinomas of skin, lung, kidney, prostate, and liver. Immunohistochemical staining showed the junctional and dermal lesional cells to be strongly and diffusely positive for S100 protein and focally and intermittently positive for MART-1/Melan-A. The dermal component was diffusely positive for p75NGFR-Rc and rarely positive for HMB-45. Negative staining for CD1a and cytokeratins excluded Langerhans and epithelial cellular proliferations, respectively. In evaluating cutaneous myxoid lesions, our report highlights both the utility of including neural crest-lineage markers (S100 protein and p75NGFR-Rc) in the immunohistochemical evaluation and the importance of considering rare melanoma variants in the differential diagnosis. Moreover, the coexpression of p75NGFR-Rc and S100 protein, in both the myxoid and spindle cell components of this tumor, provides support for the assertion that myxoid melanomas represent a desmoplastic melanoma variant.

Design: A tissue microarray was constructed from 48 different carcinomas of the skin, lung, kidney, prostate, and liver. Immunohistochemical staining with AE1/AE3 and OSCAR were performed. The staining intensity and area were scored as 0 to 3 and 0 to 4, respectively, according to a semiquantitative scale. The final score (0 to 12) was calculated as the intensity score multiplied by the area score. The average staining intensity and area were scored as 0 to 3 and 0 to 4, respectively, according to a semiquantitative scale. The final score (0 to 12) was calculated as the intensity score multiplied by the area score. The average final score was used to compare both immunostains on carcinomas of different origins.

Results: OSCAR staining in basal cell carcinomas of skin and prostatic adenocarcinomas was about twice or three times stronger than AE1/AE3 staining, whereas AE1/AE3 staining on squamous cell carcinomas of skin was nearly twice as strong as OSCAR staining (Table). Renal cell carcinoma, pulmonary adenocarcinoma, and pulmonary squamous cell carcinoma were stained similarly with OSCAR and AE1/AE3. Hepatocellular carcinoma stained only with OSCAR.

Results of AE1/AE3 and OSCAR Staining on Different Carcinomas

<table>
<thead>
<tr>
<th>Carcinoma</th>
<th>AE1/AE3</th>
<th>OSCAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal cell carcinoma (n = 8)</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Squamous cell carcinoma of skin (n = 13)</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Renal cell carcinoma (n = 10)</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Prostatic adenocarcinoma (n = 12)</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>Pulmonary adenocarcinoma (n = 2)</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Pulmonary squamous cell carcinoma (n = 1)</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Hepatocellular carcinoma (n = 2)</td>
<td>0</td>
<td>10</td>
</tr>
</tbody>
</table>

Conclusions: OSCAR may be considered as an excellent adjuvant or alternative immunostain to improve the detection rate of carcinomas of different origins.

Additional Levels and Phosphohistone H3 (PPH3) Expression Are Useful in Evaluating Proliferation Activity in Thin (T1x) Melanomas
(Poster No. 28)

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Context: According to the melanoma staging system in the 7th edition of AJCC Cancer Staging Manual, the presence of a single mitosis in a melanoma, 1 mm thick or less, is sufficient to raise the stage from T1a to T1b. The objectives of this study were to evaluate whether additional levels of the lesions originally classified as T1a would ultimately change the staging and to assess the utility of PPH3 immunostaining as an aid for detecting mitoses.

Design: A total of 60 primary melanomas were examined. In a pilot study, we analyzed 30 cases of T1x melanomas distributed among 26 cases without mitosis (T1a) and 4 cases, as controls, with 1 mitosis/mm² or more (T1b). The original hematoxylin-eosin (H&E) slides were reviewed, and 6 levels were done every 50 μm. One level (at 100 μm) was immunostained with PPH3 MAB (1/100, Cell Signaling Technology, Inc, Boston, Massachusetts) and ALP-Fast red revelation. The numbers of stained nuclei, both nonmitotic and mitotic, per square millimeter, were counted.

Results: Additional levels revealed the presence of ≥1 mitosis/mm² in 9 (34%) melanomas initially reported as T1a. PPH3 revealed the presence of mitoses in 5 other cases confirmed as T1a based on the additional H&E tests. These cases were small-cell melanomas with basophilic nuclei. In total, 53% of the melanomas initially classified as T1a according to the 2010 AJCC melanoma classification were actually T1b.

Conclusions: The 7th edition AJCC melanoma staging system puts too much emphasis on the presence of a single mitosis that is highly subjective to sampling effect. PPH3 immunostaining is useful as an additional tool to help identify mitoses.

Acquired Perforating Collagenosis in the Setting of Human Immunodeficiency Virus
(Poster No. 29)

Joel Pinczewski, MD, PhD1 (jp123ok@yahoo.com); Robert Skinner, MD; Andrzej T. Slominski, MD, PhD. 1Department of Pathology, University of Maryland, Baltimore; Departments of 2Dermatology and 3Pathology, University of Tennessee Health Science Center, Memphis.

Reactive perforating collagenosis (RPC) represents an unusual skin disorder of unknown etiology that is characterized by the elimination of altered dermal collagen through the epidermis. This results in painful, ulcerated papules that often involve the extensor surfaces. RPC occurs in both an inherited and an acquired form. The acquired form is mainly seen in the setting of uremia or diabetes mellitus. Reports of RPC in patients with nonuremic human immunodeficiency virus (HIV) are extremely rare (2 reported cases) and have exclusively been associated with the use of indinavir treatment. Here, we report a case of RPC of the lower leg in a patient with end-stage HIV following the introduction of nonindinavir containing quadruple-dose HAART therapy, which included efavirenz. RPC is believed to occur because of damage to dermal collagen, often because of superficial trauma (scratching). The patient’s medications in this case are known to cause pruritus, and this lends support to the prevailing causative theory of RPC.

An Unusual Case of Granulomatous Scarring Alopecia
(Poster No. 30)

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Scarring granulomatous alopecia is an unusual condition that is associated with sarcoidosis and syphilitic infections. The following report describes a highly unusual and aggressive case of granuloma-
Dermatofibroma: Expanding the Histopathologic Spectrum

The patient was a 95-year-old, white woman who presented with a 1-week history of pruritus of the scalp. Despite treatment with antifungal medications and steroids, the patient’s condition progressed over several months into diffuse hair loss, first involving the scalp and later extending to involve the eyebrows. Biopsies revealed granulomatous folliculitis with degeneration of the follicular structures and inflammation. The follicular inflammatory infiltrate was initially a mixed neutrophilic and granulomatous/plasmolymphocytic infiltrate, which later developed into a pure granulomatous/plasmolymphocytic infiltrate. Results of PAS-F immunohistochemical staining for fungi, Kinyoun staining for mycobacteria, and Brown-Brenn staining for acid-fast organisms were all negative as were other tests for sarcoidosis and other infectious diseases such as syphilis. This case, therefore, represents an example of a highly unusual form of granulomatous, scarring alopecia not previously described in the literature (Figure 96).

**Cellular Neurothekeoma Mimicking Cellular Dermatofibroma: Expanding the Histopathologic Spectrum (Poster No. 31)**

**B. Thakral, MBBS, MD** (beenuthakral@gmail.com); **B. C. Gleason, MD**; **A. B. Thomas, MD**; **S. D. Billings, MD**; **T. A. Victor, MD**; **T. C. Cibull, MD**. 1 Department of Pathology, NorthShore University HealthSystem, Evanston, Illinois; 2 Department of Pathology, Diagnostic Pathology Medical Group, Sacramento, California; 3 Department of Pathology, The Cleveland Clinic, Cleveland, Ohio.

**Context:** Cellular neurothekeoma (CNT) is a benign cutaneous and soft tissue neoplasm. Most CNTs demonstrate a lobulated to micronodular architecture with nests and bundles of epithelioid to spindle cells embedded in a dense collagenous stroma. Rarely, CNT can demonstrate a predominantly fascicular growth pattern, often in association with a desmoplastic stroma.

**Design:** We retrieved 3 cases of CNT that demonstrated a predominantly fascicular pattern from the files of NorthShore University HealthSystem (Evanston, Illinois). The clinicopathologic features and accompanying immunohistochemical stains were evaluated. The clones of these monoclonal antibodies, dilutions, and their sources are summarized in the Table.

**Results:** All cases demonstrated a moderately cellular proliferation of epithelioid to spindle cells, with pale to eosinophilic, slightly granular cytoplasm, vesicular nuclei, and a single nucleolus arranged in a fascicular pattern with admixed, thick collagen bundles. One case had prominent epidermal hyperplasia, and all 3 cases demonstrated collagen trapping. The neoplastic cells expressed NKI-C3, CD10, and microphthalmia transcription factor and lacked expression of factor XIIIa, S100, epithelial membrane antigen, and CD34.

**Conclusions:** Our cases show an unusual pattern of CNT with a predominantly fascicular growth pattern, collagen trapping, and occasionally, epidermal hyperplasia. The overlap with cellular dermatofibroma is striking. The lack of factor XIIIa expression, expression of microphthalmia transcription factor, and plump to epithelioid cytomorphology with visible cytoplasm and focally prominent nuclei are helpful in distinguishing fascicular CNT from cellular dermatofibromas.

**Solitary Cutaneous Rosai-Dorfman Disease (Poster No. 32)**

**Adriana Olar, MD** (olar@bcm.edu); Andrea L. Haws, MD, MS; Todd M. LeLeux, MD; Linda K. Green, MD. 1,2 1 Department of Pathology, Baylor College of Medicine, Houston, Texas; 2 Department of Pathology, Michael E. DeBakey Veterans Affairs Medical Center, Houston.

Rosai-Dorfman disease (R-DD), or sinus histiocytosis with massive lymphadenopathy, is a benign, self-resolving, histiocytic proliferative disorder of unknown etiology that commonly affects young males. Different etiologies have been proposed, including viral, immune, and familial forms of the disease, the latter of which have recently been described. Extramedullary involvement is rare and usually accompanies nodal disease. Cutaneous and subcutaneous soft tissue infiltrates are the most commonly encountered extranodal manifestations of R-DD, but infiltrates may be seen in other sites. Pure extranodal, solitary, cutaneous involvement is very rare. We reviewed the files of our institution for the past 5 years for cutaneous histiocytic lesions. The clinical and histologic findings were reviewed. There was one identified case of cutaneous R-DD in a 65-year-old, black man. Clinically, he presented with a 0.8-cm, solitary, erythematous, firm, nonpainful abdominal nodule, which was noticed during a routine skin examination. There was no evidence of lymphadenopathy or other systemic signs of R-DD. Histology showed a polymorphic inflammatory infiltrate, including S100-positive and focally CD68-positive histiocytes showing emperiploesis (S100 positivity shown in Figure 97, ×400 magnification). Because of its inflammatory appearance, solitary cutaneous R-DD may be overlooked and misdiagnosed as an abscess or infectious disorder. Although it is rare, it should be considered in cases with atypical histiocytic infiltrates, especially when emperipolesis is seen. An S100 stain is needed to confirm the diagnosis and should be performed on such suspicious cases. Very few of these patients advance to a systemic disease, and the epidemiology is different from that for the nodal disease.

**Antibodies Used for Immunohistochemical Analysis**

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Clone</th>
<th>Dilution</th>
<th>Source</th>
<th>Antigen Retrieval Method</th>
</tr>
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<tr>
<td>S100</td>
<td>DR96+</td>
<td>1:1000</td>
<td>Biocare Medical, Concord, California</td>
<td>Biocare Decloaking Chamber</td>
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<td>AC-1A1</td>
<td>Prediluted</td>
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<tr>
<td>MITF</td>
<td>D5</td>
<td>1:100</td>
<td>Dako, Glostrup, Denmark</td>
<td>Biocare Decloaking Chamber</td>
</tr>
</tbody>
</table>

**Abbreviations:** EMA, epithelial membrane antigen; MITF, microphthalmia transcription factor.
Determination of Melanocytes Within Variants of Basal Cell Carcinomas
(Poster No. 33)
Christine Lin, MD (clin@pathology.ufl.edu); Frederick L. Glavin, MD. Department of Pathology, University of Florida, Gainesville.

Context: The concept of melanomas arising from a malignant transformation of native melanocytes inhabiting basal cell carcinomas (BCCs) and thus resembling collision tumors has not been fully elucidated.

Design: This study characterized the density and distribution of melanocytes within 6 different variants of BCCs: micronodular, nodular, morphea, cystic, superficial, and infundibular cystic types. We stained 57 total cases of BCC with Melan-A antibodies.

Results: Fifty-two of 57 BCCs (91%) were populated by dendritic melanocytes. The melanocytes inhabiting basal cell lesions were of nonaggregate, singly dendritic form. Slender types of BCCs, such as micronodular, morphea, and infundibular cystic, were found to have a peripheral staining pattern. No correlation was found between the size of the nodular variant of BCC and the distribution of melanocytes. The density of melanocytes in BCCs was compared with the overlying and adjacent uninvolved epidermis. Nodular and micronodular variants had similar or more melanocytes in relation to the healthy epidermis, respectively. An increase in melanocytes at the upper portion of the nodular variant of BCCs was compared with the overlying epidermis. No correlation was found between the size of the nodular variant of BCCs and the distribution of melanocytes. The peripheral staining pattern. No correlation was found between the size of the nodular variant of BCCs and the distribution of melanocytes. The peripheral staining pattern.

Conclusions: The distribution, density, and gradient of melanocytes within the different subtypes of basal cell carcinomas were analyzed in hopes of providing further knowledge about the development of collision tumors.

Epidermodysplasia Verruciformis Arising in a Patient on Adalimumab: Report of a Rare Case and Review of Literature
(Poster No. 34)
Lanie Galman, MD (lgalman@bhs1.org); Xiangrong Zhao, MD; Daniel J. Carter, MD. Department of Pathology, Berkshire Medical Center, Pittsfield, Massachusetts.

Epidermodysplasia verruciformis (EV) is a rare, inherited disorder characterized by the development of multiple warts and pityriasis versicolor-like cutaneous lesions. Sporadic EV has been reported in patients positive for human immunodeficiency virus and in those with renal transplants. Here, we report a case of a 63-year-old woman with polyfactorial coagulopathy, Rubinstein-Taybi syndrome, trisomy 9, Turner syndrome, and Gardner syndrome.

Adalimumab: Report of a Rare Case and Review of Literature
(Poster No. 35)
Calvin Chen, DO; Tee Lang, MD (tlang@tuftsmedicalcenter.org); Miguel Stadecker, MD, PhD. Department of Pathology, Tufts Medical Center, Boston, Massachusetts.
Pilomatricoma, a benign cutaneous neoplasm with differentiation toward hair matrix, was first described by Malherbe and Chennatis in 1880 as a calcifying epithelioma. The tumor is common in children, with a slight female predominance, and most cases occur in the first 2 decades of life. The exophytic variant of pilomatricoma is rare with 2 cases cited in the literature. We report a case of a 43-year-old, white woman who presented with a 1-year history of a slow-growing, exophytic and crusted nodule on the forehead. The lesion grew rapidly during the last 2 months. The nodule was saucerized to reveal a tan-gray exophytic nodule with an irregular, crusted surface and chalky white areas on the cut face. Microscopic examination showed an exophytic, lobulated proliferation of pilomatrical epithelium with necrosis, including shadow cells. The overlying epidermis was ulcerated, and there was marked acute and chronic inflammation and granulation tissue extending to the deep edge of the biopsy. Our case displayed an unusual, exophytic variant of pilomatricoma. It is of clinical relevance because crusted, exophytic pilomatricoma can mimic squamous cell carcinoma or other neoplastic cutaneous lesions, and it should be considered a differential diagnosis in the clinical setting of a middle-age patient presenting with an exophytic, crusted skin lesion. Additionally, there are reported familial cases of pilomatricoma to be associated with myotonic dystrophy, polyfactorial coagulopathy, Rubinstein-Taybi syndrome, trisomy 9, Turner syndrome, and Gardner syndrome.

TGFβ-Like Events Mediated by Four-and-a-Half LIM Domain Members Regulates Proliferation in Melanoma Cells
(Poster No. 36)
Maria E. Romero, MD; Julio C. Valencia, MD (valencij@mail.nih.gov); Metin Ozdemirli, MD, PhD; Vincent J. Hearing, PhD. 1Department of Pathology, Georgetown University Hospital, Washington, DC; 2Laboratory of Cell Biology, National Institutes of Health, Bethesda, Maryland.
Context: TGFβ has an ambiguous, dual role in cancer progression. SMADs are direct effectors of TGFβ actions. However, other signaling pathways have been implicated as well, but the molecular mechanisms by which TGFβ receptors engage in non-SMAD pathways remain unknown. Recent evidence suggests that four-and-half LIM (FHL) family members suppress tumor cell growth through TGFβ-like signaling pathways. Our goal is evaluate whether FHL members are embedded in the proliferation mechanisms of human melanoma cells.

Design: Immunohistochemical detection of FHL members was performed in a melanoma tissue array. Signaling and molecular responses of FHL members were evaluated in melanoma cells secreting or not secreting TGFβ.

Results: Using a tissue-array of primary and metastatic melanomas, we found FHL2 up-regulated in most tumors. Exogenous TGFβ increased FHL2 and β-catenin protein levels in melanoma cells whether or not they secreted TGFβ. Surprisingly, ectopic TGFβ reduced the protein levels of SMAD 2/3 and key SMAD-target genes, such as c-myc, suggesting an inverse response toward exogenous TGFβ. Our preliminary results indicate that such response might be mediated through FHL and the Wnt signaling pathway.

Conclusions: FHL2 is a suitable marker for melanoma and might account for the different response of melanoma cells to TGFβ.

Epithelial Immunohistochemical Markers Distinguish Pigmented Basal Cell Carcinoma From Melanoma

(Poster No. 37)

Lynden P. Bowden, III, MD, MPH (pete.bowden@us.army.mil); David M. Burch, MD. Department of Pathology and Laboratory Medicine, National Naval Medical Center, Bethesda, Maryland.

Superficial pigmented basal cell carcinoma can histologically mimic melanoma in situ with conventional staining, especially when there is a prominent intraepidermal component. Misdiagnosis of melanoma may lead to more extensive and unnecessary surgical procedures, but the pathologist must also maintain a high index of suspicion. We present a case of a 73-year-old, white man who underwent a shave biopsy of a 1-cm lesion on the neck. The patient had a history of squamous cell carcinoma of the skin. The lesion was biopsied and sent for pathological evaluation. On gross examination, the biopsy showed a firm, nodular mass measuring 1 x 1 x 0.5 cm. On histological examination, the mass was diagnosed as an epidermal nevus. The patient was monitored and followed up for further evaluation. We present this case to illustrate the importance of differential diagnosis in histological evaluation of skin lesions.
An Unusual Presentation of an Adrenal Teratoma (Poster No. 40)

Maria F. Gonzalez, MD (Maferg13.Gonzalez@ttuhsc.edu); Thomas McGill, MD; Mitchell S. Wachtel, MD; Viviane Mamlouk, MD. Departments of 1Pathology and 3Pediatric Surgery, Texas Tech University Health Sciences Center, Lubbock.

We report the case of a 10-year-old girl with macroscopic hematuria and mild abdominal pain for 1 month. Results of the physical examination were normal. A renal ultrasound showed a 4.6 × 4.0 × 3.9-cm hypeechoic mass at the upper pole of the right kidney. We suspected it to be an adrenal adenoma. The patient underwent total adrenalectomy. The 34.9-g, friable specimen measured 5 × 5 × 3-cm. It was composed of bone fragments, skin, and fatty tissue. The microscopic examination showed the presence of ectomesenchymal and ectodermal elements consistent with a mature teratoma of the adrenal gland. Mature teratomas are well known for their clinical and histologic pleomorphism.

We report the relatively rare finding of a mature adrenal teratoma that presented with macroscopic hematuria and abdominal pain mimicking a radiographically suspected adrenal adenoma. This case broadens the differential diagnosis of macroscopic hematuria to include the unusual presentation of an adrenal teratoma. Hypechoic masses of adrenal glands may suggest aberrant osseous elements that heighten the probability of a rare mature adrenal teratoma.

Characterization of Cell Cycle Progression in Malignant Thyroid Neoplasms of Follicular Cell Origin by Immunohistochemical Staining (Poster No. 41)

Jing Liu, MD, PhD (Jing.Liu.18@uth.tmc.edu); Robert E. Brown, MD. Department of Pathology and Laboratory, University of Texas Medical School, Houston, TX.

Context: Malignant thyroid neoplasms of follicular cell origin include a spectrum of carcinomas, ranging from low-grade to rapidly lethal, high-grade carcinoma. Characterization of cell cycle in these neoplasms would allow for exposing therapeutic targets. This study was designed to use immunohistochemistry to investigate cell cycle progression and proliferation in various malignant thyroid neoplasms of follicular cell origin.

Design: We retrieved 10 follicular thyroid carcinomas (FTCs), 14 papillary thyroid carcinomas (PTCs)-conventional type, 9 PTCs-follicular variant, and 2 anaplastic thyroid carcinomas (ATCs). Tissue microarrays (TMAs) were constructed using 2.0-mm cores from formalin-fixed, paraffin-embedded thyroidectomy tissue blocks. The TMA sections were immunohistochemically stained for cyclin D1, Skp2, Ki-67, and p27. Nuclear staining was considered for all markers. The extensiveness (0%–100%) of immunoreactive tumor cells in each case was evaluated. Mitotic index was obtained.

Results: In PTCs, the conventional type, PTCs-follicular variant, and ATCs, mean expressions were 13.3%, 23.6%, 17.0%, and 42.5% for cyclin D1; 1.0%, 0.4%, 0.3%, and 35.0% for Skp2; 3.1%, 1.8%, 2.1%, and 42.5% for Ki-67; and 24.2%, 13.0%, 15.4%, and 1.5% for p27, with mitotic indices of 1.6, 0.8, 1.2, and 0.2% per 10 high power fields, respectively.

Conclusions: In comparison with other lower-grade thyroid carcinomas, ATCs present with increased cell cycle progression/proliferation evidenced by high expression of cyclin D1 (G1 phase), Skp2 (S phase), and Ki-67 (G1, S, G2, and M phases), increased mitotic index, and correspondingly low p27. These findings provide insight into the selection of cell cycle-specific therapeutic agents for different types of malignant thyroid neoplasms of follicular cell origin.

Finding a Needle in a Haystack: Autoimmune Adrenalitis and Peripheral Neuroblastic Tumors (Poster No. 42)

Nicole A. Cipriani, MD (nicole.cipriani@snhospitals.edu); Isil Halac, MD; Allie N. Husain, MD. Departments of 1Pathology and 3Pediatric Endocrinology, The University of Chicago, Illinois.

Adrenalitis in adults is present in >60% of autopsies involving patients older than age 60. Primary or secondary adrenal insufficiency (AI) occurs in 100 million to 200 million adults. Most people with primary AI have autoimmune adrenalitis or Addison disease (AD). AI in pediatrics is rare and is caused by congenital adrenal hyperplasia and AD. We present a case of coincident adrenalitis and neuroendocrine tumors in a 16 year old. We evaluate the prevalence of AD in resections for peripheral neuroblastic tumors: ganglioneuroma (GN), ganglio-neuroblastoma (GNB), and neuroblastoma (NB). All resected retroperitoneal/abdominal GNs, GNBs, and NBs were identified. Each case with adrenal was evaluated for adrenalitis. Other findings were noted. A total of 55 specimens were identified, 22 with adrenal: 18 pediatric and 4 adult. In the pediatric group, adrenalitis and GN were present in 1 case. CD20 and CD3 immunohistochemistry showed mainly T cells in the adrenal versus B cells in the GN. Of the remaining pediatric cases, 12 were newborn; 1 was NB and GN, and 4 were GNB. Seven cases were normal; 10 had hemorrhage, congestion, or fetal cortical involution. In the adult group, all cases with GN did not exhibit adrenalitis. Three were normal and 1 had congestion. Autoimmune adrenalitis in the pediatric population is rare and even rarer in the setting of peripheral neuroblastic tumors. In this case of coincident AD and GN, the inflammation in the adrenal and that in the tumor were unrelated because the adrenal showed a predominance of T cells, whereas the tumor showed B cells. Of the 21 adult and pediatric adrenal glands without adrenalitis, most findings were normal.

Clear Cell Variant of Pancreatic Endocrine Neoplasm in a Patient With Li-Fraumeni Syndrome: An Unusual Neoplasm With Cytohistologic Correlation (Poster No. 43)

Sherry L. Jilinski, MD (sherry.jilinski@comcast.net); Michael Roeyer, MD. Department of Anatomic Pathology, National Naval Medical Center, Bethesda, Maryland.

Li-Fraumeni syndrome is an autosomal dominant tumor syndrome due to germ-line mutations of the TP53 gene. Affected patients are susceptible to many tumors, including breast carcinoma, soft tissue sarcomas, osteosarcoma, adrenocortical carcinoma, brain tumors, leukemia, and multiple other carcinomas, such as pancreatic adenocarcinoma. However, no association has been documented between Li-Fraumeni syndrome and neuroendocrine tumors. Familial pancreatic endocrine tumors have been associated with Von Hippel-Lindau syndrome and often exhibit clear cell morphology. We report a case of a 34-year-old woman with documented Li-Fraumeni syndrome who had an incidental mass in the body of the pancreas that was discovered during a staging computed tomography scan for breast cancer radiation therapy. It was suggested to be a clear cell variant of adenocarcinoma, so the patient underwent partial pancreatectomy and splenectomy for further evaluation. Histologic examination revealed a 2-cm pancreatic endocrine neoplasm, clear cell variant. Immunohistochemistry showed positive staining for synaptophysin (strong), chromogranin (moderate), CD10 (strong), pancytokeratin (strong), and epithelial membrane antigen (weak), supporting the diagnosis. Although pancreatic adenocarcinoma is associated with Li-Fraumeni syndrome, we, herein, present a case of clear cell pancreatic endocrine neoplasm arising in a patient with this syndrome. Because these tumors may have overlapping morphologic features, we propose that pancreatic endocrine tumors, specifically the clear cell variant, may be an under-recognized tumor in these patients.

Carcinoid Tumor of the Middle Ear Presenting as Chronic Otitis Media and Conductive Hearing Loss (Poster No. 44)

Wenping Li, MD, PhD (wenping@gmail.com); Maria Romero, MD; Hun H. Kim, MD; Metin Ozcemirli, MD, PhD. Departments of 1Pathology and 2Otolaryngology, Georgetown University Hospital, Washington, DC.

This is the case of a 21-year-old woman with a history of left-sided conductive hearing loss and chronic otitis media who had a tympanos- tomy tube placed a year ago that did not improve her hearing. Two months later, she developed significant left ear pain. Computed tomography showed complete opacification of the middle ear cavity without evidence of bony erosion or ossicular chain erosion. Under the operation microscope, she had a thickened tympanic membrane. There was a yellow cystic lesion filling up the entire middle ear space extending into the eustachian tube area. This was associated with significant cholesteatoma and mucosal edema. Left tympanomastoid-ectomy and removal of a middle ear mass were performed. Pathologic examination showed fibrous tissue with infiltrative epithelioid tumors nests morphologically resembling neuroendocrine tumor and compatible with middle ear adenoma (carcinoid tumor of the ear) with chronic otitis media in the background. By immunohistochemistry, the tumor cells were positive for keratin, chromogranin, and CD56. Although CD56, chromogranin, synaptophysin, epithelial membrane antigen, and CD99 were negative for CD34, S100, desmin, and smooth muscle actin. MIB-1 proliferative index was low (less than 5%). Carcinoid tumor
of the middle ear can present as chronic otitis media and conductive hearing loss. The primary treatment is complete surgical removal. Although it is a benign tumor, it has metastatic potential. Awareness of this rare entity may allow prompt diagnosis and treatment.

**Plasmablastic Lymphoma: Usual and Unusual Presentations**  
*(Poster No. 45)*

Xuchen Zhang, MD, PhD (xuchen.zhang@downstate.edu); Alifya Oultache, MD; Constantine Axiotis, MD, Department of Pathology, Kings County Hospital Center and SUNY Downstate Medical Center, Brooklyn, New York.

Plasmablastic lymphoma (PBL) is an aggressive B-cell lymphoma, most frequently arising in the oral cavity of patients infected with human immunodeficiency virus (HIV). Although clinical features may help in the diagnosis, an extranodal, especially the colon, peripheral blood (PB), or bone marrow (BM), makes PBL more difficult to diagnose. We report 2 cases of PBL with usual (case 1) and unusual (case 2) presentations. Case 1 was a 55-year-old, African-American man with AIDS who presented with weight loss and odynophagia. Mouth examination showed fungating lesions on hard palate and parapharynx covered with white exudates. Hard palate biopsy showed medium to large sized neoplastic cell infiltration. The neoplastic cells resembled immunoblasts to cells with plasmablastic differentiation. Numerous mitotic figures and apoptotic cells were present. Immunostains revealed positivity for CD38 and negativity for CD20, CD3, and AE1/AE3. Case 2 was a 69-year-old, African-American woman with AIDS who presented with diarrhea and weakness. A PB smear showed plasmacytoid lymphocytosis. The PB flow cytometry showed CD138+, CD20+, and k-restricted B cells. A BM biopsy revealed markedly hypercellular BM (80%–90%) with infiltration by large, plasmacytoid lymphocytes. The diagnosis was then assigned to 1 of 3 categories: concordant, discordant, or deferred. The overall sensitivity was calculated using the frozen section diagnosis in relation to the permanent, paraffin-embedded section diagnosis.

**Results:** Of the 179 cases examined, the results were concordant (n = 140, 78%), discordant (n = 3, 2%), and deferred (n = 36, 20%). The overall sensitivity of the salivary gland frozen section in our institutions was 98% (excluding cases in the deferred category). Among our discordant cases, the pitfalls recognized were infarctions with squamous metaplasia mimicking squamous cell carcinoma, hypercellularity in benign lesions mimicking malignancy, and sampling issues.

**Conclusions:** Frozen section in salivary gland lesion diagnosis is often a reliable modality to provide an intraoperative consultation. Our data are comparable to those in the literature. Being wary of the diagnostic pitfalls, keeping close communication with the surgeon, and understanding the diagnostic implications are all critical in ensuring accuracy.

**Carcinoma Ex-Pleomorphic Adenoma of the Nasal Cavity**  
*(Poster No. 48)*

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Carcinoma ex-pleomorphic adenoma is a very uncommon neoplasm, especially in extraparotid and minor salivary gland sites. This tumor arises from pleomorphic adenoma following malignant transformation of the epithelial and/or myoepithelial component(s). We report a rare case of carcinoma ex-pleomorphic adenoma of the nasal cavity. Fewer than 10 such cases have been reported in the literature. A 58-year-old, white man presented with a 4-month history of worsening right nasal obstruction, anosmia, and epistaxis. Examination revealed a necrotic mass filling the right nasal cavity with septal deviation and perforation. A computed tomography scan showed a 5.5-cm mass with ethmoid extension and right-sided sinus opacification. Resected fragments grossly consisted of tan tissue with focal hemorrhage. Microscopically, a multidisciplinary approach is essential for accurate diagnosis of unusual malignancies.

**Frozen Section Diagnostic Accuracy in Salivary Gland Lesions**  
*(Poster No. 47)*

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Department of Pathology and Laboratory Medicine, University of Cincinnati, Cincinnati, Ohio.

**Context:** Frozen sections are a common modality used by pathologists to provide a rapid, intraoperative diagnosis to aid surgeons in patient management. Herein, we evaluate the level of concordance and overall sensitivity of frozen section diagnosis in salivary gland lesions and correlate our data to highlight diagnostic pearls, pitfalls, and implications.

**Design:** The consecutive records were reviewed of 1707 patients from 3 affiliated hospitals who had undergone surgeries with salivary gland involvement during a 10-year span (January 1, 2000, to December 31, 2009). Of these, 179 cases were identified in which a frozen section had been requested and performed. The diagnosis was then assigned to 1 of 3 categories: concordant, discordant, or deferred. The overall sensitivity was calculated using the frozen section diagnosis in relation to the permanent, paraffin-embedded section diagnosis.

**Results:** Of the 179 cases examined, the results were concordant (n = 140, 78%), discordant (n = 3, 2%), and deferred (n = 36, 20%). The overall sensitivity of the salivary gland frozen section in our institutions was 98% (excluding cases in the deferred category). Among our discordant cases, the pitfalls recognized were infarctions with squamous metaplasia mimicking squamous cell carcinoma, hypercellularity in benign lesions mimicking malignancy, and sampling issues.

**Conclusions:** Frozen section in salivary gland lesion diagnosis is often a reliable modality to provide an intraoperative consultation. Our data are comparable to those in the literature. Being wary of the diagnostic pitfalls, keeping close communication with the surgeon, and understanding the diagnostic implications are all critical in ensuring accuracy.

**Clinicopathologic Study of an Unusual, Bilateral Middle Ear Tumor in an Infant**  
*(Poster No. 46)*

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We report an unusual case of a malignant epithelial neoplasm with neuroendocrine differentiation in an 8-month-old female with bilateral, destructive mastoid lesions involving the external auditory canal with intracranial, extradural extension into the temporal lobes. The mother of the infant had died of cervical cancer 3 days after delivery. The patient died 3 months after initial diagnosis. Although PBL typically presents in the oral cavity, extravasation locations can be involved. Large clinical and molecular studies on oral and extracranial involvement are needed to further characterize this infrequent type of lymphoma.

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the tumor showed nodules of closely packed nests, trabeculae, and cords of atypical epithelioid and spindle cells in a myxoid and hyaline stroma (Figure 101, left). There were foci of bland epithelial cells forming tubules surrounded by myoepithelial cells merging with chondromyxoid stroma consistent with coexisting pleomorphic adenoma (Figure 101, right). Most of the tumor cells were positive for pancytokeratin, p63, and calponin, along with an increased proliferation index of 80% on Ki-67 stain (compared with <20% in the benign component), confirming the diagnosis of carcinoma ex-pleomorphic adenoma with myoepithelial differentiation. Although malignant transformation of the myoepithelial component portends an immediately aggressive clinical course in carcinoma ex-pleomorphic adenoma of the salivary glands, the few cases reported in the nasal cavity preclude a definitive prognosis in our patient. At 10 months’ follow-up, our patient remains tumor free.

Oropharyngeal Squamous Cell Carcinomas in Younger Patients Are More Likely to Be Human Papillomavirus-Related

(Poster No. 49)

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Context: The incidence of oropharyngeal squamous cell carcinoma (OPSCC) has increased, particularly among younger patients. High-risk human papillomavirus (HPV), specifically HPV-16, is recognized as an independent risk factor for OPSCC. Immunohistochemistry for p16 correlates strongly with HPV gene expression. HPV-related p16 expression is associated with improved survival and response to radiation therapy. We evaluated the immunohistochemical expression of p16 in a series of patients with OPSCC and compared the results by age, gender, and oropharyngeal site.

Design: We reviewed the biopsy specimens of 129 patients with OPSCC. Sites included tonsil, base of tongue, soft palate, and oropharyngeal wall. Immunohistochemistry for p16 was performed on formalin-fixed, paraffin-embedded tissue using the labeled streptavidin-biotin method. Tumors were classified as p16-positive (strong, diffuse, nuclear, or cytoplasmic staining) or negative.

Results: Overall, 47.5% of the OPSCCs expressed p16. Eighteen of 26 patients (69.2%) younger than 50 years expressed p16. The odds ratio was 3.14. (95% confidence interval [CI], 1.25–7.88; P = 0.02). Tonsillar carcinomas were more likely to express p16 compared with those at the base of tongue. The odds ratio was 2.3. (95% CI, 1.09–4.87; P = 0.03). Gender was marginally associated with expression of p16 (P = 0.07).

Conclusions: Younger patients (younger than 50 years) with OPSCC were more likely to have positive expression of p16 compared with older patients (older than 50 years). Tonsillar carcinomas were the most likely to be associated with positive expression of p16. Immunohistochemistry for p16 is simple, easy to interpret, and can be routinely performed on newly diagnosed patients with OPSCC to stratify cases with a more favorable prognosis and improved response to radiotherapies.

Schwannoma of Paranasal Sinus With Unusual Features

(Poster No. 50)

Aleksandar Vodovnik, MD (whauff@gmail.com); Ståle Sund, MD, PhD. Department of Pathology, Forde Central Hospital, Forde, Norway.

A subpopulation of CD34+ cells has been observed in schwannomas at various sites. However, substantial CD34 expression is unusual in schwannomas of the paranasal sinuses. A 28-year-old man of Asian-Indian origin complained of longstanding, unilateral nasal obstruction. Clinical examination and computed tomography revealed a stalked polyoid lesion arising from the left posterior nasal septum and growing into the sphenoidal sinus. Familial and personal medical history revealed no evidence of neurofibromatosis, trauma, or previous surgery. The specimen consisted of a tan-colored, firm, slightly lobular, and polyoid tissue, measuring 3 × 2 × 1 cm. Antoni A areas prevailed, and Verocay bodies were often associated with an extensive myxoid change. The tumor showed poorly demarcated borders, focally leading to ulceration. Proliferation fraction was virtually zero, and necrosis was absent. Focal degeneration, hemorrhaging, and coarse pigmentation were observed. S100 showed weak to moderate, cytoplasmic, and nuclear diffuse reaction in tumor cells throughout. CD34 expression was strong and diffuse in spindle cells, restricted to Antoni B areas (Figure 102), and accompanied by fewer CD68+ and smooth muscle actin-positive spindle cells. A few CD34+ cells were morphologically similar to those positive for S100. Desmin, Melan A, epithelial membrane antigen, and CD31 were negative. CD34 expression in schwannomas of the paranasal sinuses necessitates careful interpretation. It may be related to an increase in supportive and endoneurial fibroblastic cells in association with degeneration and duration of the lesion. Clinical, radiologic, and morphologic correlation still has a pivotal role in diagnosing cases with a divergent immunohistochemical profile.

Metastatic Clear Cell Renal Cell Carcinoma to the Tongue

(Poster No. 51)

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Clear cell renal cell carcinoma is a malignant neoplasm that most commonly metastasizes, hematogenously, primarily to the lung. Yet, it has a well-known propensity to metastasize to unusual sites. This is the case of a 53-year-old man with a history of left kidney clear cell renal cell carcinoma who presented with a large right dorsal tongue lesion. An incisonal biopsy of the lesion was performed. The microscopic examination revealed an ulcerated neoplasm with cells demonstrating clear cytoplasm and a prominent network of small thin-walled blood vessels. By immunophenotype, the tumoral cells were positive for pankeratin, vimentin, and CK10, and negative to epithelial membrane antigen, and CD34. Both the morphology and immunostains confirmed the diagnosis of metastatic clear cell renal cell carcinoma to the tongue. This is an exceedingly rare metastasis site for a renal cell carcinoma with only few cases reported in the literature.

Unusual Presentation of Metastatic Ductal Adenocarcinoma of the Pancreas

(Poster No. 52)

Kilik Kesha, MD1 (kilik.kesha@dan hosp.org); Max Llaudes, MD3; Marc Rappaport, DO2; Hadi El-Fanek, MD, 1 Departments of ‘Pathology and ‘ Medicine, Danbury Hospital, Danbury, Connecticut.

Pancreatic ductal adenocarcinoma first metastasizes to regional lymph nodes (72%–83%) and then to the liver (64%–80%) and lungs (27%–50%). Pancreatic cancer uncommonly metastasizes to the head and neck. We report the case of an 86-year-old woman with no significant past medical history who presented with a right mandibular mass. An x-ray and computed tomography scan showed an expansile osteolytic lesion in the right mandible. The patient underwent a biopsy of the mandibular mass. Grossly, the lesion showed multiple fragments of tan-pink soft tissue. Microscopically, the lesion consisted of stromal connective soft tissue infiltrated by a moderately differentiated malignant epithelial neoplasm arranged in solid nests and ductal-glandular components. Mitoses and necrosis were present. Immunohistochemistry stains were positive for CK7, CK20, carcinoembryonic antigen 19-9, and villin and were negative for estrogen receptor, progesterone receptor, TTF-1, WT-1, and CTX 2 (Figure 103). Histologic features were consistent with metastatic adenocarcinoma; primary sites included upper gastrointestinal (pancreatic and biliary) and head and neck. An abdominal computed tomography scan showed a mass in the pancreatic body. Pancreatic ductal adenocarcinoma presenting as a mandible mass is extremely rare, with only 2 previously reported cases, to our knowledge. It is believed that metastasis to this...
thyroid carcinoma. After workup and outside consultation a diagnosis of assisted in ruling out plasmablastic lymphoma. The location and focal lymphoma and being negative for human immunodeficiency virus, included plasmablastic lymphoma. However, the clinical information, negative for TTF-1 and B-cell and T-cell markers. The differential diagnosis were positive for CD138 and variably positive for cytokeratins but were Pathology of the tissue showed a predominance of pleomorphic giant cells appearance and calcifications. A total thyroidectomy was performed. weeks time. An ultrasound of the neck demonstrated an enlarged left lobe was found to have a left-sided neck mass that rapidly grew during a few weeks time. An ultrasound of the neck demonstrated an enlarged left lobe of the thyroid, secondary to a complex mass with heterogenous change is found in the angle or ramus of the mandible, the possibility of a pancreatic cancer should be kept in mind. In this case, it was the first indication of an undiagnosed, malignant tumor and prompted an evaluation for the primary tumor.

**CD138 (Syndecan 1)-Positive Anaplastic Thyroid Carcinoma**

(Poster No. 53)

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Anaplastic thyroid carcinoma (ATC) represents less than 5% of clinically recognized malignant thyroid neoplasms yet accounts for more than 50% of deaths attributed to thyroid cancer annually. The incidence is approximately 1 or 2 cases per million annually. ATC is very aggressive with a mean survival of 6 months after diagnosis. We present a case of ATC in a 64-year-old man with a history of untreated chronic lymphocytic leukemia and nontoxic nodular goiter who complained of dysphagia and was found to have a left-sided neck mass that rapidly grew during a few weeks time. An ultrasound of the neck demonstrated an enlarged left lobe of the thyroid, secondary to a complex mass with heterogeneous appearance and calcifications. A total thyroidectomy was performed. Pathology of the tissue showed a predominance of pleomorphic giant cells and a small population of plasmacytoid-appearing cells. The tumor cells were positive for CD138 and variably positive for cytokeratins but were negative for TTF-1 and B-cell and T-cell markers. The differential diagnosis included plasmablastic lymphoma. However, the clinical information, including lack of systemic symptoms that would likely be found in lymphoma and being negative for human immunodeficiency virus, assisted in ruling out plasmablastic lymphoma. The location and focal papillary carcinoma in the tumor were more consistent with anaplastic thyroid carcinoma. After workup and outside consultation a diagnosis of CD138 anaplastic thyroid carcinoma was rendered.

**Oncytic Mucopidermoid Carcinoma: Diagnostic Features of a Rare Entity**

(Poster No. 54)

Muhammad A. Raza, MD (muhammad.raza@stjohn.org); Sweety Nagori, MD; Basim M. Al-Khafaji, MD. Department of Pathology and Laboratory Medicine, St John Hospital and Medical Center, Detroit, Michigan.

We report 2 cases of oncocytic mucopidermoid carcinoma presenting as a painless parotid gland mass. Fine-needle aspiration biopsy revealed the presence of oncocytic epithelium with associated lymphocytes in one case; there was insufficient material for diagnosis in the other. Histologically, both excised parotid glands showed predominantly sheets and clusters of oncocytes admixed with scant mucocytes highlighted by a mucicarmine stain. Meanwhile, a positive intracytoplasmic granularity staining with phosphotungstic acid-hematoxylin stain highlighted the oncocytic mitochondria in both cases. The differential diagnosis of salivary gland neoplasms with oncocytic changes includes several benign entities. However, oncocytic mucopidermoid carcinoma is a low-grade, malignant neoplasm, albeit of favorable prognosis, in which a neck dissection is not indicated unless there is clinical evidence of metastasis. Pathologic distinction of this neoplasm from other benign oncocytic salivary gland neoplasms with the help of special stains, when necessary, is essential for appropriate clinical care.

**A Rare Finding of a Periparotid Lymph Node Diffusely Involved by Warthin Tumor**

(Poster No. 55)

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Warthin tumor is a benign salivary gland tumor with an unclear origin that occurs almost exclusively in the parotid gland. Although the most popular theory contends that the tumor develops from heterotopic salivary gland epithelium present in lymph nodes, little is known about the pathogenesis of Warthin tumor or its malignant potential. A lymph node involved by Warthin tumor is a rare event and has been reported as microscopic foci. They have been mistaken for metastatic carcinoma both clinically and radiologically. We report the case of a 48-year-old woman who had a parotidectomy for Warthin tumor. One of the periparotid lymph nodes demonstrated a diffuse involvement by Warthin tumor. This case report is a reminder that, although rare, Warthin tumor has the potential to involve lymph nodes. Its histologic appearance may mimic a metastatic carcinoma. However, proper distinction is important because of difference in management and prognosis. Furthermore, the lymph node involvement by Warthin tumor, which was observed in this case, merits further investigation that may help determine the pathogenesis (Figure 104).

**Simultaneous Occurrence of Medullary Carcinoma and Papillary Carcinoma in a Thyroid Gland: A Collision Tumor**

(Poster No. 56)

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We report the rare simultaneous occurrence of papillary carcinoma and medullary thyroid carcinoma within the same gland. This entity or combination of the 2 tumors represents less than 1% of all thyroid malignancies. Both tumors showed classic histologic features. Interestingly, the papillary carcinoma presented within a thyroglossal duct cyst and within the thyroid gland itself. Meanwhile, the medullary carcinoma presented within the contralateral lobe. Immunoreactivity for calcitonin, chromogranin, and thyroglobulin further aided in distinguishing the 2 tumors. These tumors may present as a mixed tumor with dual differentiation or as a collision tumor (a tumor with 2 distinct and well-defined components), as in our example. Although the cell-of-origin for papillary (follicular cell) and medullary (parafollicular C cell) neoplasms are different, a common stem cell, the ultimobranchial body, is a likely source for both tumors. Additionally, both tumors share a common genetic predisposition: the proto-oncogene rearranged during
transfection, which is rearranged in most papillary carcinomas and is also found to be mutated in 50% to 60% of sporadic medullary carcinomas. Surgical resection with lymph node dissection and clinical follow-up to identify familial cases of medullary carcinoma are indicated.

Epithelial-Myoepithelial Carcinoma of the Nasal Cavity (Poster No. 57)

Caroline C. Martin, MD (ccmartin@mcvh-vcu.edu); William J. Frable, MD. Department of Pathology, Virginia Commonwealth University, Richmond.

Epithelial-myofibroepithelial carcinoma of the nasal cavity is a rare tumor. Four cases have been reported in the English medical literature. These cases were reported in Asian countries, including Japan, China, and South Korea. We report the first case, to our knowledge, of epithelial-myofibroepithelial carcinoma of the nasal cavity in the United States. A 40-year-old, white woman, with a history of a malignant basoloid neoplasm of the right inferior turbinate, presented with a new left inferior turbinate lesion. Gross examination revealed a well-circumscribed, ulcerated, outlined, peripherally enhancing mass located between the anterior margin of the ramus of the left mandible and maxilla and protruding outward. An incisional biopsy was performed and was followed by a wide, local excision 3 weeks later. The patient recovered well postoperatively but refused follow-up chemoradiation therapy. Six months later, she presented with altered mental status, secondary to hypercalcemia from bone metastases. She was discharged to a hospice facility per her family’s request. Histologic sections of the specimens revealed a diffuse hypercellular, pleomorphic, ill-circumscribed lesion with extensive necrosis. The viable areas exhibited slit-vascular-like spaces and micropapillary architectural patterns with stromal eosinophilia (Figure 105). Focal small cellular nests with features of SCC were present. Immunohistochemistry displayed positivity for vimentin, p53, AE1/AE3, and CAM 5.2 (focally positive). All tumor cells were negative for desmin and CD34.

The Accuracy of Automated Predictive Focusing for Whole Slide Imaging Applications in Digital Pathology (Poster No. 59)

Vipul A. Baxi, BS; Richard R. McKay, PhD (rich.mckay@omnyx.com); Michael C. Montalto, PhD. Department of Hardware R&D, Omnyx, Piscataway, New Jersey.

Context: Whole slide imaging is the automated digital acquisition of an entire tissue sample for review on a computer monitor. The ability of a system’s automated focus procedure to accurately capture the optimal focal plane is an important parameter affecting the acceptance of whole slide imaging into routine practice.

Design: Sixty-seven fields of view from each of 3 different slides were imaged at 51 z-planes (0.1-μm steps). The optimal focal plane was calculated for each field of view. Automated scans of the same region were performed under normal scan conditions (3 z-planes/tile for focus calculations; continuous motion, 0.09 s/tile). To remove motion as a variable, a third set of data was acquired in a similar fashion by stopping the system at each tile (0.05 s/tile). The predicted focal plane for the continuous motion and stop-and-go methods were compared with the optimal focal plane. System repeatability (n = 10) was also performed for each method.

Results: Autofocus error for each method was calculated by comparing it to the position of the optimal focal plane (Table). Data are presented at a 95% confidence level (mean ± 2σ).

Conclusions: The tile-based, predictive, 3-point autofocus method used here displays outstanding accuracy. Although continuous motion scans displayed lower accuracy than the stop-and-go method, 95% of all tiles were within 0.2 μm of optimal focus. In fact, greater than 99.7% (mean ± 3σ) were within the system’s depth of field. Continuous motion scanning was significantly faster, demonstrating that speed and high-quality focus (autofocus is performed for each tile) are not mutually exclusive.

<table>
<thead>
<tr>
<th>Summary of Results</th>
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<tbody>
<tr>
<td><strong>3-Point Stop-and-Go Scan</strong></td>
</tr>
<tr>
<td>Repeatability, μm</td>
</tr>
<tr>
<td>Autofocus error, μm</td>
</tr>
<tr>
<td>Time to scan, s/tile</td>
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</table>

Abbreviations: s, second.

Facilitating Access to Biospecimen Research and Standard Operating Protocols Through the Biospecimen Research Database (Poster No. 60)

Andrew W. Breychak, BA1 (breychakaw@mail.nih.gov); Kelly B. Engel, PhD2; Ian Fore, DPhil3; Helen M. Moore, PhD2;1 Center for Bioinformatics and Information Technology, National Cancer Institute, Rockville, Maryland;2 Office of Biorepositories and Biospecimen Research, National Cancer Institute, Bethesda, Maryland.

Context: Pathology research and clinical practice relies on controlled procedures to minimize specimen-processing artifacts to ensure accurate analysis and diagnosis. There is a need to identify research on specimen handling in peer-reviewed journals and to identify standard operating protocols (SOPs) for broad application across multiple institutions. This will enable pathologists to validate research findings and lead to more rapid transition of translational research into laboratory and clinical practice.
Design: The National Cancer Institute’s Biospecimen Research Database (BRD) (http://biospecimens.cancer.gov/brd/) provides pathology practitioners and researchers with an annotated source of published research and review articles of specific relevance to human quality biospecimen collection and processing. More than 600 papers have been indexed according to test analyte, specimen type, and experimental variables. Additional functionality includes curation tools and experimental factor search options.

Results: An additional 700 publications have been identified for curation. Future functionality includes opportunities for community comment, meta-analysis of papers, and addition of electronic SOPs.

Conclusions: The BRD will become a definitive source of structured SOPs that can be searched individually and also be used by software systems (ie, Cancer Bioinformatics Grid–caBIG applications and others). The SOPs will exist as structured data that can be queried in cаЅGRID-enabled data services. The BRD is intended to be used by pathologists, researchers, and biorepository managers who wish to search, subscribe, and comment on SOPs and the supporting annotated, published literature. The goal of the Office of Biorepositories and Biospecimen Research is for the BRD to serve the needs of the biospecimen science and pathology communities; feedback and paper referrals are welcome and can be submitted at biospecimens@mail.nih.gov.

Incorporating Technology Into the Medical Autopsy Workflow
(Poster No. 61)

Matthew A. Smith, MD (smithma@upmc.edu); Somak Roy, MD; Lawrence Nichols, MD; Rick Nestler, MT, ASCP; Elizabeth Augustine, RN, BSN. Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania.

Context: From 2007 to 2009, there were 807 autopsies performed by the University of Pittsburgh Medical Center Autopsy Service. We used handwritten notes for initial recording of the gross pathology and handwritten and telephone communications to keep track of the decedents. We computerized these processes to improve our efficiency, biosafety, and documentation.

Design: Information Services developed a software program (Remains Tracker) that tracks decedents, documentation, autopsy status, and body transfer using input from various departments, including nursing, security, pathology, and medical records. We installed a hands-free workstation adjacent to the dissection table with access to electronic medical records, a pathology information system, and voice recognition software. We monitored qualitative improvement in decedent tracking, decedent paperwork management, biohazard/remediation prevention, rapidity of gross description, access to clinical impressions and radiologic findings, resident satisfaction, and provisional autopsy diagnosis completion.

Results: With Remains Tracker, we were better able to ascertain which deaths were for autopsy and which autopsies were complete to facilitate release of bodies to funeral directors. The computer station eliminated the burden of taking handwritten notes and transcription while completing an autopsy. Local availability allowed for access to medical records as autopsy findings created questions and the need for clinicopathologic correlation with additional studies. Resident satisfaction was mixed because autopsies were performed by different-sized teams requiring coordination of multiuser input, and a noisy environment created dictation challenges.

Conclusions: Autopsy is a uniquely labor-intensive, extensive, and complicated anatomic and clinicopathologic process that can benefit greatly from computerization; achieving those benefits requires an ongoing effort to fit the technology to the task.

Pathology Image Storage in Picture Archiving and Communication Systems Has a Positive Impact on Patient Care
(Poster No. 62)

Lisa D. Duncan, MD (lduncan@utmc.edu); Daryl R. Tharp, MD. Department of Pathology, University of Tennessee Graduate School of Medicine, Knoxville.

Context: Picture archiving and communication systems (PACS) were developed for the Department of Radiology to archive, retrieve, and view medical images. (Digital Imaging and Communications in Medicine) standardized image transfer and storage PACS to facilitate the dissemination and portability of medical information, thereby improving patient care. Because pathology is a visual specialty, these principles of image storage and retrieval can be incorporated into the implementation of pathology PACS.

Design: PACS is a storage device and can accommodate images obtained by an ordinary camera. We obtained both gross and microscopic JPEG images of a variety of cases, converted them to DICOM format using PACSScan Software, and stored these images in our hospital PACS.

Results: Stored images conform to radiology DICOM standards and are viewed on Web-based browsers or PACS monitors like radiology images. These images were displayed at cancer working conferences and were viewed remotely by a variety of physicians thus facilitating communication among caregivers.

Conclusions: Pathology PACS began as an experiment at our institution but has become a valuable tool in patient care. We use pathology images stored in PACS at intradepartmental working conferences, and they improve the quality of case discussion. Because these images are viewed in PACS, both radiology images and pathology images can thus be viewed under the same DICOM platform, and the quality of both can be assured, thereby improving patient care. Because pathology is a visual specialty,

### Automated Macro-Image Segmentation and Tissue Detection Capabilities of a Whole Slide Imaging System
(Poster No. 63)

Richard R. McKay, PhD1 (rich.mckay@omnyx.com); Weizhuo Li, PhD2; Anthony J. Demetris, MD1,2; Jeffrey L. Fine, MD2; Jonathan Ho, MD2; Drazen M. Jukic, MD2; Anil V. Farwani, MD,2; Laura M. Drogowski, BS2; Hak Sim, PhD2; Michael C. Montalto, PhD1 1Department of R&D, Omnyx, Piscataway, New Jersey; 2Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania; 3Department of R&D, Omnyx, Pittsburgh, Pennsylvania.

Context: Whole slide imaging is the automated digital acquisition of an entire tissue sample for review on a computer monitor. The capability of automatic tissue identification, compared with that of the human observer, is an important parameter affecting the acceptance of whole slide imaging into routine practice.

Design: Fifty “typical” slides, randomly selected from 9 different benches, were imaged using a custom 4.8 megapixel camera. Automated tissue identification and scan mapping were performed on each image. The region covered by the scan map was compared with a human observer viewing the glass slide at x1 magnification (naked eye) and at x4 to x10 magnification (using a standard Olympus BX41 microscope).

Results: Objects identified by segmentation were categorized based on size as ultrasmall (60–150 μm), small (150–750 μm), or main tissue (>750 μm). The number of times per slide each segmented object was (a) visible to the observer at x1 magnification, or (b) identified at higher magnification as a true positive (hematoxylin-osin-stained material as opposed to dirt, smudges, or debris) is shown in the Table.

Conclusions: The capability of macro-imaging and automated segmentation to identify regions for high-resolution scanning was significantly greater than that of the human observer. However, the system had relatively low specificity because some of the smaller objects identified were clearly not tissue. Although this can affect scan time and image review time, it presents minimal risk. To fully assess sensitivity, manual review of the entire slide must be undertaken to identify the false-negative rate of the system.

<table>
<thead>
<tr>
<th>Average Number of Regions Per Slide</th>
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<tbody>
<tr>
<td>Ultrasmall (60–150 μm)</td>
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<tr>
<td>-------------------------</td>
</tr>
<tr>
<td>Autosegmented objects (all positives)</td>
</tr>
<tr>
<td>Objects identified by eye (x1)</td>
</tr>
<tr>
<td>Objects identified at x4 to x10 (true positives)</td>
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This research was supported in part by Omnyx LLC (Pittsburgh, Pennsylvania). Partial salary was paid to Jeffrey L. Fine, Anthony J. Demetrus, Jonhan Ho, Anil V. Parwani, and Drazen M. Jukic through a corporate-sponsored research grant.

**Pixel Function That Allows Merging of Traditional Immunohistochemical Stains**

*Poster No. 64*

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**Context:** Diagnostic immunophenotyping is typically performed via “mentally” combining single immunohistochemical stains. Conversely, in research settings, colocalization predominates. The discrepancy is due to technical and/or practical hurdles (eg, antibody species incompatibility, expertise, time investment). Here, we present a simple pixel algorithm that allows electronic merging of traditional immunohistochemical stains of adjacent sections.

**Design:** We used 3 markers (rabbit-anti-CBP1, mouse-anti-TFF2, cytoplasmic; rabbit-anti-MIST1, nuclear) and a slide digitization (ScanScope XT, Aperio, Vista, California) and combined subsequent levels using synchronized virtual slides, image extraction, manual merge, and selection of pixels with higher numeric values. A customized link among several software platforms (Adobe Photoshop CS3; Aperio ImageScope10.0; ImageJ Version 10.2) was created using AutoIT (Version 3.2.12.0), a freeware BASIC-like scripting language for automating the Microsoft Windows graphical user interface.

**Results:** Antibody species incompatibility of CBP1/MIST1 (both chief-cell markers) precludes selective labeling; however, the pixel merge function allows colocalization of both markers without compromising staining specificity and, at the same time, allows marker evaluation on individual stains. Figure 106 exemplifies the merging of 2 double-immunohistochemical images (CBP1+TFF2 and MIST1+TFF2), where the merge shows nuclear MIST1 colocalized in CBP1+gastric chief cells (scale bar, 100 μm). The quality of the merge can be assessed by the exact overlap of the common TFF2 neck-cell stains.

**Conclusions:** The pixel merge algorithm is a simple way to generate colocalization images from routine immunohistochemical stains. Given that (1) immunohistochemistry is one of the most widely applied molecular assays in routine diagnostic pathology, and (2) the number of scanned glass slides will continue to increase, we believe that pixel merge shows nuclear MIST1 colocalized in CBP1+gastric chief cells.

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**Implementation of 2D Bar-Coding in the Anatomic Pathology Laboratory to Facilitate Digital Pathology Workflow**

*Poster No. 66*

Anil V. Parwani, MD, PhD1 (parwaniav@upmc.edu); Bryan J. Dagott, MD;2 Jonhan Ho, MD;2 Tony Piccoli, BS1; Tony J. Melanson, BS;2 Drazen M. Jukic, MD, PhD.1 1Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania; 2Omnyx, LLC, Pittsburgh.

**Context:** Anatomic pathology (AP) laboratories’ manual processes are barriers to digital pathology workflow implementation. Accurate specimen labeling is required for safe tissue processing and ultimately, slides sent for whole slide scanning will have barcodes for patient identification and workflow management. Our laboratory implemented bar-coding across anatomic specimen handling, from accessioning to sign-out.

**Design:** The AP workflow was analyzed, and a system was designed to integrate barcode identification throughout specimen processing. Two-dimensional (2D) DataMatrix barcodes were used for all labels. Symbol barcode scanner models 6607 and 6707 (Motorola Corporation, Schaumburg, Illinois) were installed in the accessioning room, gross room, histology laboratory, and pathologist workstations. Standon Microwriter (Thermo Scientific, Waltham, Massachusetts) and General Data (General Data Corporation, Cincinnati, Ohio) 2D DataMatrix barcode cassette printers were installed in the gross room. Slides were labeled using thermal transfer Cognitive CXI 300-dpi printers (CognitiveTPG, Lincolnshire, Illinois) and StainerShield XT chemical-resistant labels (General Data Corporation).

**Results:** The first laboratory went live a year ago, and mislabeling was reduced by 92%. Workflow efficiency and specimen tracking were improved. Slides can be aggregated, scanned, and distributed to pathologists. The 2D bar-coding allows slides to be loaded into whole slide scanners and integrated into laboratory information systems.

**Conclusions:** The AP specimen identification systems can significantly reduce laboratory errors by matching cases after scanning while speeding case delivery by reducing assembly time, thus improving patient care and safety. Additionally, our laboratory is prepared for full-scale implementation of digital workflow. Bar-coding will likely become standard in AP practice, particularly as laboratories adopt digital pathology.

This research was supported in part by Omnyx, LLC (Pittsburgh, Pennsylvania). Partial salary was paid to Johnhan Ho, Anil V. Parwani, and Drazen M. Jukic through a corporate-sponsored research grant.
Web-Based Synoptic Reporting for Cancer Checklists (Poster No. 67)

Brett W. Baskovich, MD (brett@uf.edu), Robert W. Allan, MD. Department of Pathology, Immunology and Laboratory Medicine, University of Florida, Gainesville.

Context: Synoptic reporting for cancer specimens ensures that all clinically validated pathologic information is provided. The process of developing a synoptic reporting system for all cancer specimens is arduous (see current) and the College of American Pathologists has 66 site-specific cancer checklists. We sought to automate the development of a Web-based synoptic reporting system using existing cancer checklists with the output incorporated into an anatomic pathology information system.

Design: Existing synoptic cancer checklists for genitourinary pathologic specimens were modified with element descriptors. These included radio buttons for mutually exclusive, single choices from a list; checkboxes for elements that might require multiple options to be reported; and text boxes for free-entry items, such as tumor size. A parsing algorithm was written in the PHP Hypertext Processor language to automatically convert these modified checklists into Web forms displayed with HTML and JavaScript. Additional algorithms were added as needed, such as an automatic calculation of the Stage for testicular tumors. The checklists can be edited and recompiled from the host Web site. When complete, the Web forms can generate a synoptic report that can be cut and pasted into a Microsoft Word-based anatomic pathology system.

Results: Fifteen Web-based synoptic forms were generated for genitourinary pathology specimens. The Web-based reporting method allowed access to the synoptic report elements at any workstation, formatted reports in a reproducible fashion, reduced errors and omissions, and significantly reduced transcription time.

Conclusions: Web-based synoptic reporting greatly enhances the ease of reporting cancer checklists. Using a parsing algorithm, numerous protocols can be quickly constructed from simple Word-based documents.

Digital Pathology Principles in the Histology Laboratory: A Workflow Perspective (Poster No. 68)

Chris A. Simmons, BS, AS, HTL(ASCP)1 (simmons@UPMC.EDU); Tiffany L. Sellaro, PhD; Curtis S. Stratman, MBA2; Tony J. Melanson, BS2; Drazen M. Jukic, MD, PhD.1 1Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania; 2Omnyx, LLC, Pittsburgh.

Context: Before digital pathology can be successful for high-throughput clinical use, scanner and software products must be scalable to the high-volume, high-throughput laboratories. Venturers must address efficient scanner operation and seamless integration of software components into the histology laboratory workflow.

Design: We implemented vendor scanner and software solutions (Omnyx, LLC, Pittsburgh, Pennsylvania) for digital histology workflow and evaluated their ability to address the needs of the digital anatomic pathology laboratory.

Results: Digital case compilation, rather than manual, paper-driven case compilation, was highly valued by histology. The ability to efficiently operate the scanner, review images, and manage the distribution of the cases based on quality controls is of paramount importance to digital histology workflow. Histology staff feels that a value-added feature is a comprehensive view of the case combining the hematoxylin-eosin stains with special stains to assist with quality assurance. Additionally, histology personnel are able to instantly view a magnified image if additional quality checks are needed. Lastly, communication between the laboratory and pathologist improved.

Conclusions: Although many vendors, corporations, and universities talk about digital pathology implementation, little has been studied related to the impact digital pathology will have on histology workflow. We conclude that successful implementation of digital pathology systems will depend on successful integration with a histology laboratory. Lacking the workflow perspective of the histology laboratory will result in user dissatisfaction, increased staffing requirements, reduced quality, and delayed case availability.

This research was supported in part by Omnyx LLC (Pittsburgh, Pennsylvania). Partial salary was paid to Drazen M. Jukic through a corporate-sponsored research grant.

Pathology WikiBook: The First Open-Source Web-Based Pathology Textbook With Web 2.0 Features (Poster No. 69)

M. Hanif Pathan, MD1 (hanif40@hotmail.com); Zahid Kaleem, MD, MD, 2Department of Pathology, University of Missouri, Kansas City; 2Department of Pathology, Missouri Baptist Medical Center, St. Louis.

Context: With the development of the Web and advances in technology, content creation using collective wisdom of prosumers has become common in many disciplines, with Wikipedia as the best known example. However, no such system exists to harness the collective knowledge and experience of pathologists across the world.

Design: A Web-based system could be designed in which pathologists and researchers across the world would be able to create, edit, and freely access pathology content in a simple and user-friendly module using state-of-the-art Web technologies.

Results: A "WikiBook" project for pathology content was created with Web 2.0 features at http://www.pathpedia.com/wikiBook in 14 months. The project has the following salient features: (1) open, online access; (2) comprehensive scope; (3) managed editing; (4) simple, intuitive graphic user interface (GUI) tools for content creation and management; (5) content versioning and archiving; and (6) the ability to print and download documents in PDF and Word formats, as well as the ability to e-mail content and save content links for future access. The editing function is managed in a hierarchical manner, starting with an editor-in-chief, followed by a WikiBook editor, and finally, the chapter/topic prosumers. The system also allows for "locking" of a topic by the respective WikiBook editors once the topic is deemed complete and updated.

Conclusions: The WikiBook project was successful in generating, editing, and disseminating pathology content across the world. The mass collaboration and distributed wisdom of pathologists and researchers could provide free access to any topic in pathology in the most reviewed and updated manner.

Differential Expression of Steroid Hormone Receptor Coregulators in Prostate Cancer (Poster No. 70)

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Context: Recent investigations revealed the potential implication of steroid hormone receptor (SHR) in the pathogenesis of prostate cancer. The transcriptional activity of SRs is modulated by their coregulators. In this study, we investigated the expression of a series of SHR coregulators in prostate cancer cell lines and tissue specimens.

Design: Normal prostate epithelial cell line RWPE-1 and prostate cancer cell lines, LNCaP, DU-145, and PC-3, were cultured in serum-free media. Prostate tumor specimens (N = 112) were microdissected by laser capture to obtain cancerous and noncancerous tissues. Malignant and adjacent nonmalignant regions from the same patient were compared. All specimens were reexamined by a pathologist. Expression of SHR coregulators was analyzed by quantitative reverse transcription polymerase chain reaction.

Results: The expression of androgen receptor–associated protein 55 (ARA55) was much lower in prostate cancer cell lines than in the noncancerous RWPE-1 cell line. Comparison of ARA55 expression between prostate carcinoma specimens and corresponding tumor-free tissue from the same patient revealed that ARA55 expression was significantly lower in malignant areas than in nonmalignant regions (n = 112, P < .001).

Conclusions: The differential expression of ARA55 may be associated with prostate cancer. ARA55 may be a novel candidate as a therapeutic target gene for prostate cancer.

TBX3 Is a Novel Biomarker for Advanced Prostate Cancer (Poster No. 71)

Chunyu Wang, PhD (chunyuwang2000@gmail.com); Yang Yu, MD. Department of Molecular and Cellular Biology, Baylor College of Medicine and The University of Texas MD Anderson Cancer Center, Houston.

Context: TBX3 (T-box 3) is a member of a phylogenetically conserved family of genes that share a common DNA-binding domain, the T-box. TBX3 encodes a transcription factor that plays a crucial role in the regulation of developmental processes and multiple disorders. In this...
study, we evaluated the expression and clinical relevance of TBX3 in human prostate cancer.

**Design:** The tissue microarray set consisted of 130 prostate tissue specimens, which were arrayed onto slides and used for immunohistochemical staining. Prostate cancer cell line DU-145 and PC-3 were transfected with TBX3 expression plasmids, its dominant negative mutant TBX3-Y149S, or short hairpin RNAs (shRNA) directed against TBX3. Gene expression was measured by quantitative reverse transcription polymerase chain reaction and enzyme-linked immunosorbent assay. DNA-protein interaction was analyzed by chromatin immunoprecipitation (ChIP) assay.

**Results:** TBX3 is expressed in prostate adenocarcinoma tissues. The elevated TBX3 level in prostate cancer is correlated with lymph node status, clinical stage, and Gleason score. TBX3 expression is inversely correlated with E-cadherin expression. Overexpression of TBX3 promot ed the invasion and migration of prostate cancer cells and down-regulated E-cadherin expression and stimulated the expression of matrix metalloproteinase 2, 9, and 14 (MMP-2, MMP-9, and MMP-14). MMP-14 dominant mutant of TBX3 antagonized its effect. ChIP assay demonstrated the recruitment of TBX3 protein to target gene promoters.

**Conclusions:** TBX3 expression is associated with unfavorable patient outcome. TBX3 is also associated with invasiveness in vitro. These results suggest that TBX3 is a promising novel biomarker for advanced prostate cancer.

**Fluorescent in Situ Hybridization for EML4-ALK–Positive Lung Adenocarcinomas: Selecting Patients for Targeted Therapy Trials**

(Poster No. 72)

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**Context:** The fusion product of echinoderm microtubule–associated protein-like 4 (EML4) and anaplastic lymphoma kinase (ALK) genes is a molecular marker used to select lung adenocarcinoma cases for trials of targeted therapy with a MET/ALK tyrosine kinase inhibitor. Lung adenocarcinomas positive for this gene fusion product have been resistant to traditional chemotherapeutic regimens.

**Design:** We examined 23 cases of lung adenocarcinoma that were negative for EGFR and KRAS mutations by polymerase chain reaction analysis; 2 showed signet ring cell features. Fluorescent in situ hybridization was performed on formalin-fixed, paraffin-embedded tissue using the Vysis protocol for deparaffinization and hybridization and the commercially available ALK break-apart probe (Vysis, Des Plaines, Illinois). We counted a total of 200 cells for each case. Positive cells were those that showed a clear separation of green and orange signals, and positive cases were defined as those that contained more than 5% positive cells.

**Results:** The 23 adenocarcinoma cases were all negative for EML4-ALK, although 2 cases showed 3% and 4% of cells positive for EML4-ALK. These results contrast with previous studies that have shown 1.5% to 13% of cases positive for EML4-ALK in a sampling of lung adenocarcinomas that tested negative for EGFR and KRAS mutations.

**Conclusions:** Despite the relative rarity of EML4-ALK positive cases, molecular screening for such cases will likely provide substantial benefit to a subset of patients with lung adenocarcinoma and be in high clinical demand. It may be more cost- and labor-effective to consolidate screening for relatively rare molecular subsets of adenocarcinoma cases in select molecular testing centers.

**Do Neoplastic Genetic Changes Obscure DNA Identity Testing?**

(Poster No. 73)

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**Context:** DNA fingerprinting analyzes whether an unexpected tumor on a diagnostic histologic slides belongs to the patient or represents an inadvertent tissue contaminant. Such low frequency contaminants are unavoidable in routine tissue processing so that accurate means to resolve these situations are essential. The polymorphic loci used in DNA identity testing are thought to remain stable in tumors; however, the question arises whether tumor or therapy-associated mutations could produce erroneous nonidentity results. This study examined the stability in tumors of highly polymorphic, short tandem repeat sequences that are commonly used for identity testing.

**Design:** Rectal adenocarcinomas from 28 patients were examined, including 8 following chemoradiation therapy. DNA was extracted from microdissected adenocarcinomas and paired with healthy tissues. Polymerase chain reaction amplification using the Promega PowerPlex 16 System (Madison, Wisconsin) was followed by capillary gel electrophoresis on an ABI 310 genetic analyzer (Foster City, California) for 16 polymorphic, short tandem repeat loci. Alleles of patient-matched healthy and tumor specimens were examined for false-positive tumor inconsistencies.

**Results:** Of 640 total alleles analyzed, 597 (93%) were successfully amplified, and among these, no false-positive mutations were detected in tumors that obscured identity assessment. The only variation detected was the appearance of a new third amplicon in single separate loci from 3 different tumors. Retention of the 2 original alleles in all 3 examples still permitted patient identity assessment.

**Conclusions:** The 16 short tandem repeat loci examined remained genetically stable in tumor tissue, suggesting they are robust markers for tissue identity testing of unexpected tumor fragments on patients’ diagnostic slides.

An Epstein-Barr Virus Positivity Rate of 8% in Posttransplant Patients Monitored by Quantitative Real-Time Polymerase Chain Reaction

(Poster No. 74)

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**Context:** Quantitative real-time polymerase chain reaction (PCR) testing is useful for monitoring Epstein-Barr virus (EBV) DNA levels in patients at risk of posttransplant lymphoproliferative disorder (PTLD). However, defining a clinically significant EBV viral load is laboratory specific and complicated by the lack of a standardized methodology. The purpose of the study was to determine the EBV positivity rate in a posttransplant patient population and to correlate results with symptomatology.

**Design:** DNA extracted from clinical samples was analyzed using quantitative real-time PCR. Results were retrospectively correlated with transplant history and clinical symptomatology.

**Results:** In 1 year, 773 quantitative EBV tests were performed on 493 patients after transplant. Sixty-one tests (7.9%) were positive on 45 patients (9.1%). Of the patients with detectable EBV DNA, 24 were asymptomatic (viral loads, 332–62,670 copies/mL); 13 patients had non-EBV–related symptomatology (viral loads, 360–62,325 copies/mL); 4 had fever or symptoms of an upper respiratory tract infection (viral loads, 420–13,165 copies/mL); 1 patient had no available clinical information; and 3 patients had a histologic diagnosis of PTLD (viral loads 1170 to >11 million copies/mL). Even excluding results too high to be quantified, the average viral load seen in patients with PTLD was significantly higher (234,000 copies/mL) than seen in the other groups (P < .001).

**Conclusions:** We determined that 7.9% of quantitative EBV tests performed on posttransplant patients were positive. Viral loads were similar in asymptomatic patients, those with non-EBV–related symptomatology, and those with upper respiratory tract symptoms. Patients with PTLD had significantly higher EBV viral loads.

A Novel Method of Molecular DNA Methylation Biomarkers in Acute Myeloid Leukemia and Potential Applications for Detection of Minimal Residual Disease

(Poster No. 75)

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**Context:** Acute myeloid leukemia (AML) is the most common, malignant myeloid disorder in adults. Standard treatment provides complete remission in 60% to 80% of patients. However, minimal residual disease (MRD) often occurs, leading to high rates of AML relapse. aberrant DNA methylation is a hallmark of AML that can be used to detect MRD. This study investigated the use of a novel molecular technique known as methylation-sensitive restriction enzyme polymerase chain reaction (MSR-PCR) to detect DNA methylation and MRD in AML.
Design: Sixty-five bone marrow and peripheral blood samples from patients with AML were tested using MSR-PCR. Some patients had multiple samples from progressive disease stages. DNA was extracted from the samples, subjected to methylation-sensitive enzyme digestion, and amplified using PCR. Eight studied genes (HIN1, NO.1, p15, KLF4, SOCS1, CXCR4, PCDHA12B, and SLC26A4) were evaluated in each sample. Gel electrophoresis of PCR products was used to detect methylation. Three patients with samples from progressive disease stages were evaluated for methylation of HIN1 and PCDHA12B.

Results: DNA methylation was detected in 57 of 65 (87.7%) of the samples. All 8 genes were found to be hypermethylated with a range of 9.2% (SLC26A4) to 73.8% (HIN1set2) (Table). All patients evaluated for HIN1 and PCDHA12B lacked methylation at initial diagnosis and remission; however, they demonstrated methylation at relapse.

Conclusions: These initial results indicate that MSR-PCR can detect DNA methylation in AML and could be used to detect MRD in the proper context.

### Data Summary

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### MAP3K3 Is a Novel Therapeutic Target for Prostate Cancer

Chunyu Wang, PhD (chunyuwang2008@gmail.com); Yang Yu, MD. Department of Molecular and Cellular Biology, Baylor College of Medicine and The University of Texas MD Anderson Cancer Center, Houston.

**Context:** MAP3K3 gene (also known as MEKK3/MAPKKK3) is located in 17q23 and encodes mitogen-activated protein kinase/extracellular-regulated kinase kinase kinase 3. MAP3K3 protein directly regulates the extracellular signal-regulated protein kinase pathway and regulates a variety of downstream targets to exert its biologic effects. In this study, we investigated the role of MAP3K3 in prostate cancer.

**Design:** Quantitative polymerase chain reaction was used to detect gene copy number. MAP3K3 gene and short hairpin RNA (shRNA) expression constructs were transfected into prostate cancer cell lines. Cell proliferation, cytotoxicity, and apoptosis were measured.

**Results:** MAP3K3 is amplified and/or expressed in a panel of human prostate cancer cell lines and prostate tumor tissues. Overexpression of MAP3K3 gene induced the proliferation of prostate cancer cells, accompanied by elevated cyclin D1 levels. The shRNA knockdown of MAP3K3 gene expression inhibited prostate cancer cell proliferation. Similar effects were observed in a xenograft mouse model. Prostate cancer cells overexpressing MAP3K3 were more resistant to apoptosis-inducing drugs (taxol, doxorubicin, and 5-fluorouracil). These cells expressed more cell survival factors, such as bcl2 and less cleaved caspases, compared with control cells. Exposure of cells transfected with MAP3K3 shRNA to the apoptosis-inducing drugs dramatically decreased proliferation and clonogenicity.

**Conclusions:** MAP3K3 is a candidate oncogene that is amplified and overexpressed in human prostate cancer. Overexpression of MAP3K3 results in increased cell proliferation and resistance to apoptosis. Suppression of MAP3K3 gene expression decreases cell proliferation and enhances drug sensitivity. Therefore, MAP3K3 may serve as a potential promising therapeutic target for prostate cancer.

### Identification of Tissue Contamination by Polymorphic Deletion Probe Fluorescent In Situ Hybridization

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**Context:** Specimen mix-up and floater contamination are problems in surgical pathology practice. Current molecular techniques to identify tissue contaminants include fluorescent in situ hybridization (FISH) identification of X and Y chromosomes and polymerase chain reaction microsatellite analysis. Polymorphic deletion probes (PDP), recently developed FISH probes based on copy number variants, are highly polymorphic and can genetically distinguish between tissues on glass slides from any 2 individuals. Using a panel of 3 PDPs from chromosomes 2p, 4q, and 8p, we compared the genotypes of presumed tissue contaminants and patient tissues to demonstrate the practical utility of PDP FISH in cases of specimen mix-up and floater contamination.
Design: The PDP FISH and XY FISH were performed on formalin-fixed, paraffin-embedded tissue from 20 cases of potential specimen mix-up or floater contamination.

Results: The PDP FISH was successful in all cases. Clear genotypes were identified for all tissues. In 13 cases, PDP FISH confirmed that the genotype of the potential tissue contaminant was distinct from that of the patient tissue, confirming tissue contamination. Of these 13 cases, XY FISH was informative in only 4 cases. In 7 cases, PDP FISH confirmed that the genotype of the potential tissue contaminant was identical to that of the patient tissue.

Conclusion: The PDP FISH is a novel, accurate, cost-effective, and practical molecular technique for the identification of tissue contamination and specimen mix-up in surgical pathology specimens.

$t(5;9)(q13;q32)$: A Previously Unreported Translocation in T-cell Large Granular Lymphocytic Leukemia

(Poster No. 79)

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We report a case of a 57-year-old man with T-cell large granular lymphocytic leukemia (T-LL) with a previously unreported, apparently balanced ($t(5;9)(q13;q32)$) translocation. The patient had lymphocytosis for 9 years, with a steady and unintentional weight loss. Examination of his peripheral smear showed a predominance of intermediate-sized lymphocytes with round nuclei that were often notched or folded and were surrounded by moderate amounts of cytoplasm-containing azurophilic granules. Flow cytometry revealed a population of T cells with a CD4:CD8 ratio of 1.8. These cells coexpressed CD56 and CD57, suggestive of large granular lymphocytes. Karyotype analysis of the bone marrow showed a clonal translocation, $t(5;9)(q13;q32)$, in 9 out of 20 cells in metaphase with no other abnormalities. The $9q32$ locus encodes a helix-loop-helix protein TAL2 and has been reported to be involved in rearrangements with 1p34, 1p32, 1q24, 1p13, 1q22, and 1p13 in T-cell malignancies. This protein and other homologous proteins (TAL1 and LYL1) are proto-oncogenes that are upregulated as a result of gene fusions. It is likely that the 5;9 translocation resulted in an up-regulation of the TAL2 gene. The other involved region at 5q13 is poorly annotated. However, rearrangements of the SSBP2 gene mapped to 5q13 resulting in fusion genes have been associated with pre–B cell acute lymphoblastic leukemia. Another potential candidate for a possible fusion partner at the $5q13$ locus is BT3F, a transcription factor gene. The molecular impact of the translocation is currently in progress and will define a new fusion gene in the etiology of T-LL.

Gene Expression Profiling in the Pathogenesis of Bladder Tumors

(Poster No. 80)

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Context: A variety of genetic alterations and gene expression changes are involved in the pathogenesis of bladder tumors.

Design: To explore expression changes in bladder tumors, microarray analysis was performed.

Results: Analysis yielded 1131 known genes and 796 expressed sequence tags that were changed when comparing tumors to healthy epithelia. Altered genes included cell cycle–related genes, epidermal growth factor receptor–Ras signaling genes, apoptosis genes, growth factor receptors, and oncogenes. Using the pathway visualization tool GenMAPP, we found that these genes can be grouped along several pathways that control apoptosis, cell cycle, and integrin-mediated cell adhesion. Thirteen members of the S100 gene family were confirmed by real-time polymerase chain reaction to be differentially expressed in human bladder cancers, with overexpression of S100A2, S100A3, S100A5, S100A7, S100A9, S100A10, S100A11, S100A12, S100A14, S100A16, and S100P and underexpression of S100A1, S100A4, and S100B. S100A1, S100A2, S100A3, S100A8, S100A9, S100A10, S100A12, S100A14, and S100A16 showed similar patterns of differential expression in bladder cancers from mouse, rat, and human.

Conclusions: These results suggest that multiple pathways are involved in bladder tumorigenesis, and the differential expression of S100 gene family members is characteristic of bladder cancers. Moreover, these genes may play important roles in bladder tumorigenesis and progression.

Implementation of a Comprehensive Internet-Deployed Hematopathology Database for Resident Education

(Poster No. 82)

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Context: Training in hematopathology requires a multiparametric approach. Pathologists-in-training can view cases via the Web interface. Automated whole slide image capture was performed at ×40 magnification, using an Aperio T2 (Aperio Technologies, Vista, California) 5-slide scanner. Digital slides and supplemental data (flow cytometry histograms, etc) were referenced by hyperlink in a Microsoft Access database. A ColdFusion (Adobe, San Jose, California) application was used at the front end to present the data in an organized Web page. Results: Pathologists-in-training can view cases via the Web interface. Within each case, the patient’s history, digital slides, relevant testing results, and diagnostic information are available. There are no limitations on the number of whole slide images or the type of supplemental data that can be integrated into the site.

Conclusions: A comprehensive collection of digital slides and supplemental test data that is integrated with clinical information is a significant move toward improving resident training in hematopathology. The Internet-deployed database is very well suited to standardizing pathology resident education.
Primary Ewing Sarcoma/Primitive Neuroectodermal Tumor of Soft Tissue in the Perinephric Region
(Poster No. 83)

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Primary Ewing sarcoma/primitive neuroectodermal tumor of soft tissue is a rare entity. We describe a primary Ewing sarcoma/primitive neuroectodermal tumor of soft tissue in the perinephric region in a 36-year-old man who was admitted with acute pyelonephritis. Computed tomography scan revealed left renal enlargement with multiple hilar masses and a posterior left perinephric nodule. Computed tomography-guided fine-needle aspiration biopsy of the posterior left perinephric nodule showed characteristic cytologic and histologic appearances of a small blue cell tumor, with focal Homer-Wright rosette formation. The tumor cells showed diffuse positivity with CD99, vimentin, BCL2, neuron-specific enolase, and synaptophysin. They were negative for muscle markers (desmin, myogenin, and smooth muscle actin), melanoma markers (S100, HMB-45, MART-1, and tyrosinase), epithelial markers (pankeratin, epithelial membrane antigen, CK7 and CK17), and lymphoid markers (CD45, CD3, and CD20). Fluorescent in situ hybridization analysis using dual-color DNA probes for the Ewing sarcoma breakpoint region 1 on chromosome 22q12 revealed a rearrangement of the Ewing sarcoma breakpoint region 1 locus, confirming the diagnosis of Ewing sarcoma/primitive neuroectodermal tumor. To our knowledge, this is the first intact documentation of primary Ewing sarcoma/primitive neuroectodermal tumor of soft tissue in the perinephric region with an immunohistochemical panel and cytogenetic analysis.

A Much Needed Competency: How To Bring a New Test In-House
(Poster No. 84)

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Context: Pathology residents must learn to provide consultation on the choice and interpretation of a wide range of laboratory tests. They must also understand how to bring in a new test, which is central to their competency in systems-based practice. This abstract reports our method of teaching residents how to analyze new tests.

Design: All residents review laboratory tests requested by physicians and prepare a recommendation at a formal presentation to laboratory medicine faculty and residents, which includes background information, critical review of at least 3 current articles comparing the new test to the current gold standard, costs involved (instrumentation, supplies, and technical support), as well as the clinical perspective. An estimation of the test volume is also taken into account. In this work, 2 recent examples will be elaborated in the presentation were the Candida albicans PNA FISH (AdvantDX, Woburn, Massachusetts) assay for candidemia and the Quantiferon-TB Gold In Tube Test (Cellestis, Valencia, California). Each evaluation included multiple steps that were taken by the residents rotating in clinical pathology. In the case of C. albicans PNA FISH assay, the residents found that the number of tests being performed did not clinically or financially justify its setup in house. However, Quantiferon-TB Gold In Tube Test was brought in to help screen hospital staff with positive tuberculosis skin tests and a history of Bacillus Calmette-Guérin vaccination.

Conclusions: This exercise gives residents the understanding of potential pitfalls from clinical pressures to financial interests. As a bonus, they learn how to critique the literature and perfect presentations to other physicians and laboratory administration.

Teaching Basic Pathology to High-School Students
(Poster No. 85)

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Context: With health care reform underway, there is interest in having students study human disease before medical school (ie, at the college or high school level).

Design: For 2 years, 3 pathology professors conducted a 6-week summer program in general pathology for high-school students who had no prior premedical college exposure. Teaching methods included lectures, histopathology virtual image laboratories, and scholarly resource training. The Institutional Review Board approved this study. Six students enrolled in 2008, and 9 students enrolled in 2009. In the 2009–2010 academic year, a 6-month course (2 hours weekly) was added for 10 senior students from a magnet biosciences high school.

Results: The summer students attended 74.75 instructional hours. The year-long students attended 42 hours. The content was that of a medical school general pathology course. Teaching methods by percentage of time used included lectures (28% summer, 38% during year); virtual slide image laboratories (20% summer, 17% during year); scholarly resource training (11% summer, 3.5% during year); review (11% summer, 19% during year), dialogues with professional role models (7% summer), and other methods (21% summer, 23% during year). Approximately 35% of the teaching was performed by videoconference. All students passed the course; one-third performed at honors level. All students successfully completed an independent study project with a scholarly presentation. The courses received a rating of 4.8 out of 5 for student satisfaction.

Conclusions: High-school students are capable of mastering medical school-level content in general pathology, raising the possibility of introducing the study of human disease earlier than previously undertaken.

Evaluation of an In-House Telepathology System Used for Remote Resident Education
(Poster No. 86)

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Context: We studied a system developed in-house that is used for our multifacility resident-training program and that consists of virtual slide and real-time telepathology components. The goal was to evaluate the usefulness of the remote teaching system. This system provides high-quality, audiovisual educational conferences, including case studies and keynotes lectures, to every resident who is in rotation at our various hospitals. This system synchronizes remote education and enables residents to benefit from all possible learning opportunities.

Design: Using the virtual slide component, participants previewed the case study slides via the Internet at any time and location. Then, the cases were discussed at a conference using the real-time slide images on a Web page through an intranet connection among the hospitals. We used slides from 20 cases at 5 conferences. We received 53 valid responses in a questionnaire format.

Results: Based on statistical analysis, users found that pattern recognition and cytologic features were satisfactory with low magnification (73%) and high magnification of the hematoxylin–eosin, virtual slides. They were confident in making a diagnosis based on review of the virtual slides. However, they were dissatisfied with moving slides from one field to another because of the resulting broken images. Cytology images were unsatisfactory because of a layering focus issue.

Conclusions: This study shows that the 2 main components of our system were well received by participants; however, there are still issues that need to be resolved and details that need to be standardized and enhanced. The system is inexpensive and easy to build.

Improving Frozen Section Turnaround Time Using a Collaborative Problem-Solving Tool
(Poster No. 87)

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Context: Rapid, frozen section (FS) diagnosis turnaround time (TAT) is critical for patient care and compliance with College of American Pathologists regulations. We used a collaborative problem-solving tool (FastTrac, Orion Advisory, Charlotte, North Carolina) to identify objectives and FS TAT components and recommended process improvements. Our goal was to improve FS TAT from our baseline of 70.0% FS compliance (reported in 20 minutes) without increasing FS discrepancy rates.
Application of Chapter 48, Carcinoma of the Eyelid, in the Seventh Edition of the American Joint Committee on Cancer Staging Manual
(Poster No. 89)

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Context: We conducted a quality improvement, applied practical review of the staging system in chapter 48, “Carcinoma of the Eyelid,” in the 7th edition of the American Joint Committee on Cancer Staging Manual.

Design: We conducted a 15-year, consecutive, retrospective review of all cases of excisional biopsy for carcinoma of the eyelid.

Results: During a 15-year review period, 52 cases of excisional biopsy for carcinoma of the eyelid were identified. We were able to assign clear-staging to 50 cases using the available pathology data. The results were stage IA (72%), stage IB (22%), stage II (6%), stage III (2%), and stage IV (0%).

Conclusions: Chapter 48, “Carcinoma of the Eyelid,” proved to be a practical tool for carcinoma staging of the eyelid. Although there may be disparate findings on largest tumor dimension, depending on how it is measured, we found that largest tumor dimension remains an effective predictive factor. Medial canthal location had a slightly higher staging association. High-grade pathologic prognostic factors, such as tumor necrosis or perineural spread, had a 100% association with final stage of II or greater. Concordance and compliance were 100% for the recommended, site-specific, pathologic risk factors. Newly required data points, including Clark level, tumor thickness in millimeters, and a statement that the tissue was not derived from the ear or nonhairy lip, had 0% reporting during the 15-year period. The newly recommended prognostic site-specific tumor factors appear to work in high concordance with staging severity and have a strong community acceptance rate.

Repeatability and Analytic Validity of a Pretreatment Prostate Cancer Prognostic Assay (Prostate Px Plus)
(Poster No. 90)

Michael J. Donovan, MD, PhD2; Faisal M. Khan, MS2 (faisal.khan@aureon.com); Douglas Powell, PhD2; Valentina Bayer-Zubek, PhD2; Allison Mott, BAT3; Paul O’Dwyer, BA2; 1Department of Pathology 2Machine Learning 3Prognostics, and 4Laboratory Operations, Aureon Laboratories, Yonkers, New York.

Context: We report on a systems-based, prostate cancer model (Prostate Px+, Aureon Laboratories, Yonkers, New York) that predicts the risk of disease progression (DP; castrate prostate-specific antigen rise, systemic disease, and/or death from disease) and the probability of extracapsular pathology (ECP; prostatectomy stage ≥T2, no Gleason grade 4 or 5, and prostate-specific antigen nadir) at diagnosis. The test uses pretreatment clinical variables and a feature template derived from image analysis and quantitative, biomarker multiplexing from a formalin-fixed, paraffin-embedded prostate needle biopsy. The result is an integrated score (DP) and probability (P) that stratifies the patient’s risk for DP and ECP. To evaluate performance by equation and analytic validity, we performed a repeatable study on patients evaluated at our CLIA/College of American Pathologists–certified laboratory.

Design: We randomly selected 50 previously processed patients; they were anonymously and blindly reprocessed with routine samples. The DP score, DP-P, DP relative risk, and PP-P (Table) were generated and compared, along with patient risk classification. A method-of-moments analysis estimated the variance, reliability, bias, and random error; a percentage of statistical agreement was calculated.

Results: There was 94% agreement for the variables measured between (same) patients, including DP score, DP-P, DP relative risk, and PP-P (Table). There was good consistency for the low/high risk DP (90%; 45 of 50 patients) and FP (92%; 46 of 50 patients) predictions. Average DP scores changed by 4.7%; average FP-P changed by 7.6%.

Conclusions: There was excellent reliability between same patient materials when assayed with Prostate Px Plus. The overall performance supports the validity of the analytic platform and robustness of the feature development process.

Patents have been applied for regarding the Prostate Px+ test mentioned in this abstract. Michael Donovan and Faisal Khan are the abstract authors listed on these patents. The patent applications are as follows: Systems and methods for treating, diagnosing and predicting the occurrence of a medical condition, 462,041, filed July 2009; and Systems and methods for treating, diagnosing and predicting the occurrence of a medical condition, 12,584,048, filed August 2009.
The Use of a Fat-Dissolving Solution in Identifying Lymph Nodes in Colon Cancer Resection Specimens

Poster No. 92

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Context: Higher lymph node (LN) yields lead to better prognostic information for patients with colon cancer. Therefore, pathologists should attempt to find every LN within the pericolonic fat. This often demands a significant time commitment. We investigated whether a fat-dissolving solution (FDS) could expedite LN dissections while increasing yields of all LNs and positive LNs, leading to possible up-staging of patients.

Design: A single observer performed LN dissections on 87 T1 to T4 colon cancer specimens randomly assigned to formalin fixation (n = 45) or pretreatment with FDS (n = 42). The LNs were categorized by size and whether they harbored metastatic carcinoma (Table). A Mann-Whitney 2-sample test was used to compare the groups across all categories, and negative binomial regressions were run to adjust for the amount of tissue examined.

Results: The total number of LNs was significantly higher in the FDS group (P < .001) (Table). There was no significant difference between the number of positive LNs identified. More LNs <2 mm in size were found in the FDS group (P < .001). There was no difference across other size categories (all, P > .10). The average time of dissection in both groups was essentially equal (44.5 minutes FDS versus 45.6 minutes formalin).

Conclusions: Pretreatment with FDS increases detection of total LNs in colon cancer specimens, improving overall yields. This method primarily helps to identify LNs <2 mm in size. It does not increase yields of positive LNs and consequently does not affect staging. Additionally, a FDS does not improve the time of dissection.

Epitope (In)stability in Archival Paraffin Sections: A Word of Caution for Biorepository Research

Poster No. 93

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Context: The intestine-specific, caudal-related homeobox gene CDx2 plays an important role in differentiation and maintenance of epithelial function. CDx2 has recently been described as a highly sensitive marker of intestinal metaplasia, which may supplement the histologic identification of Barrett esophagus (BE).

Design: Archival specimens (N = 232; 155 BE);7 77 BE−) from 103 patients who were BE− were stained with CDx2 (Cell Marque, Rocklin, California) using the Ventana Benchmark automated platform. Any nuclear staining within the specimen was considered positive. Simultaneously run colonic tissue served as positive and negative controls. Four recent BE cases were used as comparative positive control.

Results: CDx2 expression was identified in 122 of 155 (sensitivity, 79%) BE− specimens and 13 of 77 (false-positives, 17%) BE− specimens. CDx2 expression was not identified in 35 of 155 (false-negative, 21%) BE− nor in 64 of 77 (specificity, 85%) BE− specimens. Per-patient archived and recently diagnosed CDx2 BE sensitivity was 69% (71 of 103) and 100% (4 of 4), respectively. Qualitatively, all archived specimens exhibited significantly less CDx2 staining intensity and quantity than controls, often staining at times as only single cells within the specimen (Figure 109, A). Comparatively, the 4 recent BE cases stained strongly and diffusely within all affected areas (Figure 109, B).

Conclusions: CDx2 holds promise as a method to detect intestinal metaplasia in esophageal biopsies of BE. Tissue block age appears to significantly affect tissue antigenicity qualitatively and quantitatively.
Loss of antigenicity in stored tissues is of clinical importance, and immunohistochemistry use must be considered carefully in research and clinical settings to reduce errors in interpretation.

**Review of Recombinant Activated Factor VII Use and Proposed Protocol for Off-Label Use**

(Poster No. 94)

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**Context:** Clinical applications of recombinant activated factor VII (rFVIIa) are well documented, primarily involving treatment of hemophiliac patients with inhibitors. However, its off-label use as a hemostatic agent in non-hemophilic settings continues to raise questions about its appropriate clinical use and effectiveness. This is especially true under circumstances when a patient's physiologic state may render rFVIIa ineffective (ie, acidosis). At present, our institution has no formal protocol guiding the clinical decision to use rFVIIa. At a cost of approximately $6000/dose, evaluation of its usage is worthwhile.

**Design:** We performed a retrospective chart review of 92 patients at our institution who had been treated with rFVIIa, gathering data on the clinical indications and laboratory parameters proximal to administration (eg, blood pH, complete blood cell count, and administered blood products).

**Results:** Of 92 patients, 8 (9%) had an established indication for use of hemophilia A with high-titer inhibitor (n = 4), Glanzmann thrombasthenia (n = 2), acquired factor VIII inhibitor (n = 1), and congenital factor VII deficiency (n = 1). Of the patients receiving off-label doses, 27 of 84 (32%) had blood pH less than 7.2.

**Conclusions:** Off-label use of rFVIIa outpaces established indications for use at our institution. Using a protocol similar to that suggested by the Israeli Multidisciplinary rFVIIa Task Force could have resulted in an estimated $91,000 in annual savings when considering blood pH alone. A proposed protocol has been developed, and further cost-savings data are being collected.

**Sepsis Masquerading as an Acute Transfusion Reaction**

(Poster No. 95)

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Acute transfusion reactions present with an array of symptoms ranging from urticaria to shock. The most severe reactions, hemolytic, anaphylactic, and transfusion-related acute lung injury, can present with overlapping symptoms, making the diagnosis and classification of a true acute transfusion reaction challenging. We present a case that exemplifies this situation. A 23-year-old woman with lupus nephritis, who was receiving immunosuppressants, presented to the hospital with headache, nausea, vomiting, and a hematocrit of 12% without fever. After receiving 2 units of packed red blood cells, she immediately became hypotensive and hypoxic. Hemolysis was excluded by a negative direct antiglobulin test (DAT) and no plasma hemoglobin. However, new pulmonary interstitial edema and a drop in her leucocyte count led the pathology resident to suspect transfusion-related acute lung injury. Subsequently, she experienced cardiac arrest, was transferred to the intensive care unit, and was noted to have a bullous skin rash. Upon consultation, intracuticular bacteria, as well as 60% bands, toxic granulation, and Döhle bodies, were identified in her blood smear. That sample subsequently grew Escherichia coli, and gram-variable rods were seen in the bileaue fluid. Despite full support, she remained hypotensive and expired the next day. Postmortem examination showed no anatomic cause of death, and sepsis was the most likely explanation for her clinical picture. This case illustrates the difficulty in discerning an acute cause of death, and sepsis was the most likely explanation for her clinical and expired the next day. Postmortem examination showed no anatomic sample subsequently grew *Escherichia coli* guiding the clinical decision to use rFVIIa. At a cost of approximately $6000/dose, evaluation of its usage is worthwhile.

**Conclusions:** The sharp decline in outdated platelets from 28.4% to 6.3% with a net difference of 21.1% (P < .05), which corresponds to an actual reduction of 77.82%.

**Prevalence of Rhesus D Variants Confirmed by Molecular Genotyping in a Multiethnic Prenatal Population**

(Poster No. 97)

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**Context:** Rhesus (Rh) D determination in pregnant women is critical to facilitate Rh immune globulin prophylaxis for D-negative women. The RhD antigen comprises more than 30 epitopes; a single amino acid change can cause epitope loss, resulting in "partial D" variants. Individuals with some partial D variants may develop anti-D antibodies against the missing epitope after pregnancy or transfusion. Red blood cells with partial D may type as D+ or D depending on the reagent used. This study screened for Rhd variants.

**Design:** Routine blood bank samples from 501 prenatal patients were tested for RhD using 3 serologic reagents according to manufacturers' directions. Discrepent results were referred for molecular Rh genotyping at Progenika, Inc (Cambridge, Massachusetts).

**Results:** Median age was 27 (range, 16–46 years). The demographics were 41.6% African-American, 19.8% white, 14.8% Hispanic, 12% African, 5.8% Asian, 5.8% Portuguese, and 0.8% unknown. RhD was positive in 88% and negative in 10% of cases; these cases showed consistent reactivity with all 3 methods. Discordant results were found in 11 patients. Weak D (n = 5) and partial D (n = 5) variants were confirmed by molecular genotyping in all but one case.

**Conclusions:** RhD variants, confirmed molecularly, occurred in 2% of our multiethnic population. Some authorities recommend interpreting a 2+ or weaker D test result as D-negative; however, this may not be explicitly stated in the manufacturer's directions. Molecular Rh genotyping is now available to resolve serologic discrepancies. Consideration of the patient's ethnic background, and close cooperation between pathologists and obstetric providers, facilitates optimal prenatal care in these cases.

**New Insights From Longitudinal Analysis of von Willebrand Factor Multimeric Patterns in Thrombotic Thrombocytopenic Purpura**

(Poster No. 98)

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**Context:** ADAMTS13 deficiency and subsequent formation of unusually large von Willebrand factor (ulVWF) multimers are known pathologic factors that underlie clinical development of idiopathic thrombotic thrombocytopenic purpura (TTP). Details about ulVWF formation and the natural history of TTP are unknown. We aimed to define the timely relationship between VWF multimer patterns and the clinical course of TTP.

**Improved Efficiency of Platelet Use Through Active Consultation**

(Poster No. 96)

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**Context:** The short shelf life of platelet products makes their inventory management challenging. Our 530-bed tertiary-care teaching hospital does not keep platelets in inventory; they are ordered from regional blood collection establishments as health care professionals (HCP) request them for transfusion. However, more than 25% of platelets ordered remained in inventory until they were outdated. We tried to determine whether close observation and expert consultation by blood bank staff could help improve platelet use and lower the occurrence of outdated platelets.

**Design:** A retrospective analysis of platelet use was performed. During an 11-month period, all platelet requests were evaluated by blood bank staff according to our guidelines, and expert consultation was offered as needed to HCP. At all times, the decision to transfuse was made by the HCP. A postanalysis was performed using the chi-square test.

**Results:** In the 4 months before active consultation (October 2008 to January 2009), 109 units of apheresis platelets were requested for transfusion by HCP. Thirty-one units (28.4%) were not transfused; they remained in inventory until their expiration date and were discarded. In the 11 months of active consultation, 284 units of platelets were requested by HCP. Of these, only 18 units (6.3%) were not transfused. We observed a sharp decline in outdated platelets from 28.4% to 6.3% with a net difference of 21.1% (P < .05), which corresponds to an actual reduction of 77.82%.

**Conclusions:** The data indicate that active consultation and cooperation between HCP and blood bank staff can significantly reduce the number of platelets that become outdated.
Design: We performed VWF multimeric analyses in more than 300 serial samples longitudinally collected from 15 TTP patients at various clinical stages.

Results: During acute presentation, we observed the persistence of excessive uVWF multimers in patients who died from TTP or who were refractory to daily plasma exchange treatment, indicating a correlation between the severity of uVWF multimers and thrombosis. We also detected severe forms of uVWF multimer patterns in patients who responded to daily plasma exchange treatment but soon experienced episodes of TTP exacerbation. For patients who experienced TTP relapses, some started to show clearance of uVWF multimers from blood 1 to 2 weeks before the clinical event of TTP relapse. In other cases, uVWF multimer levels appeared to persist in blood until several days after patients had received daily plasma exchange. In the course of this study, ADAMTS13 activity levels were also precisely determined using surface-enhanced laser desorption ionization time-of-flight mass spectrometry to establish correlation between ADAMTS13 activity measured in vitro and VWF multimeric patterns formed in vivo.

Conclusions: Our study, for the first time to our knowledge, defines dynamic changes of VWF multimeric patterns in relation to evolution and natural history of TTP and to ADAMTS13 activity levels.

A Maternal Hypercoagulable State May Predispose to Syndromic Microcephaly with Perinatal Asphyxia and Hypoxic-Ischemic Encephalopathy

(Poster No. 99)

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We present a rare case of a young woman with combined heterozygosity for the G20210A prothrombin gene mutation and heterozygosity for the A1298C mutation in the methylene tetrahydrofolate reductase gene. This patient was not aware of her genetic status and delivered her first male infant with microcephaly, perinatal asphyxia, and hypoxic-ischemic encephalopathy. A concomitant intervillosal thrombus with fetal nucleated red blood cell counts (RBCCs) was found in the placenta. The patient subsequently underwent extensive testing regarding hypercoagulopathy, including tests for protein C, S, factor V, antithrombin III, anticardiolipin immunoglobulin G (IgG), plasminogen, hexagonal phase phospholipid, and dilute Russell viper venom. All results were within reference ranges. However, prothrombin and methylene tetrahydrofolate reductase genotyping revealed that the patient was heterozygous for the G20210A and A1298C mutations, respectively. Her management included aspirin and folic acid daily, as well as avoidance of hormonal contraception. Low-molecular weight heparin was prescribed during pregnancy, and her subsequent 2 pregnancies, carefully monitored with coagulation profiles, were both uneventful. The patient revealed that her mother’s past medical history was significant for prolonged bleeding and that both her mother and sister had deep venous thromboses in their 30s with recurrent pregnancy losses. Although single heterozygosity for either prothrombin or methylene tetrahydrofolate reductase present only minimal risk of coagulopathy, the combination of these 2 mutations has the potential to result in severe hypercoagulable complications to the fetus. Screening for these factors in patients of child-bearing age with a family history of thrombosis is highly recommended to reduce the risk of severe consequences both for the mother and for child.

Prevalence of Heparin in Samples Submitted for Lupus Anticoagulant Testing

(Poster No. 100)

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Context: Lupus anticoagulant (LA) testing can be affected by the presence of antiphospholipid medications. For instance, high concentrations of heparin can cause false-positive results. Current guidelines advise caution when performing and interpreting LA testing for patients who are on anticoagulants. We searched our reference laboratory database to determine the prevalence of heparin in samples submitted for LA testing.

Design: We reviewed results of 18,676 LA reflexive test panels. Heparin was identified by medications. For instance, heparin (time before and after heparin neutralization), thrombin time, and reptilase time. Samples were classified as follows: those containing any heparin (any degree of thrombin time prolongation), and those containing a potentially significant heparin concentration (thrombin time, >150 seconds).

Results: There were 1909 LA-positive panels (10%). There were 2111 samples (11%) containing some heparin, and of these, 322 (16%) were LA-positive. Six hundred sixteen samples demonstrated thrombin time prolongations (5% of all samples containing heparin). Eighty of these (13%) were LA-positive, representing 4% of samples containing heparin and 0.4% of all samples.

Conclusions: The LA testing guidelines indicate that samples should be obtained before, or in the absence of, anticoagulant therapy. Despite these recommendations, our data show that a significant number of these samples contain heparin (11%); however, the number of LA-positive samples with a potentially significant heparin concentration were few (0.4% of all samples). We conclude that the laboratory LA-testing algorithms should employ assays to identify and neutralize heparin, and laboratories should provide education regarding appropriate samples for LA testing.

Impact of a Retrospective Audit of Recombinant Factor Seven (NovoSeven) Use in a Tertiary-Level Medical Center

(Poster No. 101)

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Context: Recombinant factor VIIIa (NovoSeven) is frequently used off-label to attempt to control bleeding from intracerebral hemorrhage or cardiovascular surgery. Its use carries a risk of thromboembolic complications. This retrospective chart review was performed to label (MedWatch 2010). Audits of NovoSeven are appropriate and frequently become the responsibility of the transfusion service. We report the impact of a retrospective audit of NovoSeven use on subsequent clinical practice.

Design: In September 2009, NovoSeven use was retrospectively audited for a 12-month period (period 1). Subsequent use was prospectively audited (period 2). Cases were reviewed for clinical history, blood product use, service, complications, and survival.

Results: In period 1, 19 patients received NovoSeven. Ten patients (53%) died a median of 1.5 days after receiving NovoSeven. Five patients (26%) developed complications of DIC and/or thrombosis. Median age of survivors was 54 years; median age of deaths was 61 years. Neurosurgery (56%) accounted for most requests, followed by cardiothoracic surgery (20%) and hematologic-oncology (16%). In period 2, 6 patients received NovoSeven; 2 (33%) died. Median age of survivors was 73 years; median age of deaths was 76.5 years. No complications occurred from NovoSeven. No patients in DIC or renal failure received NovoSeven. Most patients are from neurosurgery (83%). Preliminary data was discussed in October 2009. Subsequently, NovoSeven use decreased from an average of 1.6 per month to once a month with survival outcome improving from 47% to 66%.

Conclusions: Auditing of NovoSeven use may enhance physician awareness of its complications and result in reduced and more appropriate use.

Type 3 von Willebrand Disease Mimicking Hemophilia A in a 50-Year-Old Man With Persistent Hemarthrosis

(Poster No. 102)

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The clinical presentation of von Willebrand disease (vWD) is variable and ranges from mild mucocutaneous bleeding to soft tissue bleeding with hemarthrosis based on subtype. Hemophilia A and type III vWD are both characterized by markedly decreased factor VIII levels and similar clinical presentations of soft tissue bleeding and hemarthromas. However, in type 3 vWD, von Willebrand factor antigen is markedly decreased, whereas patients with hemophilia A have normal or near-normal levels. We report on a 50-year-old man with hemophilia A who was diagnosed at 18 months secondary to prolonged bleeding time and decreased factor VIII activity. Since then, he has had recurrent spontaneous and trauma-induced hemarthromas in the ankles and knees, gastrointestinal and soft tissue bleeding, and bleeding with dental procedures. He was treated with cryoprecipitate infusions. He presented to our institution with left knee hemarthrosis. Admission laboratory work revealed the following results: von Willebrand factor antigen, 16%; factor VIII activity, 2%; ristocetin cofactor, <12%; and normal vWF

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multimer distribution at barely detectable levels. Based on these results, he was rediagnosed with type III vWD. Recombinant antihemophilic factor/von Willebrand factor complex therapy was initiated with stabilization of his bleeding. Recognition of the overlap between these disorders is important for selecting appropriate laboratory testing and for obtaining an accurate diagnosis and appropriate treatment. Severe type III vWD should be considered in the differential diagnosis of patients with soft tissue bleeding and decreased factor VIII activity, and appropriate testing should be performed to render an accurate diagnosis.

The Benefit of Computer Physician Order Entry in Blood Management
(Poster No. 103)

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Context: To avoid inappropriate transfusions, we implemented transfusion guidelines with associated clinical indications for computer physician order entry. We sought to determine the frequency of inappropriate transfusions, patient-specific predictors of inappropriate transfusions, and reasons for bypasses and overrides.

Design: The transfusion guidelines were prepared by reviewing those from many different hospitals and from published data to reflect evidence-based transfusion practices: hemoglobin ≤8% or hematocrit ≤24% for red blood cells; prothrombin time >15, international normalized ratio >1.5 or partial thromboplastin time >45 for fresh frozen plasma (FFP); and <10 000 or >10 000 platelets with clinical reasons. Prospective and retrospective audits were conducted to determine compliance. "Other reasons" that fell outside the indicators were evaluated to determine reasons for bypasses and overrides.

Results: Of all orders processed during a 6-month period, "others reasons" were 0% (0 of 2547) for red blood cells, 22.5% (308 of 1368) for FFP, and 28% (100 of 357) for platelets. The FFP and platelet requests originated mostly from open heart surgery, neurosurgery, and cases of intraoperative and postoperative bleeding. We reviewed laboratory values and clinical information and determined that most of the reasons were in an acceptable range. Some patient-specific predictors associated with inappropriate transfusions required lengthy discussions with physicians.

Conclusions: The computer physician order entry implementation achieved consistency in ordering patterns, educational opportunities for clinicians, greater ease in monitoring transfusion appropriateness for laboratory personnel, and improved evidence-based transfusion practices. Ongoing retrospective review and an open dialogue with clinicians appears to be crucial for appropriate blood management. A prospective audit and front-end interventions targeted at the deciding provider are in progress.
CORRECTION

The authors of an abstract that appeared in the September 2010 issue of the Archives are shown in an incorrect order. The corrected reference is: Czyszczon I, Sahoo S, Alatassi H. Signet-Ring Cell Carcinoma of the Gallbladder in a 22-Year-Old Man: Case Report and Literature Review [CAP abstract]. Arch Pathol Lab Med. 2010;134(9):1289.