Endoscopic Ultrasound-Guided Fine Needle Aspiration Cytology Diagnosis of Solid Pseudopapillary Neoplasm: Three Case Reports with Review of Literature

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Solid pseudopapillary neoplasm of the pancreas (SPN) is relatively rare and it occurs almost exclusively in women. We recently experienced three cases of SPN diagnosed by endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA). These three cases were two male and one female patient whose age was 29, 37, and 44 years old. Radiological diagnosis was pancreatic endocrine tumor (PEN) showing solid with a heterogeneous echogenicity. EUS-FNA cytology specimens consisted of single cells and aggregates of uniform cells, forming microadnexal structures, branching, papillary clusters with delicate fibrovascular cores. In conclusion, a single diagnosis of SPN based on clinical and radiological findings would be risky because there is a possibility of it being misdiagnosed as PEN or other malignancies. An EUS-FNA is therefore essential for establishing the diagnosis. In addition, the pathologists should recognize the characteristic cytologic findings with immunoprofiles of SPN to prevent misdiagnosis of SPN.

CASE REPORTS

Clinical findings
Case 1

A 44-year-old man with no previous medical history presented to the hospital complaining of the right lower quadrant ab-
Abdominal pain. The patient had no history of injury, melena, fever, hematochezia, nausea or vomiting. On ultrasonography and CT scans of the abdomen, there was a pancreatic head mass (Fig. 1A). The patient was therefore transferred to our hospital for further evaluation and treatment. The patient underwent EUS. This showed that the patient had a well-circumscribed, 4 cm-sized heterogeneous echogenic mass in the pancreatic head (Fig. 1B). Then, the patient underwent EUS-FNA, whose findings were initially suggestive of PEN. The patient underwent pylorus preserving pancreatico-duodenectomy but received no further treatment. At the time of writing, the patient had no evidence of residual tumor.

Case 2

A 37-year-old previously healthy woman incidentally had a 1.7 cm-sized pancreatic mass detected on abdominal ultrasonography during the regular medical check-up. The patient was transferred to us for further evaluation and treatment. On abdominal CT scans, there were findings that are suggestive of a small, low-attenuated mass in the pancreatic body with a mi-

Fig. 1. (A) A well-defined, partly enhancing 4.0 cm-sized mass is present in the pancreatic head of case 1 (arrows). (B) An endoscopic ultrasound image shows a 4.0 cm-sized, round, well-defined and heterogeneously hypoechoic solid mass in the pancreatic head. (C) A whitish-tan, solid mass with hemorrhage is noted in the pancreatic head on the resected specimen (arrows).
nal dilatation of the distal pancreatic duct. Under the clinical impression of pancreatic cancer, the patient underwent EUS for further evaluation of the pancreatic lesion. This showed that the patient had a well-defined, homogeneously echogenic mass in the pancreatic body. The patient underwent EUS-FNA followed by the distal pancreatectomy without adjuvant chemotherapy.

Case 3

A 29-year-old previously healthy man presented to the hospital complaining of dyspepsia and constipation. In spite of the conservative medication, the patient had no symptoms improved. On abdominal CT scans, there was a benign-looking, 5 cm-sized mass in the pancreatic tail. The impression was a microcystic serous cystadenoma or a pancreatic cancer, for which the EUS was performed. Then, the EUS showed that there was a well-circumscribed, homogeneous echogenic mass with a mostly solid containing calcification. This was followed by the FNA.

Following this, the patient underwent spleen-preserving distal pancreatectomy.

Pathologic findings

FNA findings

The smears were highly cellular with a population of small, uniform cells in cohesive, often branching and papillary cell clusters, or interspersed with many single cells. The background was clean or filled with hemorrhage. Delicate fibrovascular cores with myxoid stroma were noted. Because cell clusters were admixed with hemorrhage, characteristic architectures were not clearly indentified in case 1, which lead to misdiagnosis of PEN. Individual tumor cells are uniform with round-to-oval nuclei, smooth to slightly indented or grooved nuclear membranes, even finely granular chromatin and inconspicuous nucleoli (Fig. 2A). The cytoplasm is scanty to moderate. Some tumor cells show rosette formation with luminal myxoid globule (Fig. 2B).

![Fig. 2.](http://dx.doi.org/10.4132/KoreanJPathol.2012.46.4.399)
Liquid-based cytology smear was performed in one patient (case 2). The cytologic findings were similar to those of conventional smears. In comparison with conventional smear, however, papillary cell clusters were more frequent and more easily detected (Fig. 2C) in clean background without hemorrhage (Fig. 2D). Individual cells showed finely granular chromatin with more prominent nucleoli. There are no differences in the indentation or nuclear grooves between the two methods.

Gross findings
All tumors were well-circumscribed and demarcated from the pancreatic tissue without capsule. In case 1, the tumor was 4 cm in size and located in the pancreatic head and its cut surface was grayish-white, solid with focal hemorrhage. No cystic change was identified (Fig. 1C). In case 2, the tumor was 1.7 cm in size and located in the pancreatic body. The tumor was grayish tan, solid with hemorrhage in 20% of tumor volume. No cystic changes or capsule were noted. In case 3, there was a 5 cm-sized, well-demarcated solid mass in the pancreatic tail. The mass showed a hemorrhage without cystic change.

Microscopic findings
All tumors were composed of sheets of relatively uniform, loosely cohesive or distracted cells with eosinophilic slightly granular cytoplasm and uniform nuclei with nuclear grooves. There were delicate background vasculatures (Fig. 3A). By this dyscohesive nature of tumor cells, cells were loosely adherent to the blood vessels, forming characteristic pseudopapillae. Cores of pseudopapillae stroma or either myxoid or hyalinized (Fig. 3B and 3C). Foam cells and red blood cells were scattered among the neoplastic cells. Some of the neoplastic cells had not only a clear, almost vacuolated cytoplasm but also intracytoplasmic eosinophilic globules. But there was a lack of mitotic figures. Immunohistochemical staining was performed in all the three cases (Fig. 4), whose results are summarized in Table 1.

DISCUSSION
Diagnosis of SPN is important for the clinical management of patients. Diagnostic modalities including CT and MRI can only suggest a diagnosis of SPN. CT findings include an encap-
sulated lesion with a well-defined margin and variable central areas with cystic degeneration, necrosis or hemorrhage. Calcifications may occasionally be seen. MRI is helpful for identifying the characteristic internal signal intensities of blood products, which is useful in making a differential diagnosis of SPN from other cystic pancreatic tumors.12 Advances in technology have permitted the performance of FNA biopsy under EUS guidance.13

EUS permits a better evaluation of SPN, but the findings also are not specific. Because SPN occurs almost exclusively in women, with an approximate female-to-male ratio of 9:1, it might be difficult to make a preoperative diagnosis if the case presents with unusual clinical and radiologic findings for which an accurate preoperative diagnosis using EUS-FNA cytology

![Image](http://www.koreanjpathol.org)

Fig. 4. In case 3, the tumor cells show an immunopositivity for vimentin (A), progesterone receptor (B), and β-catenin (C) and an immunoreactivity for a loss of E-cadherin (D).

Table 1. Summary of immunohistochemical findings

| Anti-serum | Source | Dilution | Case 1 | Case 2 | Case 3 |
|------------|--------|----------|--------|--------|--------|
|            |        |          | CB     | Tissue | CB     | Tissue | CB     | Tissue |
| Synaptophysin | Dako    | 1:300    | Positive | Positive | ND     | ND     | ND     | ND     |
| Chromogranin | Dako    | 1:200    | Negative | Positive | Negative | ND     | ND     | ND     |
| Vimentin    | Ventana | RTU      | ND      | Positive | Positive | ND     | Positive | ND     |
| PR          | Ventana | RTU      | ND      | Positive | Positive | ND     | Positive | ND     |
| CK          | Dako    | 1:400    | ND      | Negative | ND     | Negative | ND     | Negative |
| CD10        | Novocastra | 1:400   | ND      | Positive | ND     | Weakly Positive | ND     | Positive |
| β-catenin   | Transduction | 1:600  | ND      | Positive | ND     | Positive | ND     | Positive |
| E-cadherin  | Transduction | 1:800  | ND      | Negative | ND     | Negative | ND     | Negative |

CB, cell block; ND, not done; RTU, ready to use; PR, progesterone receptor; CK, cytokeratin.
would be highly desirable. This is because a local surgical excision is usually curative in SPN. Since Bondeson et al. first made a correct diagnosis of SPN on the preoperative FNA, 57 cases of SPN have been diagnosed based on cytologic findings on the percutaneous FNA. 

Recently, some cases of SPN have also been diagnosed on the EUS-FNA. We summarized EUS-FNA cytologic features of SPN (Table 2) and their immunohistochemical profiles (Table 3) according to a review of the English literatures. FNA cytomorphic features are highly characteristic and distinct from those of other cystic or solid tumors of the pancreas. On aspirated materials, the most frequent features are the presence of marked cellularity with pseudopapillary fragments composed of fibrovascular cores lined with one to several layers of tumor cells intermingled with dis cohesive neoplastic cells. As shown in our cases, inter- or intra-cellular pink hyaline globules, mucus-like globules are surrounded by the stromal cells and cellular debris, which is also one of the frequent features. Histologic differential diagnosis of SPN from PEN or pancreatic adenocarcinoma is important. This is because SPN have a much better prognosis compared with PEN or pancreatic adenocarcinoma, with only 10% to 15% of cases recurring or metastasizing. More than 95% of SPN are cured by complete surgical resection alone. The uniform, bland-appearing, often dispersed epithelial cells of SPN can greatly resemble those of PEN. When the papillary architecture is absent in SPN cytologic specimens, a careful attention to the nuclear details that are commonly seen in many cases of SPN, including the presence of nuclear grooves, indentations, the occasional perinuclear vacuole or intracytoplasmic hyaline droplet, will be useful in making a differential diagnosis between the two disease entities. In an actual clinical setting, however, it would be almost impossible to make a differential diagnosis between the two disease entities without an ancillary test. In case 1, it was particularly difficult to make a diagnosis of SPN because the tumor cells were arranged in solid nests and pseudopapillary architectures were not prominent. The possibility of PEN could not be completely ruled out even in the resected specimens. We could therefore make a diagnosis based on immunohistochemical stains. The aspirated tissue from any lesion can be prepared in a number of different ways: direct smears, cytospins, liquid-based preparations and cell blocks. Direct smears are the most common, therefore make a diagnosis based on immunohistochemical stains. The aspirated tissue from any lesion can be prepared in a number of different ways: direct smears, cytospins, liquid-based preparations and cell blocks.
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