Pancreatoblastoma

A Rare, Adult Pancreatic Tumor With Many Faces

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Pancreatoblastomas are malignant epithelial neoplasms of the pancreas that are heterogeneous and have variable cellular differentiation, complicating the diagnosis. We report a case of pancreatoblastoma occurring in an adult patient, presenting as a pancreatic head mass with liver metastasis and jaundice. The initial liver biopsy diagnosis was metastatic neuroendocrine carcinoma based on morphology and synaptophysin positivity. At pancreatic resection, the diagnostic features of pancreatoblastoma were recognized. We review the radiologic and pathologic differential diagnosis, histologic heterogeneity, clinical presentation, and associated genetic syndromes for this unusual tumor that can mimic other types of pancreatic neoplasia.


REPORT OF A CASE

A 37-year-old man who was previously healthy presented with abdominal pain, jaundice, and elevated liver enzymes. During the clinical investigation of this condition, an abdominal computed tomography scan was performed, revealing masses in the pancreatic head and liver. The patient was also found to have a bile duct obstruction. Clinically, this constellation of findings was believed to be most suggestive of a hepatic metastasis from a primary pancreatic neoplasm. Therefore, a needle biopsy of the liver mass was obtained and was initially diagnosed as a neuroendocrine carcinoma, consistent with metastasis from a pancreatic primary. The patient underwent a surgical procedure to remove the pancreatic tumor and to alleviate his biliary obstruction.

PATHOLOGIC FINDINGS

On gross examination, a tumor was found in the head of the pancreas, measuring 7 cm. The cut surfaces of the mass were gray and fleshy. It obstructed both the pancreatic and common bile ducts and abutted the retroperitoneal margin. Histologically, the mass was heterogeneous (Figure, A through D). Most of the tumor was composed of geographic nests of monotonous-appearing cells, separated by dense, fibrous septa, some of which contained atrophic pancreatic lobules and residual ducts. Many of the neoplastic cells in these nests had a “neuroendocrine” appearance, with basophilic nuclei and scant cytoplasm. In some areas, however, the cells had an appearance more suggestive of pancreatic acinar differentiation with vaguely granular, amphophilic cytoplasm; central nuclei; and prominent nucleoli. In a few places, such cells formed rosettelike structures around small, central tubules. In the stroma surrounding the nests, the tumor itself seemed to form some ductlike structures, lined by columnar epithelium with basally located nuclei. Rarely, there were small collections of cells with a squamoid appearance, composed of polygonal cells with abundant eosinophilic cytoplasm, well-delineated cell borders, and, focally, keratinization. Mitotic figures were scattered throughout the tumor.

The various morphologic components of the tumor were also immunohistochemically distinct. The neuroendocrine-appearing component was positive for synaptophysin, which was also seen in the original liver biopsy and which helped lead to the initial diagnosis of neuroendocrine carcinoma. The ductular component stained with antibodies against cytokeratin 7. There was patchy positivity in the acinar-appearing component with antibodies against anti-trypsin and anti-chymotrypsin. Cytokeratin 20 results were negative. Based on these morphologic and immunohistochemical features, a diagnosis of pancreatoblastoma was rendered.

COMMENT

Pancreatoblastoma is a rare, malignant pancreatic epithelial neoplasm with a heterogeneous appearance, reflecting multiple types of cellular differentiation. Its occurrence has a bimodal distribution, with tumors presenting in both children (mean age, 2.4 years) and adults (mean age, 40 years), although its incidence (or perhaps simply its diagnosis) is more common in the young. Pancreatoblastoma may occur sporadically or in association with genetic syndromes, such as Beckwith-Wiedemann syndrome or familial adenomatous polyposis syndrome.

Clinical Presentation

Patients typically present with nonspecific symptoms, such as abdominal pain, diarrhea, weight loss, and...
vomiting. The tumor can produce α-fetoprotein, and serum α-fetoprotein may be used to follow the clinical response to therapy in patients whose tumors produce it.

**Radiologic Findings**

The radiologic differential diagnosis for these tumors is broad and includes a number of benign and malignant processes, such as mucinous cystic neoplasm, serous microcystic adenoma, ductal adenocarcinoma, pancreatic endocrine neoplasm, acinar cell carcinoma, solid pseudopapillary tumor, and autoimmune pancreatitis. On imaging studies, pancreatoblastomas tend to appear circumscribed and heterogeneous with a mix of solid and cystic areas. Fibrous septa separating collections of tumor cells can be detected on both magnetic resonance imaging and computed tomography scans and are often calcified.1-5

**Pathologic Findings**

Grossly, the tumors are often large, well-circumscribed, and partially encapsulated, occurring with equal frequency in the head and tail of the pancreas. Tumors occurring in adults tend to be particularly large, ranging up to 20 cm.6 The cut surfaces are gray or tan with a soft consistency, and focal necrosis may be found. A cystic variant can be found in patients with Beckwith-Wiedemann syndrome.

Microscopically, the tumor is organized into nests of primitive-appearing cells separated by dense, variably cellular stromal bands. There can be a variety of components, including those with endocrine differentiation, ductal differentiation, and even heterologous elements, such as bone and cartilage. The most characteristic histologic finding, and an important clue to the correct diagnosis, is the presence of squamoid corpuscles. These appear as variably sized foci of squamoid cells, which occasionally keratinize. They can be subtle and difficult to detect, or they can appear overtly squamous.

Our case is similar to previously reported cases of adult pancreatoblastoma.7

**Pathologic Differential Diagnosis**

The diagnostic challenge in correctly identifying these lesions stems from their histologic heterogeneity. Com-
monly considered entities include acinar cell carcinomas, pancreatic endocrine neoplasms, poorly differentiated adenocarcinomas, and solid pseudopapillary tumors (SPT).

Acinar cell carcinoma and pancreatoblastoma are histologically similar, both containing abundant acinar cell differentiation. The most distinguishing feature is the squamoid corpuscle, which is present in pancreatoblastomas and absent in acinar cell carcinomas.

Pancreatic endocrine neoplasms present another potential diagnostic dilemma. Both pancreatic endocrine neoplasm and pancreatoblastoma grow in a nested architecture. Pancreatoblastomas also often contain a neuroendocrine component that stains with antibodies against synaptophysin and chromogranin, adding to the confusion. In our case, the liver metastasis had a nested growth pattern of cells with a neuroendocrine appearance, and it expressed synaptophysin, leading to the original diagnosis of metastatic neuroendocrine carcinoma. Helpful distinguishing features include the characteristic monotonous, the “salt-and-pepper” chromatin pattern of neuroendocrine tumors, and the lack of other cell lineages, such as acinar cells or squamid corpuscles, which are present in pancreatoblastoma. Immunohistochemistry for chymotrypsin or trypsin can be helpful in identifying the acinar phenotype in pancreatoblastomas, as they were in this case.

Generally, the clinical presentation of ductal adenocarcinoma varies greatly from that of pancreatoblastoma. Unlike our case, pancreatoblastomas are generally found incidentally or in association with nonspecific symptoms because they are slow growing, whereas pancreatic adenocarcinomas commonly present with jaundice and weight loss, and are much smaller than pancreatoblastomas at presentation. The unusual presentation of the patient with rapid-onset jaundice in this case added to the diagnostic confusion. Histologically, pancreatoblastomas can have a tubular component, but that is often a small percentage of the tumor. In contrast to ductal adenocarcinoma, the cytologic appearance of the epithelium lining the tubules in pancreatoblastoma is low grade, and the desmoplastic response seen with adenocarcinomas is absent.

Occasionally, SPT can present a diagnostic challenge. Grossly, SPTs are large, solitary, encapsulated masses, similar to pancreatoblastoma. Infrequently, SPTs can be predominantly solid, lacking the characteristic pseudopapillary structures and fibrovascular cores that typically separate SPT from other, solid pancreatic tumors. Both tumors can show evidence of neuroendocrine differentiation and stain with synaptophysin. In addition, both tumors can show abnormal nuclear staining with β-catenin. Again, a search for the characteristic squamoid corpuscles is most helpful, and antibodies against the exocrine enzymes (trypsin and chymotrypsin) can be helpful in the differential diagnosis.

Cytology

Pancreatoblastoma has only rarely been reported in the cytology literature. The reported cases have been in children and young adults. 8-11 The material sampled on fine-needle aspiration included variable components; however, an acinar component and a stromal component were always identified. Most reports also identified a neuroendocrine component, highlighting the importance of recognizing the heterogeneity of these tumors and the sampling problems they present.

Genetics and Hereditary Syndromes

Some studies have evaluated the importance of genetic alterations in pancreatoblastomas. A number of studies have found alterations in the Wnt signaling pathway, especially at the 11p locus. 12-14 That locus is also affected in children with Beckwith-Wiedemann syndrome, a syndrome that has been associated with congenital pancreatoblastoma and other congenital anomalies. Abraham and colleagues 15 reported a case of pancreatoblastoma occurring in a patient with familial adenomatous polyposis. That tumor had a genetic alteration in the adenomatous polyposis coli/β-catenin pathway, which was also demonstrated in 5 of 8 sporadic tumors (62%) by Abraham et al. 16,17 tested.

Therapy

Pancreatoblastomas are treated primarily by surgical resection. Complete resection has been associated with significantly better long-term survival. 6 Chemotherapy and radiation have been used in unresectable cases and recurrent disease with variable response. 15,16 Pancreatoblastoma is an aggressive disease, and adults with this disease tend to have poorer long-term survival than do children. This is particularly true when they present with distant metastasis, which occurs in about one-quarter of cases, most commonly in the liver. 6

References