Solid Pseudopapillary Neoplasm of the Pancreas Associated with Familial Adenomatous Polyposis

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Abstract

A man in his thirties visited our hospital for an evaluation of a 12×10-mm pancreatic solid tumor that was accidentally detected on computed tomography performed for follow-up of familial adenomatous polyposis (FAP). We diagnosed the patient with a solid pseudopapillary neoplasm (SPN) based on endoscopic ultrasound-guided fine-needle aspiration, and he underwent pancreaticoduodenectomy. Small SPN tumors appear as solid tumors, without typical features of SPN, making the definitive diagnosis more difficult. The genetic background of FAP patients can predispose them to SPN, and imaging of the pancreas should be performed at prescribed intervals in FAP patients.

Key words: solid pseudopapillary neoplasm, familial adenomatous polyposis, β-catenin, endoscopic ultrasound-guided fine-needle aspiration


Introduction

Solid pseudopapillary neoplasms (SPNs) of the pancreas are rare, accounting for approximately 0.17-2.7% of all exocrine pancreatic tumors (1). Most SPN patients are women; less than 10% of reported SPN patients in the literature are men (2). SPN is usually detected as a heterogeneous mass with a combination of solid and cystic areas, with larger tumors containing areas of calcification in the tumor wall. In contrast, small SPN tumors appear as solid tumors and lack these typical features, making the definitive diagnosis more difficult.

We herein present a case of SPN with a very small lesion in an adult man. SPN was accidentally detected during follow-up for familial adenomatous polyposis (FAP). The clinicopathological features of SPN remain uncertain. However, it is possible that the genetic background of patients with FAP predisposes them to developing SPN (3, 4). In fact, patients with SPN associated with FAP have been reported, although the number of cases is very few (5). We believe that the present case is informative with respect to the relationship between SPN and FAP. We thus present this case along with a review of the literature.

Case Report

A Japanese man in his thirties visited our hospital for an evaluation of a pancreatic tumor accidentally detected on computed tomography (CT) performed for the follow-up of FAP. The patient had a history of FAP and colon cancer, while his father, paternal grandmother and all six paternal uncles and aunts also had colon cancer and his sister had colon polyposis. He currently had no symptoms, and the laboratory findings were normal, including the levels of tumor markers (Table). CT of the abdomen revealed a 12×10-mm round solid mass in the pancreatic head (Fig. 1). The tumor was increasingly enhanced, although the extent of enhancement was less than that observed in the non-tumor parenchyma of the pancreas (Fig. 2). No cystic areas or sites

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Table.  Laboratory Findings.

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<tr>
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<tr>
<td>CEA</td>
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<tr>
<td>RBC</td>
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<tr>
<td>Albumin</td>
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<tr>
<td>CA19-9</td>
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<tr>
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<tr>
<td>ALP</td>
<td>191 IU/L</td>
</tr>
<tr>
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<tr>
<td>CRP</td>
<td>0.07 mg/dL</td>
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![Figure 1](image1.png)

Figure 1.  Abdominal computed tomography. (a) axial view; (b) coronal view. Computed tomography of the abdomen revealed a 12×10-mm round, solid mass (arrow) in the pancreatic head.

of calcification were detected in the tumor. T1-weighted magnetic resonance imaging (MRI) of the lesion showed a low signal intensity, whereas T2-weighted and diffusion-weighted images showed hyperintense signals (Fig. 3). However, no signs of hemorrhage or low-intensity rims were detected on T2-weighted MRI. Meanwhile, ¹⁸F-fluorodeoxyglucose-positron emission tomography (FDG-PET) showed abnormal accumulation in the tumor (maximum standardized uptake value, 3.6) (Fig. 4); no abnormal accumulation was observed in any organs on FDG-PET. Furthermore, endoscopic ultrasonography (EUS) revealed a low echoic, round tumor that was well demarcated from the surrounding pancreas (Fig. 5). The intratumoral echo density was slightly heterogeneous; however, no cystic components were observed. Although endoscopic retrograde cholangiopancreatography (ERCP) showed no abnormalities of the pancreatic duct, the duodenal papillae exhibited swelling, and adenoma was diagnosed based on the findings of the biopsy specimen (Fig. 6).

According to these results, we set out to diagnose the duodenal papillary adenoma and pancreatic head tumor. We considered that the pancreatic tumor may be an adenocarcinoma, acinar cell neoplasm, neuroendocrine neoplasm, SPN or metastatic lesion. However, it was difficult to make a definitive diagnosis based solely on the imaging results. We therefore performed endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) of the pancreatic head tumor. Tissue samples were successfully obtained, and microscopy revealed that the tumor cells contained eosinophilic cytoplasm and small, round nuclei. Immunohistochemically, the tumor cells demonstrated positive staining for CD10, vimentin and β-catenin (Fig. 7). Based on these findings, we suspected a diagnosis of SPN, and pancreaticoduodenectomy was performed.

The examination of the surgically resected specimen revealed a 12×10-mm solid tumor in the pancreatic head. The
Figure 2. Dynamic contrast-enhanced computed tomography. (a) non-enhanced; (b) arterial phase; (c) portal venous phase; (d) equilibrium phase. The pancreatic head tumor was increasingly enhanced, although the extent of enhancement was less than that observed in the non-tumor parenchyma of the pancreas.

Figure 3. Magnetic resonance imaging. (a) T1-weighted images (in phase); (b) T1-weighted images (out of phase); (c) T2-weighted images; (d) diffusion-weighted images. T1-weighted magnetic resonance imaging of the pancreatic head tumor (arrow) showed a low-intensity signal; T2- and diffusion-weighted images showed a hyperintense signal.

cut section contained a yellow, solid tumor that was well demarcated from the surrounding pancreas. The tumor did not contain cystic components, and the histological findings were similar to those of the EUS-FNA specimen. In particular, tumor cells with eosinophilic cytoplasm and small, round nuclei were arranged around fibrovascular stalks and displayed a pseudopapillary structure (Fig. 8). The final pathological diagnosis of the pancreatic head tumor was SPN. In contrast, the duodenal papillae was diagnosed as low-grade adenoma without malignancy. No other lesions were observed in the resected area, including the duodenum.

Discussion

SPN of the pancreas was first reported by Frantz in 1959 (6). According to the WHO classification, SPN is “a low-grade malignant neoplasm composed of poorly cohesive, monomorphic epithelial cells forming solid and pseudopapillary structures. These neoplasms frequently undergo hemorrhagic-cystic degeneration and occur predominantly in young women (7).” The reported incidence of SPN is extremely low, accounting for only 0.17-2.7% of all exocrine pancreatic tumors (1). In addition, only 10% of reported
SPN patients are men (2). Most SPNs occur in the body or tail of the pancreas and form large tumors (average size, 10 cm) (8). SPN lesions usually display calcification and signs of degeneration, including hemorrhage and necrosis. Therefore, diagnostic imaging, including CT, MRI and EUS, often shows heterogeneous tumors with a combination of solid and cystic areas. SPNs are initially solid tumors, although they change over time into heterogeneous tumors with solid and cystic areas exhibiting degeneration. Therefore, small-sized tumors may not present with the typical features of SPN. In fact, the tumor in the current case was very small (12×10 mm) and appeared to be completely solid, with no typical features of SPN, such as cystic areas, thick walls or calcification. In addition, MRI showed the tumor to be almost homogeneous, and no signs of hemorrhage or necrosis were observed. Furthermore, our patient was an adult man, and the tumor occurred in the pancreatic head. We were unable to diagnose the tumor solely based on the imaging results. The relative risk of pancreatic adenocarcinoma in patients with FAP is reported to be 4.5 (9), and various tumor complications, such as acinar cell carcinoma, may occur (10). Therefore, EUS-FNA was performed to obtain a definitive diagnosis in this case.

EUS-FNA has been established to be a useful tool with good diagnostic accuracy for detecting pancreatic tumors (11), including SPNs (12). Romics et al. proposed an algorithm for the diagnosis and treatment of SPN (13), according to which, surgery should be performed if the tumor shows typical features of SPN on US, CT and MRI. If the radiological diagnosis is equivocal and further confirmation is required, EUS-FNA is recommended. Even in cases involving a tumor size of ≤10 mm, the diagnostic accuracy of EUS-FNA is reported to be very good (14). The tumor in the present case was 12×10 mm in size, and the tissue ob-
Figure 6. Endoscopic retrograde cholangiopancreatography (ERCP) showed no abnormalities of the pancreatic duct (a); however, the duodenal papillae were swollen (b), and adenoma was diagnosed based on the biopsy specimen.

Figure 7. Histopathology of the EUS-FNA specimen. Hematoxylin and Eosin staining (a) showed that the tumor cells contained eosinophilic cytoplasm and small, round nuclei. Immunohistochemically, the tumor cells stained positively for CD10 (b), vimentin (c) and β-catenin (d).

tained via EUS-FNA was immunostained adequately, allowing us to diagnose the tumor as SPN.

FAP is an autosomal dominant disease caused by a germ-line mutation in the adenomatous polyposis coli (APC) gene, resulting in the formation of hundreds to thousands of large intestine adenomas. Colorectal cancer inevitably develops unless the tumors are removed (15, 16). FAP patients may also develop a variety of extra-large intestinal and extra-intestinal lesions, including duodenal papillary tumors, desmoid tumors and thyroid tumors (10, 17). A point mutation in exon 3 of CTNNB1, which encodes β-catenin, is detected in most cases of SPN. Cytoplasmic β-catenin is ex-
pressed at low levels under normal conditions and increased in most patients with SPN (18, 19). The FAP-related mutation in APC activates the Wnt/β-catenin signaling pathway. As a result, the cytoplasmic β-catenin expression increases, as it does in cases involving the SPN-related CTNNB1 mutation (20). Therefore, patients with FAP may develop tumors commonly seen in those with CTNNB1. However, based on our literature search, we were able to find only one case of concurrent FAP and SPN (5). The fact that both FAP and SPN are rare diseases and FAP can easily complicate cases of pancreatic and duodenum papilla cancer may explain the reduced rate of concurrent SPN cases. The current patient was confirmed to have an APC mutation on a genetic examination, and the tumor specimen was shown to express cytoplasmic β-catenin. These factors suggest that this case of SPN occurred as a result of the FAP-related mechanism described above. Furthermore, the present patient was male with primary onset in the pancreatic head, which is atypical for SPN. A case of FAP with primary onset in the pancreatic head has also been reported in a woman (5). Therefore, a causal relationship with the site of onset is suspected, although the details remain unclear due to the lack of available cases.

SPN is classified as a low-grade malignant neoplasm. SPN patients treated with complete surgical resection have a good prognosis (21). However, approximately 15-20% of cases of SPN manifest with malignant behavior, including perineural or vascular infiltration and metastasis (22, 23). Fatal cases of recurrence have been reported (24). Therefore, the diagnosis of SPN and subsequent surgical resection should be performed without delay. In the present case, we detected the tumor at a very early stage by chance because CT was performed for the follow-up of FAP. As patients with FAP may develop a variety of tumors, routine imaging of the pancreas should be conducted at designated intervals and practitioners should keep in mind the fact that FAP can predispose patients to SPN.

The authors state that they have no Conflict of Interest (COI).

References
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