Pathologic Quiz Case

A Multicystic Mass of the Pancreatic Body in a 70-Year-Old Man

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A 70-year-old asymptomatic man was found to have a large cystic mass of the pancreas by abdominal computed tomography when staging for his recently diagnosed prostate cancer took place. Magnetic resonance imaging demonstrated an 8.2-cm complex cystic mass in the body of the pancreas that encompassed 80% of the circumference of his superior mesenteric vein without invading it. Celiac and superior mesenteric arteriograms did not show encasement or displacement of vessels. There was no definitive mural nodularity or solid component. No other masses or lymphadenopathy in the abdomen was present. A distal pancreatectomy and splenectomy were performed.

The specimen consisted of the body and tail of the pancreas that measured 16.0 × 6.5 × 2.5 cm and an intact unremarkable spleen. Most of the pancreatic parenchyma was replaced by a fairly well-demarcated, multilocular cystic mass that measured 7.0 × 6.0 × 2.8 cm and contained multiple small thin- and smooth-walled cysts ranging from 0.3 to 2.0 cm (Figure 1). The cysts contained a straw-colored serous fluid. No central scar was noted. Histologic examination revealed that the cysts were lined by low cuboidal-to-flattened epithelial cells and separated by thin fibrous tissue (Figure 2; hematoxylin-eosin, original magnification ×100). The lining cells were bland and had clear cytoplasm and centrally located round nuclei with inconspicuous nucleoli (Figure 3; hematoxylin-eosin, original magnification ×400). No mitotic figures or necrosis was evident. The epithelial cells contained abundant cytoplasmic glycogen that was periodic acid–Schiff (PAS) positive (Figure 4, A; PAS stain without diastase digestion) and that was also sensitive to diastase digestion (Figure 4, B; PAS stain with diastase digestion). The epithelial cells were negative for mucin and nonreactive to monoclonal antibody against carcinoembryonic antigen. Twenty peripancreatic lymph nodes showed no evidence of metastasis.

What is your diagnosis?

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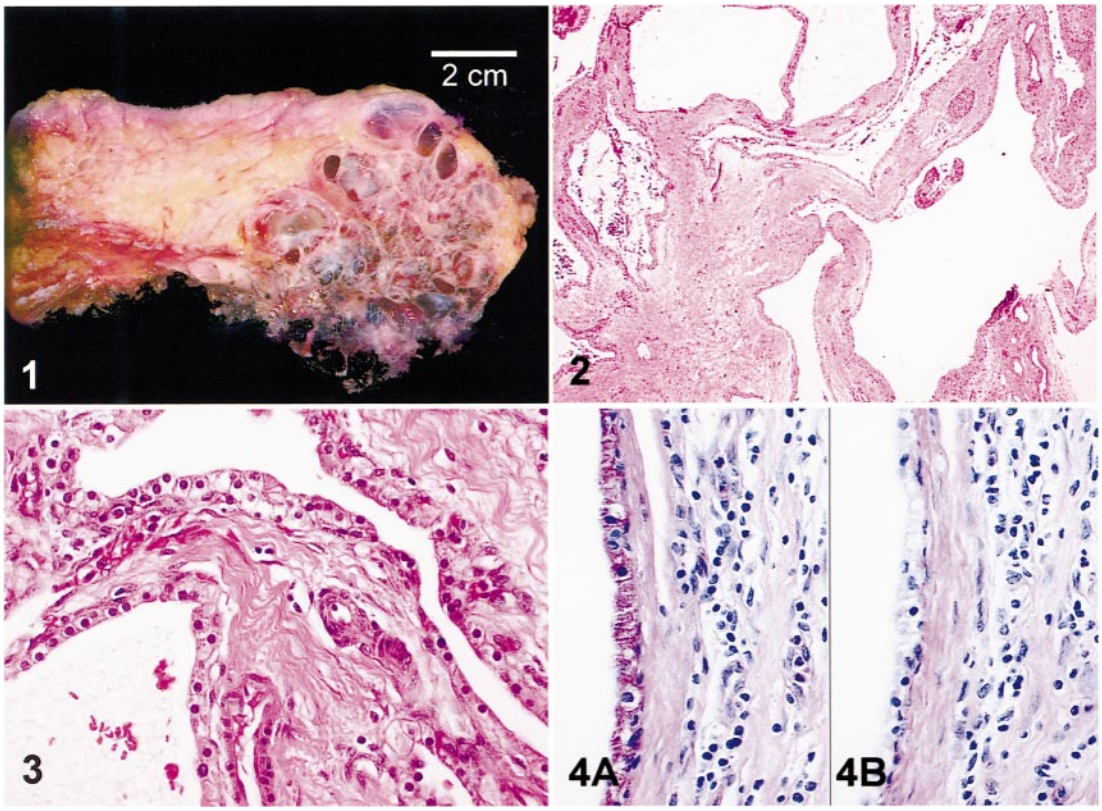

Pathologic Diagnosis: Serous Microcystic Adenoma of the Pancreas

Serous microcystic adenoma of the pancreas, also known as microcystic adenoma, glycogen-rich cystadenoma, and serous cystadenoma, is a benign tumor with an excellent prognosis. It is composed of numerous small cysts lined by bland epithelial cells with clear cytoplasm. Serous microcystic adenoma of the pancreas is uncommon and accounts for 1% to 2% of all exocrine pancreatic tumors.[1,2] Serous microcystic adenoma of the pancreas is commonly found in elderly women in the seventh to eighth decades of life (70% women; mean age, 66 years). Although the etiology and pathogenesis of the neoplasm are still unknown, an association with von Hippel-Lindau syndrome has been reported and confirmed by recent genetic analysis.[3] Serous microcystic adenoma of the pancreas is thought to arise from the ductular or centroacinar cells in the pancreas.[1,2]

Two thirds of patients with serous microcystic adenoma of the pancreas seek care for symptoms related to local mass effects, such as abdominal pain, nausea and vomiting, and weight loss. One third of patients are identified incidentally on a routine physical examination or at autopsy. Jaundice is an uncommon physical finding, even when the neoplasm involves the pancreatic head.[1,4,5] These lesions are rarely multiple, particularly when associated with von Hippel-Lindau syndrome. Up to two thirds of serous microcystic adenomas of the pancreas are located in the body or tail of the pancreas, and the remaining cases are located in the head of the pancreas. It is usually solitary, well circumscribed, slightly bosselated, and round, measuring 1 to 25 cm in greatest diameter (average, 6–10 cm). The cut surface is composed of innumerable tiny cysts that range from 0.1 to 2.0 cm. The cysts are filled with serous or serosanguinous fluid. The cysts are separated from each other by thin fibrous septa and arranged around a centrally located, dense fibrous core from which fibrous septa radiate to the periphery, sometimes forming a central stellate scar.[1–3] Microscopically, the cysts are filled with proteinaceous fluid and are lined by a single layer of cuboidal-to-flattened epithelial cells. The tumor cells have distinct cell borders, clear-to-occasionally eosinophilic cytoplasm, and round-to-oval central nuclei with inconspicuous nucleoli. There is no cytologic atypia, mitotic activity, or necrosis. Occasionally, the tumor cells form intracystic papillary projections, usually without a fibrovascular stalk. The stroma between the cysts is composed of fibrocollagenous tissue with islets of Langerhans, acini, ducts, and nerves that are occasionally trapped inside this tissue.[1–3,6] The cytoplasm of the epithelium in the serous microcystic adenoma of the pancreas is rich in glycogen and lacks mucin. Therefore, the tumor cells are positive for PAS without diastase digestion and negative for PAS with diastase digestion and Alcian blue.[1–3] Immunohistochemical stains can be helpful in the evaluation of serous microcystic adenoma of the pancreas. They are positive for epithelial membrane antigen and cytokeratins 7, 8, 18, and 19. Some studies have also shown focal positivity for CA 19-9 and B72.3. Serous microcystic adenoma of the pancreas is negative for carcinoembryonic antigen, trypsin, chromogranin A, synaptophysin, S100 protein, desmin, vimentin, and factor VIII–related antigen.[1,2,7,8]

Ultrastructural features that characterize serous microcystic adenoma of the pancreas include a uniform row of epithelial cells lining the cysts that are connected by occluding junctions and belt desmosomes resting on a basement membrane. The belt desmosomes are often in contact with intracytoplasmic filament bundles. The cytoplasm contains numerous collections of glycogen granules; however, zymogen and neurosecretory granules are absent. There are scattered mitochondria and profiles of endoplasmic reticulum in the cytoplasm, but Golgi complexes are usually absent. The apical surface of the cells can show short or poorly developed microvilli. Bundles of filaments lie in the apical and basal portions of the cells.[7,8]

The main differential diagnosis for serous microcystic adenoma of the pancreas includes mucinous cystic neoplasm, lymphangioma, serous cystadenocarcinoma, and metastatic clear cell carcinoma. Mucinous cystic neoplasms of the pancreas on gross examination are usually unilocular or oligolocular tumors that contain viscous mucin, while serous microcystic adenomas of the pancreas are multicystic, commonly with a central stellate scar, and contain watery fluid. Histologically, mucinous cystic neoplasms contain columnar cells with basally located nuclei and are rich in cytoplasmic mucin. Mucinous cystic neoplasms are positive for PAS, with and without diastase digestion, and Alcian blue, while serous microcystic adenomas of the pancreas are PAS positive but diastase sensitive and are negative for Alcian blue. Mucinous cystic neoplasms are immunoreactive for carcinoembryonic antigen and CA 19-9, whereas serous microcystic adenomas of the pancreas are negative for both. The distinction between these 2 entities is very important because of the much greater malignant potential of mucinous tumors.[1,2,6,7] Pancreatic lymphangiomas sometimes can closely resemble many cystic neoplasms, especially if they are cavernous or cystic. The endothelial cells lining the cysts in lymphangioma are more flattened than the tumor cells in serous microcystic adenoma of the pancreas and do not contain glycogen (PAS negative). Immunohistochemical markers may be helpful in differentiating serous microcystic adenoma of the pancreas from lymphangioma. Lymphangiomas are negative for cytokeratins but positive for CD31, CD34, and factor VIII–related antigen.[1,2,6] Serous cystadenocarcinomas are very rare malignancies of the pancreas that may share some features with serous microcystic adenomas of the pancreas; the carcinomas may be histologically so similar to serous microcystic adenomas of the pancreas that the diagnosis depends on the presence of metastasis. Nuclear pleomorphism and perineural invasion, when present, suggest a diagnosis of carcinoma.[1,2,4] The clear cytoplasm of the tumor cells raises the possibility of metastasis of clear cell renal cell carcinoma. Clear cell renal cell carcinomas are prone to the formation of small and large cysts, but they typically have a network of delicate, small blood vessels in addition to the clear cytoplasm of tumor cells. The tumor cells commonly show nuclear atypia. The tumor cells contain cytoplasmic lipid and glycogen; therefore, PAS staining may not be helpful. Immunohistochemically, these tumor cells are positive for vimentin.[9]

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