Oral mucosal melanoma (OMM) is an aggressive and uncommon subtype of melanoma, comprising less than 1% of all melanomas in the United States. Little is known about its molecular underpinnings, although recent data suggest a molecular profile distinct from its cutaneous counterparts. Herein, we describe a case of lethal OMM with a novel targetable ROS1 gene fusion identified by integrative targeted molecular profiling.

Case Report: A 60-year-old man presented with a 1-month history of an ulcer of the posterior maxillary tuberosity. Biopsy and subsequent maxillectomy demonstrated ulcerated invasive mucosal melanoma. Despite adjuvant radiation therapy, 5-month postoperative imaging revealed metastatic progression. To identify potential targetable therapeutic options for chemotherapy, targeted next-generation DNA sequencing (DNaseq) was performed and was negative for hotspot mutations in BRAF, CTNNB1, GNA11, GNAQ, KIT, MAP2K1, and NRAS. The patient’s health rapidly deteriorated, and he died 7 months following diagnosis. Given the lethal course of this patient’s OMM and lack of identified targetable therapeutic alterations, targeted molecular profiling was performed posthumously on tumor tissue using targeted next-generation DNaseq and RNA sequencing (RNAseq). Targeted RNAseq identified a highly expressed GOPC-ROS1 gene fusion transcript, uniting GOPC exons 1 to 4 to ROS1 exons 5 to 12. Targeted DNaseq demonstrated two-copy loss of CDKN2A and chromosome 8 gain without prioritized somatic variants. Conclusion: Here, we describe a case of OMM with a novel GOPC-ROS1 gene fusion. Tyrosine kinase inhibitors, including crizotinib and entrectinib, have demonstrated activity against ROS1-associated signaling pathways and are used to treat advanced carcinomas with ROS1 gene fusions. A recent report described a patient with metastatic acral lentiginous melanoma harboring a GOPC-ROS1 gene fusion that showed a durable response to entrectinib therapy. Thus, patients with aggressive noncutaneous head and neck mucosal melanoma may benefit from comprehensive molecular profiling beyond the canonical melanoma-associated oncogenic mutations, in order to identify potential novel targetable molecular alterations.

Cholestasis and Ductopenia: Case Report and Etiological Considerations in an Adult

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Introduction: Ductopenia represents intrahepatic cholestasis with a paucity of interlobular bile ducts, which is related to a variety of conditions such as adverse drug reactions, autoimmune diseases, viral infections, chronic rejection, graft vs host disease, and neoplasms. Most of these associations suggest an immune-mediated pathogenic mechanism. The liver biopsy is characterized by marked cholestasis without significant hepatitis but with a characteristic loss of bile ducts in the portal triads. Clinical outcome is hepatic failure unless the underlying factors are addressed.

Case Presentation: A 28-year-old male with a 6-month history of intermittent back pain was treated with Celebrex, tramadol, and hydrocodone. He traveled to the Philippines frequently. He developed dark urine, nausea, jaundice, and weight loss. AST, ALT, and total bilirubin were 90 U/L, 150 U/L, and 4 mg/dL. An abdominal ultrasound and MRI/MRCP of the liver were normal. Laboratory investigations revealed no viral hepatitis B, C, and E by PCR; antinuclear and anti-smooth muscle antibodies were negative, and the serum ceruloplasmin levels were normal. Histologic sections of the liver biopsy were compatible with an acute cholestatic disease due to loss of intrahepatic bile ducts. Later, the patient presented with worsening of lower back pain and new-onset bilateral neck lymphadenopathy. Ultrasound and subsequent PET/CT revealed multiple bilateral enlarged cervical and chest lymph nodes with diffusely increased uptake; markedly increased uptake was seen in L4 as well. A left lymph node core biopsy showed disrupted lymphoid architecture and scattered mummified and lacunar cells that were positive for CD30, CD15, and fascin. The tumor cells were partially dimly positive for CD20, confirming the B-cell lineage. Staining for CD3 was equivocal. The patient was diagnosed with stage IVB Hodgkin lymphoma.

Conclusion: We report a rare case of HL-associated ductopenia. The hepatic improvement coincided with the treatment of HL, supporting the pathogenic link.

Intracholecystic Tubulopapillary Neoplasm of the Gallbladder: A Case Report

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Objective: Intracholecystic papillary-tubular neoplasms (ICPNs) are rare precursor lesions of gallbladder cancer. They are considered homologous to intraductal papillary and tubulopapillary neoplasms of the pancreas and biliary duct. In contrast with the commoner flat-type precursor gallbladder cancer lesions, they form exophytic masses that follow a more indolent clinical course and probably have different genetic pathways to carcinogenesis.

Case Study: We report a case of a 68-year-old woman who presented with right upper quadrant pain. Imaging studies revealed a gallbladder polyp confined to the lumen. The gallbladder was removed laparoscopically.

Results: Grossly, the gallbladder contained a 1.6 × 1.0 × 0.2-cm aggregate of detached polyloid...
A Rare Case of Langerhans Cell Histiocytosis With Solitary Hepatic Involvement in an Adult Patient: Challenging Diagnosis, Transplantation, and Recurrence

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Langerhans cell histiocytosis (LCH) rarely involves liver without systemic manifestation, especially in an adult population. We describe a case of LCH with solitary hepatic involvement that was initially diagnosed as antimitochondrial antibody (AMA)-negative primary biliary cholangitis (PBC), requiring transplantation. When disease recurred, the allograft was lost and the patient required a second transplantation. We have reviewed histopathologic material from both native and allograft specimens, including all biopsies and explant hepatectomies, and clinical data accumulated over a 10-year interval. A 46-year-old woman with a clinical history of panhypopituitarism presented with jaundice and pruritus. An initial hepatology workup including liver biopsy led to diagnosis of AMA-negative PBC with advanced fibrosis. Within a year, the patient progressed to decompensated cirrhosis requiring transplantation. Her posttransplantation course was complicated by frequent bouts of markedly elevated alkaline phosphatase (>1,000 mg/dL) and gamma-glutamyl transferase with transaminases elevated above 100 mg/dL. These abnormalities, together with the liver biopsy findings of bile duct injury and portal eosinophilic infiltrate, were thought to be episodes of acute cellular rejection that occurred frequently during the first 2 years after transplantation. Her liver enzymes would show some improvement without complete normalization on high-dose steroid therapy and become elevated once the therapy stopped. Three years after transplantation, the diagnosis of LCH was established, and 4 years later, the patient lost the liver graft. The explanted allograft revealed patchy distribution of disease, confirming difficulty of LCH diagnosis on a core biopsy. A gold standard for LCH diagnosis relies on morphological and immunohistochemical examination. Establishing a diagnosis of LCH in the liver without systemic involvement is challenging due to the patchy nature of the disease and nonspecific inflammatory infiltrate with eosinophils that can mimic PBC and acute cellular rejection. Awareness of morphological features is crucial for pathologists to render the diagnosis when liver presents as solitary involvement.

Role of Immunohistochemistry in the Classification of Glioblastoma and Anaplastic Astrocytoma in Kenyatta National Hospital

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Objectives: To describe the role of immunohistochemistry in the classification of glioblastoma and anaplastic astrocytoma at Kenyatta National Hospital.

Methods: Laboratory-based retrospective descriptive study conducted at KNH/UON. Study included diagnosed glioblastoma and anaplastic astrocytoma cases (46). Patients' data and histopathological reports were retrieved from the archives and reanalyzed to identify those with a glioblastoma and anaplastic astrocytoma. Histopathology evaluation was done using formalin-fixed, paraffin-embedded blocks and routine H&E and Ki-67, a cell proliferative marker. Immunohistochemical markers isocitrate dehydrogenase (IDH1) and ATRX were done on tissue microarray blocks and routine H&E and Ki-67, a cell proliferative marker. The data were processed in STATA. Descriptive analysis and bivariate analyses were performed to correlate ATRX expression with IDH1 in the cases. The results were presented in the form of charts, tables, and figures.

Results: The lesions were multisited but most commonly in the cerebral cortex. On review of the previous vs current diagnosis: previous WHO grades III and IV (GBM 89.1%, AA 6.5%, AT/RT 2.2%, oligoastrocytoma 2.2%) and current diagnosis after consensus (GBM 95.6%, AA 2.2%, and one case of no tumor). There were 44 GBM cases: classical subtype (77.3%) and one case of oligodendroglioma (2.3%). Forty-five cases underwent IHC. In the majority of the cases (28/44), Ki-67 had a mitotic score (mean [SD] 27.1% [15.1%]) of the GBM cases. The AA case mitotic rate was 7%. IDH1 mutations were present in 11 of 44 GBM cases and in the AA case. ATRX loss was in 17 of 44