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Solid Pseudopapillary Tumor of Pancreas: Presentations and Management.

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Abstract:

Objective: To report a case series of pancreatic pseudopapillary solid cystic tumor as a rare low grade malignant abdominal tumor, which is relatively frequent in young women, with a discussion about its presentations and management to carry out a review of literature.

Materials and methods: We report a case series of 5 Solid pseudopapillary tumors of pancreas .Then all published series of this tumor since 1952 will be analyzed according to our series. The reviewed parameters included demographic data clinical manifestations, therapeutic modalities, and clinical outcomes.

Results: Eighty percent of patients were female with mean age of 22.4 years. Two were presented with acute abdominal signs following blunt trauma, 2 with mass sensation, and 2 were incidentally found. They were all diagnosed pre-operatively through computed tomographic (CT) scan and all tumors had benign characteristics. No abnormalities were found in the follow up period and control CT scans.

Conclusion: Solid pseudopapillary tumors of pancreas have benign behavior, and the treatment of choice consists of surgical resection. It may spread outside the pancreas, particularly in peritoneal cavity. Metastatic spread may be promoted by trauma, including tumor biopsies, which should never be performed. The outcome after surgical resection is excellent with 90% survival in the long term. Recurrence has been reported in approximately 10% of patients.

Keywords: solid pseudopapillary tumor of the pancreas.

Introduction

Solid-pseudopapillary tumor of the pancreas is a rare condition of which only about 300 cases have been reported in literature. This tumor was first described in 1959. It is known as FRANTZ tumor, named after the author who first described it, also as solid cystic tumor[1]; papillary epithelial neoplasia; solid and papillary epithelial neoplasia; and papillary epithelial tumor. The origin of solid-pseudopapillary tumor has not ever been clarified. It is argued that it does originate either from ductal epithelium[2], Acinar cells[3], or endocrine cells.[4] Another hypothesis is that this tumor arises from pluripotent embryonic cells of the pancreas or from the ridge ovarian analogue related cells, which were attached to the pancreatic tissue during early embryogenesis.[5]

Solid-pseudopapillary tumor of the pancreas has a tendency to predominantly affect young women.[6,7,8] This tumor rarely affects men and is characterized by a long asymptomatic course and nonspecific symptoms. Therefore, it is not uncommon that solid-pseudopapillary tumor is detected only when it has grown to a remarkable size (8-10cm).[7] One feature of this tumor is its low malignant potential. Although the liver is found to be the mostly affected site by metastases, these are only rarely seen.[5,7,9]

In this paper, we study the presentations and demographic specifications of patients who were operated in our center from 2000 to 2005 and their pathologic reports indicated that they suffered from solid pseudopapillary tumor of pancreas.

Materials and Methods:

This is a case series study to assess different presentation, diagnostic methods and demographic specifications of this rare disease. We reviewed the patients' files with pathology report of pseudopapillary tumor of pancreas that were operated in our center from 2000 to 2005. We collected and recorded these data: age, sex, signs and symptoms, past medical history, physical examinations, pre-operational diagnostic measures, laboratory data, per-operational findings, macroscopic and microscopic features of tumors, post-operation and follow up of the patients. In the follow up period, the patients were visited in planned intervals (after 2 weeks, 3 months, 6 months, and then every 6 months) by the operating surgeon. A control computed tomographic (CT) scan with oral and intravenous contrast was performed 6 months after the surgery. Finally, as the tumor is rare, we try to discuss our results with regards to other reported series.

Results:

From 2000 to 2005, five patients were operated in our center with final pathologic diagnosis of solid pseudopapillary tumor of pancreas. The group consisted of four females and one male at the age of 14, 16, 22, 28 and 32. (mean=22.4 years). The disease was presented as acute abdominal pain following slight abdominal blunt trauma in two cases, and as an incidental finding during abdominal sonography (for pregnancy and abnormal uterine bleeding and abdominal pain) in others.

Fullness of the epigastric region was the main complaint by two of our patients, but others were completely symptom-free with no accompanying gastro-intestinal complaints. None of them had positive drug history including hormonal medications. Physical examination revealed a well defined abdominal mass occupying the epigastria and left hypochondriac region in three cases and the other two had no positive abdominal finding. In all cases, primarily, an abdominal sonography showed a cystic mass which was followed by a spiral abdominal and pelvic CT scan with oral and intravenous contrast that confirmed a cystic mass in left side of upper abdomen, posterior to the stomach with multiple solid components and mural enhancement. One of them showed linear areas of hyperdensities within the cyst suggesting hemorrhage. Solid pseudopapillary tumor of pancreas was mentioned as a possible differential diagnosis in the radiology reports (Figure 1). We did not try to take a tissue diagnosis in our cases. Laboratory data including complete blood count, blood chemistry, serum amylase level and coagulation profiles were normal in all cases. Four cases were operated as elective cases and another one urgently. Midline laparotomy was the chosen incision. The extend of resection in two patients was distal pancreatectomy alone, distal pancreatectomy and splenectomy in the other case, distal pancreatectomy, splenectomy plus partial gastrectomy and segmental resection of colon in another one and distal pancreatectomy, splenectomy and left nephrectomy in the last one. In macroscopic examination, there was a spherical or partially spherical lesion with maximum diameter of 5, 13, 16 and 20 cm (in two cases), tan grey in color covered by capsule and lobulated (Figure 2). In cute sections multiple cysts containing necrotic material or bloody fluid was seen. In serial sections for microscopic evaluation, a low grade invasive malignant neoplasm of pancreas characterized by solid cellular sheets with papillary fronds composed of rather uniform epithelial cells arranged around small and large vessels and cystic spaces with fibrinohyalinized borders were observed in all cases. The nuclear grades were 1 and there were no vascular or perineural invasion in these sections (figure 3). All surgical margins were free of tumor. Postoperatively patients were hospitalized for 5-7days and then discharged without complications. Follow up period times were 48, 36, 40, 36 and 30 months. There was no abnormality in control CT scans (table 1).

Discussion:

There is a variety of cystic neoplasms in the pancreas. These include benign serous cystic neoplasms, benign and malignant mucinous cystic neoplasms, and benign and malignant forms of intraductal papillary-mucinous neoplasms. It is important not to assume that all fluid-filled pancreatic abnormalities represent pseudocysts, or that a dilated pancreatic duct represents only chronic pancreatitis. The presence of a solid component in a cystic lesion, septations within the cyst, and the absence of a clinical history of pancreatitis are factors that should alert the surgeon to the possi-

ble presence of a neoplasm. Cystic neoplasms with septation and irregular nodularity of the cyst wall are more suspicious for malignancy. In an effort to establish a preoperative diagnosis of malignancy, the cyst fluid can be aspirated using endosonography and then analyzed.[10]

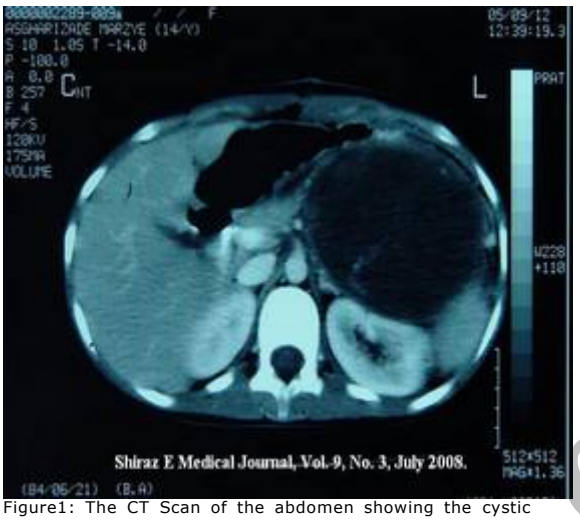

Figure1: The CT Scan of the abdomen showing the cystic lesion in left side of upper abdomen.: The cyst contains multiple enhancing solid components and shows mural enhancement.

Figure 2: A macrograph of the resected operative specimen comprising distal of pancreas, a part of stomach and large bowel and spleen.

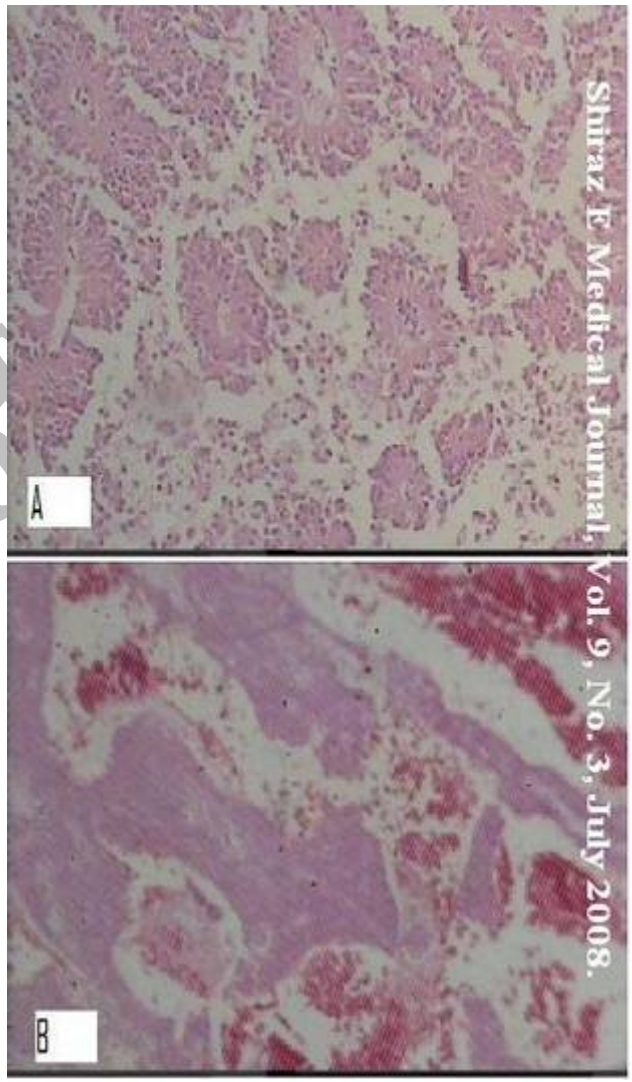

Figure 3: Micrographs showing, A: Tumor cells radially around fibro vascular stalks forming rosette-like pattern. (H & E stain). B: cystic degeneration with solid and pseudopapillary formation and red blood cell in the cystic space.

Table1- Case series patient demonstrations (tumor size is in centimeters).

Case	Sex	Age	Patient complaint	Tumor size	Extent of Surgery
1	F	14	Acute abdominal pain Following blunt trauma	13*10*8	Distal pancreatectomy
2	F	16	Mass	5*4*3	Distal pancreatectomy +splenectomy
3	F	28	Nothing	20*18*10	Distal pancreatectomy
4	F	32	Nothing	16*10*9	Distal pancreatectomy +splenectomy+ Partial gastrectomy + segmental colectomy
5	M	22	Abdominal pain and mass	20*16*8	Distal pancreatectomy +splenectomy +left nephrectomy

However, solid-pseudopapillary tumor (SPPT) is the preferred term for a distinctive type of pancreatic tumor, also known as papillary and solid epithelial neoplasm, papillary-cystic neoplasm and cystic-solid papillary carcinoma. Solid-pseudopapillary tumor of the pancreas has a tendency to predominantly affect young women aged between 25 and 35 years.[6,7,8] Age is reported to range from 8[6] to70 years[2], however, no relationship with oral contraceptives has been proven.[7] This tumor rarely affects men and is characterized by a long asymptomatic course and nonspecific symptoms. Therefore, it is not uncommon that solid-pseudopapillary tumor is detected only when it has grown to a remarkable size (8-10cm).[8] A tumor size of 20 cm in diameter has been reported once in the literature.[9] In our series, we had two tumors of approximately 20 cm in diameter. One feature of this tumor is its low malignant potential. On cross-section it often contains areas of hemorrhage and necrosis .Most cases are surrounded by a well developed capsule, but in some instances, the edges are those of a solid infiltrative neoplasm. Although the liver is found to be the mostly affected site by metastases, these are only rarely seen.[5,9] Furthermore, there are only few reports about invasive growth.[2,7] Survival time has been reported to reach up to 21 years.[1]

Mao in a cumulative review of the literature found that 90%of the patients were female with a mean age of 23.9 years and male/female ratio of 1:9.[5] In our series 80% of patients were female, the mean age was 22.4 years and the m/f ratio was 1:4.

Review of the literature revealed some 24 cases of solid-pseudopapillary tumors of the pancreas reported in children (Table 1) with an average age of 10.8 years (range: 8-16 years) and a male/female ratio of 1:4.75 [11-24] (Table 2). Four cases, 3 girls and a boy of 13-16 years, presented acutely following blunt abdominal trauma in a fashion similar to our cases [11,17,20,21] upon whom Whipple procedure was performed in some cases.[20] In our series one patient was operated emergently following blunt trauma and acute abdominal pain.

Table2- reported cases of solid pseudopapillary tumors of the pancreas in children.

Reference	Year	Cases	Sex	Age(years)
Person et al [11]	1996	1	F	16
Wang et al [12]	1998	3	1 M, 2F	10, 11, 14
Herskovits et al [13]	1999	1	M	13
Jung et al [14]	1999	6	2M,4 F	8-13
Rebhandl et al [15]	2001	4	F	12-16
Akiyama et al [16]	2002	1	F	15
Cervantes-Monteil et a[17]	2002	1	F	15
Sabatino et al [18]	2003	1	F	13
Carrinburu et al[19]	2003	1	F	9
Porte et al [20]	2003	1	M	14
Jiang et al [21]	2003	1	F	13
Andronikou et al [22]	2003	1	F	15
Saw et al [23]	2004	1	F	12
Bardales et al [24]	2004	1	F	13

Patients are often asymptomatic, and the cyst discovered accidentally on physical examination or radiological studies.[25] Occasionally, the tumor may present with a growing abdominal mass associated with vague abdominal discomfort or it may rarely present with an acute abdomen due to tumor rupture and hemoperitoneum as it happened for our patient. Rebhandle et al. reported 4 girls 12-16 years of age presenting with abdominal pain and mass (diameter 7-15 cm), located in tail (n=2), body and tail (n=1) and head (n=1) of pancreas. Only one case developed recurrences, and metastases were found despite of surgical resection and adjuvant chemotherapy.[15] Generally the tumor tends to be fairly benign in young females but appears more aggressive in older males whose mean age is about 10 years older than women.[26] We have not found any malignant behavior in our series.

Among 17 published cases of metastatic pseudopapillary and solid tumor of the pancreas (including 6 cases with peritoneal carcinomatosis), trauma was described in 11 cases (including 3 cases of peritoneal carcinomatosis). Pseudopapillary tumor may spread outside the pancreas, particularly in the peritoneal cavity. Metastatic spread may be promoted by trauma, including tumor biopsies which should never be performed.[27] Usually, there is no evidence of pancreatic insufficiency. Abnormal liver function test, cholestasis, elevated pancreatic enzymes or an endocrine syndrome and tumor markers are all unremarkable.

Given the good prognosis of the disease, it is important to make the diagnosis preoperatively, if possible so that adequate resection will be undertaken. Therefore, imaging studies should be carefully assessed; fine needle aspiration (FNAC) is sometimes considered.[27]

Abdominal ultrasound and CT-scan show a well encapsulated complex mass with both solid and cystic components and displacement of nearby structures. There may be calcifications at the periphery of the mass and intravenous contrast enhancement inside the mass suggestive of hemorrhage.[28]

Procacci et al. reported the accuracy of CT scan in diagnosing cystic pancreatic masses to be about 60%.[28] According to Cantisani et al. MRI is better than CT to distinguish certain tissue characteristics; such as, hemorrhage, cystic degeneration, or the presence of a capsule, particularly as indicated by high signal intensity on Tl-weighted imaging and slightly progressive heterogeneous peripheral contrast enhancement, seen after gadolinium adminis-

tration on dynamic examination.[29] Angiography usually demonstrates an avascular or hypovascular pancreatic tumor and may help to delineate the mass from other involved and adjacent structures.[28] Although some radiological signs are suggestive of SPPT, radiologically guided FNAC may be needed to obtain a preoperative diagnosis. In a study reviewing over 150 cases of SPPT, after having done preoperative FNAC, over70% of lesions were definitely diagnosed as SPPT or had SPPT or low-grade epithelial neoplasm in the differential diagnosis.[27] In our series all cases were diagnosed preoperatively by CT scan. The origin of this tumor remains an enigma. Kosmahl[30] attempted to correlate the immunoprofile of tumors in 59 patients with a cellular origin for SPPT. They used different stains, including exocrine markers of acinar differentiation (trypsin, chymotrypsin), ductal differentiation (glycoproteins), and neuroendocrine markers (synaptophysin and chromogranin). They found that the most consistent positive markers were vimentin, NSE, α-antitrypsin, α-amichymotrypsin and progesterone receptors, present in more than 90% of tumors. Cytokeratin was demonstrated in 70% and synaptophysin in 22%; however, their results failed to reveal a clear phenotypic relationship with any of the defined cell lines of the pancreas. Differentiation along exocrine cell lines has been postulated for SPPT on the basis of trypsin and chymotrypsin positivity. However, NSE and synaptophysin[30] positivity favors an endocrine origin. The female predominance along with the presence of progesterone receptors[31], in some reported cases, suggests a neuroendocrine origin. In a study by Pezzi, SPPT had immunohistochemical and ultrastructural evidence of both an endocrine and acinar-ductal differentiation, suggesting that this tumor may arise from a pluripotent stem cell.[32] Although progesterone receptors have been found by some investigators, estrogen receptors have not been demonstrated.[31,32] Another hypothesis by Kosmahl is that there is a close relationship between the pancreas and the genital ridges during embryogenesis so that the tumor cells may be derived from the celomic epithelium and rete ovarii.[30] These stem cells may become attached to pancreatic tissue during early embryogenesis.[30,31]

The differential diagnosis of SPPT of the pancreas includes any solid or cystic pancreatic disease entity; such as, mucinous cystic tumor, microcystic adenoma, islet cell tumor, cystadenocarcinoma, acinar cell carcinoma, inflammatory pseudocyst, mucus secreting tumor ,pancreatoblastoma, and a vascular tumor-like hemangioma. The first four are usually seen in older patients and have no particular gender preponderance.[33] Pancreatoblastoma is usually found in younger individuals of either sex. Radiologically, a linear sunburst pattern of calcification is the usual finding in microcystic adenoma. A hypervascular pattern on angiography is suggestive of islet cell tumor rather than SPPT.[33]

Grossly, SPPT is a well-encapsulated spherical mass, usually measuring about 8 to 10 cm. The cut surface shows large spongy areas of hemorrhage alternating with both

solid and cystic degenerations. The histological appearance is very distinctive and is considered diagnostic. It is fundamentally a solid tumor with extensive degenerative changes forming solid cellular and hypervascular regions without glands. Areas of degeneration may then develop into pseudopapillary structures. Other studies reported a case of hepatic metastases in which there was DNA aneuploidy and elevated proliferative index.[34]

Surgery is the mainstay of treatment that is usually curative for localized disease. There are evidences for prolonged survival after adequate surgical resection even with metastases. Even if the disease is extensive at the time of presentation, surgical debulking favors prolonged survival. Intraoperative frozen section may be helpful to ascertain the adequacy of the resection margins. There have been only a few reports regarding the use of radiotherapy or chemotherapy[35], so it's difficult to judge the value of such measures.

In conclusion, SPPT of the pancreas is a rare indolent neoplasm with an unclear origin that typically occurs in young females. The diagnosis depends on histological confirmation, but its appearance on imaging is fairly characteristic. Surgical resection has generally been curative, but close follow up is recommended, particularly when the histological appearance suggests a more aggressive tumor.

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