Solid Pseudopapillary Tumor of the Pancreas

Pankreasın Solid Psödopapiller Tümörü

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Abstract

Solid pseudopapillary tumors of the pancreas, known as Frantz tumors, are rare pancreatic tumors that occur predominantly in women, with very few cases reported in men. We present the case of a 27-year-old female patient who came to the emergency room with an intense upper abdominal pain associated with nausea and vomiting and a palpable mass in the left upper quadrant. She was initially diagnosed with a post-traumatic pancreatic pseudocyst. The patient underwent distal pancreatectomy with splenic preservation; the histopathological report showed a pseudopapillary solid tumor of the pancreas without malignant cells. In this report, a case of rare solid-pseudopapillary tumor of the pancreas is described. Our objective was to report an infrequent case of pancreatic pseudopapillary tumor and to carry out a review of the literature.

Keywords: Pseudopapillary, Tumor, Pancreas

Özet


Keywords: Psödopapiller, Tümör, Pankreas

The Eurasian Journal of Medicine
Introduction

Solid and papillary tumors of the pancreas (SPTs) are unusual benign or low-grade malignant epithelial tumors occurring predominantly in women under the age of 25 years (91%) [1-5]. SPTs are extremely rare, accounting for only 0.17 to 2.7% of all non-endocrine tumors of the pancreas [1,3-6]. Approximately 500 cases of SPT have been described in the last 40 years [2,4,7]. This tumor was first described by Frantz [8] in 1959 as a ‘papillary tumor of the pancreas’. Since 1970, several other terms have been used, including solid and cystic acinar cell tumor, papillary epithelial neoplasm, solid and papillary neoplasm, papillary-cystic tumor, solid cystic tumor, and papillary tumor of the pancreas [Frantz’s tumor]. In 1996, the World Health Organization (WHO) renamed this tumor as SPT for the international histological classification of tumors of the exocrine pancreas [9,10]. The lesions are frequently encapsulated and degenerative cystic changes are commonly observed [3]. Curative resection is the treatment of choice and prognosis is usually excellent [2]. Here, we report the pathological findings of a case of rare SPT.

Case Report

A 27-year-old woman presented with a two-month history of upper abdominal pain. Two days before presentation, the patient had noticed increasing left upper quadrant abdominal pain with associated nausea and vomiting. There was no previous history of trauma or pancreatitis. The patient said that she had no history of alcohol abuse. The patient had no other relevant history.

On physical examination, the patient was noted to be in some discomfort and afebrile with stable vital signs. The patient had anicteric sclera. Abdominal examination revealed an obvious mass in the epigastric region extending to the left upper quadrant. The mass was moderately tender with voluntary guarding but no peritoneal signs. The mass was non-pulsatile, and no bruit was audible. The rest of the examination was unremarkable.

Laboratory studies revealed a hemoglobin of 12.2 g/dL, white count 10.5 x10^3/μL, amylase 599 IU/L, lipase 997 IU/L, total bilirubin 1.1 mg/dL, alkaline phosphatase 86 IU/L, aspartate transaminase 22 IU/L, and albumin 4 g/dL. Electrolytes were within normal limits. CT scan revealed a solid mass [14 x 16 cm] arising from the body and tail of the pancreas, and there was no mass in the liver (Figure 1). This lesion was reported to be consistent with a pancreatic tumor.

The patient underwent surgical exploration. A distal pancreatectomy and splenectomy were performed. The postoperative course was uneventful.

Pathological Examination

All tissues obtained during surgery were routinely fixed in formalin and embedded in paraffin. Sections were stained with hematoxylin-eosin, periodic acid-Schiff (PAS), and Grimelius stains. Using an avidin-biotin complex method with diaminobenzidine as the chromogen, immunoperoxidase staining was performed with the following antibodies: carcinoembryonic antigen (CEA; dilution 1:500; Dako Japan, Kyoto, Japan), 1-antitrypsin (AAT; 1:300; Dako), CA19-9 (1:10; Compagnie Oris Industrie S. A., France), chromogranin A (1:100; Lipshaw, Detroit, MI, USA), neuron-specific enolase (NSE; 1:200; Dako; Chemicon Int. Inc., Temecula, CA, USA), vimentin (Biogenex Labs; San Ramon, CA 1:8,000), and synaptophysin cytokeratin AE1/AE3 (Boehringer-Mannheim, Germany; 1:400), CD34, epithelial membrane antigen (EMA) and S-100. The tumors were round to oval-sized and measured an average diameter of 7.9 cm (range 4.5-12 cm). On the cut section, the tumor was encapsulated by fibrous connective tissue and showed necrosis and hemorrhage. The solid regions displayed a variegated appearance with dark red to pink to tan coloration and were typically soft and friable with areas of hemorrhage and necrosis. The resected pancreatic tumor measured 14x13x10 cm.

The solid portions of the tumors revealed sheets of uniform polygonal cells with well-vascularized stroma and variable degenerative changes. The best-preserved areas were found nearest the fibrous pseudocapsule where the tumor cells displayed uniform oval nuclei, smooth to focally irregular nuclear contours, small nucleoli, and abundant granular eosinophilic cytoplasm. No mitotic figures were noted. Toward the cystic regions of the tumor, the tissue assumed a pseudopapillary appearance with a projection of friable epithelial cells surrounded by hemorrhage and debris. The solid tissue nearest the cystic spaces contained abundant necrotic material, blood, cholesterol crystals, and small aggregates of xanthoma cells (foam cells) (Figure 2).

Histopathologic staining with PAS and mucicarmine demonstrated the epithelial cells as glycogen-rich and without evidence of mucin, respectively.

Upon immunohistochemical examination, tumor cells were absent with staining for synaptophysin, chromogranin A, EMA, cytokeratin and S-100. The specimen stained positively for vimentin, alfa-1 antitrypsin and neuron-specific enolase.

Discussion

SPTs are rare benign or low-grade neoplasms of the pancreas [1-4]. These tumors have specific clinicopathological features that differ from those of adenocarcinoma, cystadenocarcinoma, and insula-originating tumors [1].

Unusual presentations include multicentric tumors in the pancreas and extrapancreatic sites, such as the mesocolon, ret-
properitoneum, omentum, liver and duodenum. Although this tumor occurs in all races, a large number of cases have been reported in the Asian and Black populations [2].

The cell of origin for SPTs remains controversial, but most authors agree on a theory of a primitive epithelial cell as the cell from which this tumor differentiates. Kloppel et al. [9] have suggested that SPTs originate from acinar cell differentiation due to the well-developed Golgi complexes and the presence of alpha-1 antitrypsin. The idea that these tumors originate from pluripotent embryonic cells that are not yet differentiated into either endocrine or exocrine cells has also been proposed on the basis of immunohistochemical and electronic microscopy studies [9]. Kosmahl et al. [10] correlated the immunoprofile of SPTs with that of cells derived from the coelomic epithelium and the rete ovarii. Sex hormones have a role in the growth of Frantz tumors, and pregnancy is associated with stimulation of tumor growth [8].

Most patients with an SPT are female, and their average age is 21 years [5,6]. Notably, the initial symptom of acute abdomen seen in 8% of cases may actually reflect hemoperitoneum in the lesser sac, as a result of spontaneous or traumatic rupture of the capsule. Jaundice, which is associated with tumors located in the pancreatic head, is very rare because of the nature of tumor growth [9]. Patients normally have a slowly growing abdominal mass with or without abdominal pain [7]. Tumor markers are usually normal as well [3,4].

Frantz’s tumors may be discovered by chance during diagnostic imaging procedures or may be suspected in the presence of an asymptomatic palpable mass, or an abdominal swelling in young women [2,4]. Ultrasonography and CT scans may show a well-circumscribed mass located in the pancreas, generally demarcated by a peripheral pseudocapsule. In these masses, there are solid or solid and cystic components and occasionally evidence of calcification [2,4,6,9].

Given a reasonable index of suspicion, an accurate preoperative diagnosis is highly desirable; this diagnosis is possible by fine-needle aspiration cytologic analysis. Awareness of the cytologic features of SPT is important in order to establish an accurate preoperative diagnosis that can lead to a more conservative resection. Performing fine-needle aspiration under EUS guidance has been cited as an appropriate next step in the diagnostic approach for this lesion [2].

Frantz’s tumors have a mean diameter of 10 cm (range 2-20 cm) at the time of diagnosis. They occur more frequently in the body and tail of the pancreas. They appear macroscopically as well-encapsulated and totally or partially cystic in 92% of cases; SPTs are yellow to tan, soft to firm and lobulated masses. In the cut section, the tumor was encapsulated with fibrous connective tissue and showed partially cystic necrosis and hemorrhage. Invasion of the adjacent structures is very unusual [2,4]. The resected pancreatic tumor measured 14x13x10 cm. The cut margin area of the pancreatic tail showed no tumor cell invasion.

Light microscopy generally does not present diagnostic problems [1]. Microscopic findings include a fibrous capsule with a tumor beneath forming a pseudopapillary pattern. In contrast, a pseudocyst wall is composed of granulation and fibrous tissue without an epithelial lining and is therefore easily differentiated histologically from solid pseudopapillary tumors [7,9]. The tumor showed small carcinoma cells with eosinophilic or vacuolated cytoplasm. Typical features are sheets and cords of polygonal cells with pseudopapillary structures with fibrovascular stalks or pseudorosettes [4]. Additional features observed include small dyscohesive cell aggregates, degenerative changes such as hyaline droplets or pink cytoplasmic inclusions with a May-Grunwald-Giemsa stain, mucoid-like material often accumulated in the fibrovascular stalks or surrounded by stromal cells, foamy histiocytes and/or reactive multinucleated giant cells, and calcifications resembling psammoma bodies [2]. Cholesterol clefts and calcification were seen around the capsule. Capsular invasion of the tumor cells was also present at the surgical margin of the peritoneal side. There were foci of marked necrosis; however, neither atypia nor mitosis was observed. In addition, vascular and/or neural invasion was not present. PAS stain showed PAS-positive granules within the tumor cells, but Grimelius staining was negative [8]. Tumor cells invaded the pancreatic tissue to a radius of 3 mm. In the cyst wall, the tumor structure showed a solid pattern with variable stromal sclerosis.

Immunophenotyping shows a distinctive pattern that does not correspond to any of the normal pancreatic cell types but that may aid in diagnosis in a problematic case [1]. Solid PTs are typically positive for vimentin, neuron-specific enolase [NSE], alpha-1 antitrypsin and alpha-1 antichymotrypsin. Vimentin and NSE were diffusely positive in the tumor cells, and alpha-1 antitrypsin also stained strongly. Tumor cells were positive for grumerius, chromogranin A and synaptophysin in a small population of tumor cells. However, keratin, CD34, EMA and S-100 were negative. Most studies, including ours, did not demonstrate reactivity for pancreatic hormones. This point distinguishes SPTs from non-functioning endocrine tumors (the main differential diagnosis on microscopic examination) [2,4].

Electron microscopic findings are inconsistent, usually showing zymogen-like granules and very rarely neurosecretory granules [4]. The malignant potential of these tumors is low, and there is a good overall prognosis [3,6,7,9]. Prognosis after complete resection of this tumor is excellent, with more than 95 percent of patients being cured [2]. Local recurrences are rare despite the use of radical excision [9]. Overtly malignant lesions such as pseudopapillary carcinomas do exist, as do tumors that are ‘borderline’, which show subtle or limited morphological malignant characteristics. Aggressiveness is generally associated with cellular atypia, mitotic activity, and invasion of vascular spaces, perineural interstitium, or neighboring organs. In fact, a local recurrence rate of 6.2% is reported in cases treated by radical surgi-
cal excision, and hepatic or Krukenberg-type distant metastases develop in 5.6% of cases. Frantz’s tumors should be managed with surgery. Conservative resection, when technically possible, is the treatment of choice [8] since chemotherapy and radiotherapy have both proven ineffective [3,7,8].

**Conflict interest statement** The authors declare that they have no conflict of interest to the publication of this article.

**References**