Solid-Pseudopapillary Tumor of the Pancreas Showing a Remarkable Reduction in Size over the 10-year Follow-up Period

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Abstract

An 18-year-old healthy woman was admitted to our department for further evaluation of a pancreatic mass (45 mm in diameter) by transabdominal ultrasound at a general health check. Solid-pseudopapillary tumor (SPT) was suspected from the findings of diagnostic images. Therefore, surgery was recommended. The patient and her family, however, refused surgery. Ultrasound-guided transcutaneous biopsy revealed proliferation of tumor cells with small nuclei showing a pseudopapillary arrangement. PAS positive granules and alpha-1-antitrypsin positive cells were proven, which led to the diagnosis of SPT. As the grade of atypism of the tumor cells was low, the patient underwent follow-up examination once a year at our outpatient department thereafter. The tumor gradually decreased its maximum diameter in 10 years from 45 mm to 15 mm. Thus far, there have been very few reports on the natural course of SPT, and this is the first report describing marked spontaneous shrinkage of a tumor in a long follow-up period.

Key words: solid-pseudopapillary tumor, natural course, pancreatic tumor

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Introduction

Solid pseudopapillary tumor of the pancreas (SPT) is a relatively rare neoplasm of the pancreas with a high prevalence in young women. Most SPTs are considered to be benign. However, the natural course or natural history of SPT has not yet been clarified due to a lack of reports in the literature on cases with a long follow-up period and several reports have emphasized the presence of cases with SPT showing malignant behavior. We herein report an unusual case of SPT in which the tumor showed a marked decrease in size from 45 mm to 15 mm in 10 years without any treatment. This is the first report describing such marked spontaneous shrinkage in a long-term follow-up.

Case Report

An 18-year-old healthy woman was admitted to our department for further evaluation of a pancreatic mass 45 mm in diameter detected by transabdominal ultrasound (US) at a general health check in 1997. She had no history of abdominal injury. Her body height, body weight, pulse rate, blood pressure, and body temperature were 156.0 cm, 82 kg, 72/min, 120/70, and 36.6, respectively. Neither anemia nor jaundice was present in the conjunctiva. Physical examination revealed a soft, flat abdomen with no palpable mass or tenderness, and no enlargement of superficial lymph nodes. Laboratory data on admission showed no abnormalities in serum hormone levels such as insulin, glucagon, gastrin, secretin, and VIP, nor in tumor markers (CA 19-9 and CEA) (Table 1). US and endoscopic ultrasonography visualized a globe-shaped hypoechoic solid mass in the pancreatic head 45 mm in diameter without dilation of the main pancreatic duct (Fig. 1). On CT, the mass was 45 mm in diameter showing slight enhancement with administration of contrast at the late phase. No involvement of the bile duct or the portal vein, or lymph node enlargement was detected. Mag-
Table 1. Laboratory Data on Admission

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>7000</td>
</tr>
<tr>
<td>RBC</td>
<td>4.25 x 10^12/µL</td>
</tr>
<tr>
<td>Hb</td>
<td>12.8 g/dL</td>
</tr>
<tr>
<td>Ht</td>
<td>39.2 %</td>
</tr>
<tr>
<td>PLT</td>
<td>275 x 10^9/µL</td>
</tr>
<tr>
<td>PT</td>
<td>100 %</td>
</tr>
<tr>
<td>TP</td>
<td>7.5 g/dL</td>
</tr>
<tr>
<td>Alb</td>
<td>4.6 g/dL</td>
</tr>
<tr>
<td>T-bil</td>
<td>0.8 mg/dl</td>
</tr>
<tr>
<td>D-bil</td>
<td>0.3 mg/dl</td>
</tr>
<tr>
<td>GOT</td>
<td>23 IU/L</td>
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<tr>
<td>GPT</td>
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<tr>
<td>ALP</td>
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<tr>
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<td>AMY</td>
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<td>Glu</td>
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<tr>
<td>T-cho</td>
<td>183 mg/dL</td>
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<tr>
<td>TG</td>
<td>111 mg/dL</td>
</tr>
</tbody>
</table>

Figure 1. EUS. The tumor was visualized as a solid mass without cystic components. The internal echo of the tumor was homogeneous (1997).

Figure 2. MRI. A mass, 45 mm in size, showing hypointensity in T1WI and hyperintensity in T2WI compared with the neighboring normal pancreas (Fig. 2). Endoscopic retrograde cholangiopancreatography showed a slight shift of the pancreatic duct by the tumor without stenosis or dilatation. Angiography revealed a faint tumor stain in the pancreatic head associated with extension and shift of the arteries without encasement in that area, the feeding artery being the gastroduodenal artery. From these findings, a solid-pseudopapillary tumor (SPT) was suspected and surgical resection was recommended. The patient and her family refused surgery. Ultrasound-guided transcutaneous biopsy revealed proliferation of tumor cells with small nuclei showing a pseudopapillary arrangement around fibrovascular bundles (Fig. 3a). PAS positive granules and alpha-1-antitrypsin positive cells were proven (Fig. 3b and 3c), which led to the diagnosis of SPT. The nuclei were small and the grade of atypism of the tumor cells was low without mitosis. The tumor cells were negative for grimelius and chromogranin stains, p53 protein overexpression was not seen, and the Ki-67 labeling index was low.

All these findings were suggestive of low malignant potential of this tumor. Immunohistochemical stainings of insulin, glucagon, somatostatin, serotonin, gastrin, vimentin, and cytokeratin were all negative. The patient underwent follow-up examination once a year at our outpatient department thereafter. The maximum diameter of the tumor gradually decreased (31 mm in 2001, 26 mm in 2003, 19 mm in 2005, and 15 mm in 2007). Four years after the biopsy, CT demonstrated a tiny cystic area in the periphery of the tumor, which had disappeared at the time of CT performed the next
year. In 10 years, the tumor had shrunk from 45 mm to 15 mm in diameter on CT (Fig. 4). She is presently doing well and continuing follow-up in our department.

Discussion

Solid-pseudopapillary tumor of the pancreas (SPT) was first reported by Frantz in 1959 (1), and subsequently this tumor has been given various names such as Frantz tumor, solid cystic tumor, and solid-pseudopapillary tumor. In 1981, Kloppel et al (2) refined the essential concept of this tumor and summarized its clinical features. Nowadays, giving priority to histological findings, the term solid-pseudopapillary tumor is used in the General Rules for the Study of Pancreatic Cancer.

SPT is a relatively rare tumor of the pancreas with a high prevalence in young women as in the case in this paper. In a report by Mao et al (3), the age of patients with SPT ranged from 2 years to 72 years with an average of 23.9 years. In their report, including 302 cases of SPT, Yoshioka et al (4) reported that the average age was 29.9 years, the first decade being predominant (37.9%), followed by the second (17.2%), third (13.9%), fourth (23.6%), and fifth decades (8.3%).

With the development of diagnostic imaging and accumulation of cases, characteristic findings of SPT in diagnostic imaging have been elucidated, which has made it possible to establish a preoperative diagnosis of SPT in selected cases.
Typical findings are a tumor bulging from the contour of the pancreas with eggshell-like calcification, existence of both solid and cystic components with a thick fibrous capsule, and hypovascularity. When a mass in the pancreas shows the above-mentioned features and age and gender are taken into consideration, it is possible to make a diagnosis of SPT. However, there have been some reports of woman cases, aged cases, and those without cystic components. SPTs without cystic components tend rarely to be associated with calcification, capsule formation, or central necrosis. Differential diagnosis of SPT includes nonfunctioning endocrine tumor, pancreatoblastoma, pseudocyst, and old hematoma. A nonfunctioning endocrine tumor with hypovascularity is especially difficult to differentiate from SPT. In our experience, the internal echo level is a little higher in SPT than in endocrine tumors (5-7). In the present case, although there was no cystic component detected, taking age and gender into consideration, the patient was diagnosed as having SPT.

As for histological features of SPT, Yoshioka et al (4) reported the positive rate of PAS, alpha-1-antitrypsin (AAT), and neuron specific enolase (NSE) stains to be 85.5%, 92.2%, and 82.9%, respectively. Biopsy of the tumor in this patient verified PAS positive granules and AAT positive cells. Recently, some authors have suggested the usefulness of beta-catenin and galectin-3 as useful markers to distinguish SPT from neuroendocrine tumor (8-10).

The prognosis of SPT is generally good with a low prevalence of recurrence after resection and death due to the disease. However, it is also true that there have been reports of cases developing metastasis (11-16), invasion (17-19), or recurrence (20-22). Malignant potential and its marker in SPT have not yet been elucidated. Yoshioka et al (4) reported that although capsule/parenchymal invasion was seen in 13% of SPT cases, the recurrence rate was not high in such patients compared with that in those without. Mao et al (3) reported a good clinical prognosis in patients having SPT with distant metastasis or invasion of adjacent organs. In their study, 43 out of 292 cases (14.7%) of SPT developed distant metastasis or invasion of adjacent organs, only 3 of which died of SPT during a mean follow-up period of 48.3 months. Even histologically diagnosed as malignant, SPTs reportedly seldom show abnormalities in K-ras and p53 genes (21). Enosawa (22) reported that Ki-67 labeling indices (LI) in the area of invasion and intrapancreatic area showed no difference. We previously reported a case of SPT showing an increase in size in 4 years with a doubling time of 720 days, in which overexpression of p53 protein was not observed in the area showing an increase in size and Ki-67 LI was uniformly low in the tumor, showing no difference with observations in the case described here (23). Based on these facts, neither p53 nor Ki-67 LI is deemed to be a marker of malignancy.

In this particular case, the patient refused surgery and we recommended transabdominal biopsy to achieve histological evidence to confirm the adequacy of follow-up. Although there have been no reports on cases developing dissemination following biopsy of SPT, we should be prudent in performing biopsy of SPT as its malignant potential has not yet been clarified well.

A literature search using Medline and Igaku Chuo Zassi with solid-pseudopapillary tumor, prognosis, and outcome as keywords revealed surgically treated cases but no publications on cases showing tumor shrinkage without any intervention during a long follow-up were found. Hata et al (24) reported a case of SPT showing shrinkage of the tumor from 6 cm to 4.5 cm in size during a preoperative period of 2 months. In the present case, shrinkage of the tumor may be attributable to continued degenerative change, including minor hemorrhage and necrosis, and absorption. The tumor of this patient was a hypovascular one with slight enhancement in the late phase as shown by contrast enhanced CT and faint tumor staining as revealed by angiography. During follow-up, CT demonstrated the tumor as essentially a homogeneous solid mass. The CT performed 4 years after establishment of the diagnosis by biopsy showed slight cystic change in the periphery of the tumor, which had disappeared at the time of CT performed the next year. This observation may also support the hypothesis that shrinkage results from the development of degenerative change, including hemorrhage and necrosis followed by absorption. Furthermore, the CT number of the tumor has slightly increased in 10 years, suggesting development of some change in the components of the tumor with a lapse of time, which may also support the speculation that continued/repeated regeneration and absorption as the cause of tumor shrinkage. These observations are extremely rare in other cystic diseases of pancreas.

As for management of SPTs, some investigators state that surgical resection is the treatment of choice as SPTs are categorized as borderline malignancies (25, 26). However, preservation of the organ and its function should be considered seriously and unnecessary surgery should be avoided as SPTs develop mostly in young women.

Differentiation of SPTs with high malignant potential from those with low potential realizes a tailor-made treatment, including follow-up. Further study is necessary on indications for surgical resection, timing of surgery, and grading of malignant potential with biopsy specimens.

References

3. Mao C, Guvendi M, Domenico DR, Kim K, Thomford NR,


