【 CASE REPORT 】

Perivascular Epithelial Cell Tumor of the Pancreas Diagnosed Preoperatively by Endoscopic Ultrasound-guided Fine-needle Aspiration

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Abstract:

We herein report a 49-year-old woman with a perivascular epithelial cell tumor (PEComa) of the pancreas. Imaging studies demonstrated a relatively well-demarcated mass, measuring approximately 40 mm in diameter, located in the pancreatic tail. It was heterogeneously enhanced almost to the same degree as the surrounding pancreatic tissue in both the arterial and portal venous phases. We performed endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) using the Acquire® 22-gauge needle and preoperatively obtained a definitive diagnosis with a sufficient sample. Clinicians should consider pancreatic PEComa in their differential diagnosis of patients with a pancreatic mass.

Key words: perivascular epithelial cell tumor, pancreatic PEComa, EUS-FNA, Acquire®

Introduction

Perivascular epithelioid cell tumors (PEComas) are a rare neoplasm derived from mesenchymal tissue with histological and immunohistochemical (IHC) characteristics of perivascular epithelioid cells (PECs) (1). PECs, which are distributed in the perivascular region in a radial pattern, show epithelioid features when near vessels but become spindle-shaped when distant from vessels. PECs are members of the PEComa tumor family, which includes tumors arising from the kidney and liver, such as angiomyolipoma, as well as clear-cell "sugar" tumors of the lung and extrapulmonary sites and lymphangioleiomyomatosis. On IHC staining, these neoplastic cells express melanocytic markers, including human melanoma black 45 (HMB-45) and melanoma antigen (Melan-A), as well as myogenic markers, such as α-smooth muscle actin (α-SMA) and desmin (1-6). PEComas can occur in any part of the body but tend to arise in bone, soft tissue, abdominopelvic organs, the gastrointestinal tract, and retroperitoneal organs. However, PEComas arising in the pancreas are extremely rare (7). Accordingly, the clinical and imaging manifestations of pancreatic PEComas have not been fully clarified.

The diagnosis of solid pancreatic masses using imaging modalities is sometimes difficult. To plan surgical resection of the pancreas, a histopathological examination is required preoperatively for a definitive diagnosis. It was reported previously that suspected pancreatic malignancy can be evaluated accurately using endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA), regardless of the size or location of the lesion, and the accuracy in all subgroups was > 90% (8). Thus, it is possible to diagnose the majority of pancreatic lesions using EUS-FNA with considerably high accuracy. However, sufficient samples are necessary for a histopathological assessment, such as IHC staining, to obtain a correct diagnosis.

We herein report a rare case of PEComa of the pancreas

Figure 1. Contrast-enhanced abdominal computed tomography revealed a relatively well-demarcated mass, measuring approximately 40 mm in diameter, located in the pancreatic tail (arrows). It was heterogeneously enhanced almost to the same degree as the surrounding pancreatic tissue in both the arterial and portal venous phases. (A) Plain scan. (B) Arterial phase. (C) Portal venous phase.
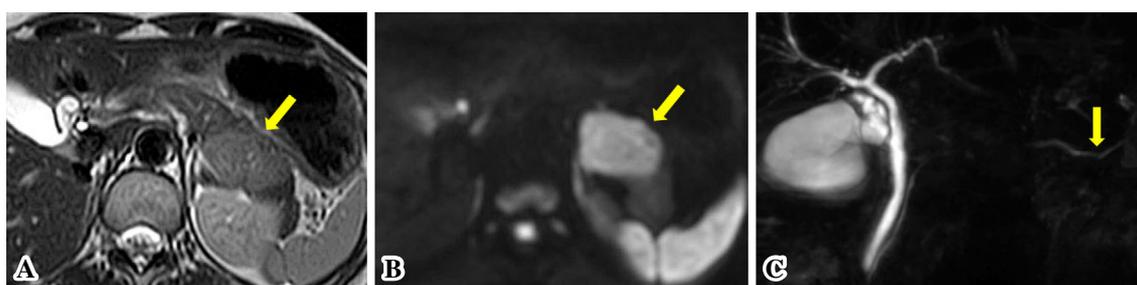
Figure 2. The pancreatic mass was slightly hyperintense on T2-weighted magnetic resonance imaging (MRI) (arrows) (A). Diffusion-weighted imaging showed that the lesion was clearly hyperintense on MRI (arrows) (B). Magnetic resonance cholangiopancreatography showed that the main pancreatic duct was translocated to the inferior side (arrows). Disruption and dilatation of the upstream main pancreatic duct were not found (C).

diagnosed preoperatively by EUS-FNA.

Case Report

A 49-year-old woman was referred to our hospital for the further examination of a mass in the pancreatic tail that was incidentally discovered by a clinical survey using abdominal ultrasound. She had no remarkable medical history and did not consume alcohol. Her family history was not relevant to her current disorder. She did not have any symptoms, and her physical examination showed no significant abnormal findings.

Laboratory tests, including hematological, serological, biochemical, and tumor marker analyses, revealed no significant abnormal findings. IgG4 was also within normal limit at 38.3 mg/dL (normal range, 4.5-117 mg/dL). Abdominal contrast-enhanced computed tomography (CT) demonstrated a relatively well-demarcated mass, measuring approximately 40 mm in diameter, located in the pancreatic tail (Fig. 1). It was heterogeneously enhanced almost to the same degree as the surrounding pancreatic tissue in both the arterial and portal venous phases. This mass was slightly hyperintense on T2-weighted magnetic resonance imaging (MRI) (Fig. 2A). Diffusion-weighted imaging (DWI) showed that the lesion was clearly hyperintense (Fig. 2B), and an apparent diffusion coefficient map demonstrated hypointensity on MRI. Magnetic resonance cholangiopancreatography

(MRCP) revealed that the main pancreatic duct in the tail was translocated to the inferior side. Disruption and dilatation of the upstream main pancreatic duct were not found (Fig. 2C). There was no evidence of distant metastasis, direct invasion to adjacent organs, or extension of the lesion into the surrounding soft tissues. In addition, enlarged lymph nodes in the peri-pancreatic region were not detected by either CT or MRI. EUS revealed a well-defined hypoechoic mass region in the pancreatic tail, and contrast-enhanced harmonic EUS using Sonazoid® showed the tumor as iso-enhanced compared to the surrounding pancreatic tissue (Fig. 3A). Neuroendocrine neoplasm (NET), ductal adenocarcinoma, solid-pseudopapillary neoplasm (SPN), and pancreatic lymphoma were considered as differential diagnoses based on CT findings of heterogeneous enhancement of the pancreatic solid mass (9, 10). However, as neither disruption nor dilatation of the upstream main pancreatic duct were revealed on MRCP, there was little possibility of pancreatic ductal adenocarcinoma. Tumor-forming pancreatitis was also suggested due to an isovascular pattern on contrast-enhanced harmonic EUS (11). Therefore, NET, SPN, tumor-forming pancreatitis, and other rare tumors of the pancreas were considered based on these preoperative imaging studies.

Since a malignant tumor could not be ruled out, the patient underwent EUS-FNA to establish a definitive diagnosis. We performed EUS-FNA with a total of three punctures
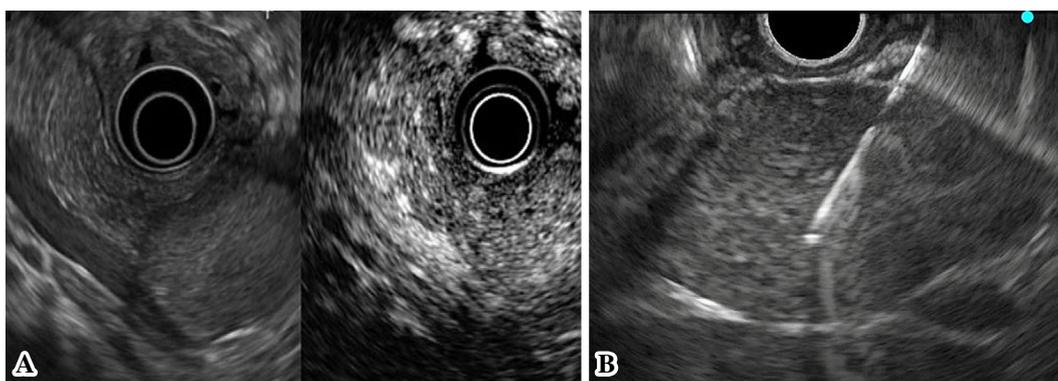
Figure 3. EUS revealed a well-defined hypoechoic mass region in the pancreatic tail, and contrast-enhanced harmonic EUS using a Sonazoid® showed the tumor as iso-enhanced compared to the surrounding pancreatic tissue (A). The mass was relatively hard; however, the puncture was achieved with little effort, and the needle never bent during the procedures (B).
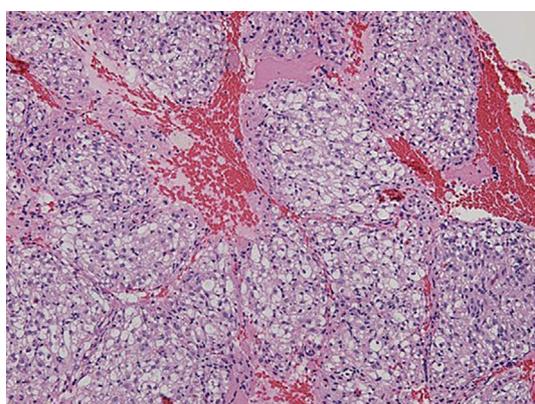
Figure 4. Histological section of fragments of the pancreatic mass lesion obtained by EUS-FNA consisting of epithelioid to spindle-shaped cells with abundant eosinophilic cytoplasm, round-to-oval nuclei, and indistinct small nucleoli proliferating in a sheet-like fashion (Hematoxylin and Eosin staining ×200).

Table 1. Results of Immunohistochemical Analysis.

Antigen	Results
HMB-45	+
Melan-A	+
cyclin-D1	+
vimentin	+
α-SMA	+
β-Catenin	+
AE1/AE3	-
CD10	-
CD34	-
CD56	-
chromograninA	-
synaptophysin	-
c-kit	-
DOG1	-
desmin	-
S-100	-
Ki-67	<5%

using the Acquire® device with a 22-gauge needle (Boston Scientific Corporation, Marlborough, USA), because a high rate of procuring a sample sufficient for a histological evaluation with a high diagnostic accuracy was reported with this device. The mass was relatively hard; however, the puncture was achieved with little effort, and the needle never bent during the procedures (Fig. 3B). We used the negative pressure suction technique with a 20-mL syringe and the fanning method, and the needle was moved back and forth approximately 30 times for each puncture. A rapid on-site evaluation by the Diff-Quick method revealed sufficient amount of specimen, and clusters of tumor cells were present with slightly hypertrophied nuclei. Histologically, the tumor was composed of epithelioid to spindle-shaped cells with abundant eosinophilic cytoplasm, round-to-oval nuclei, and indistinct small nucleoli proliferating in a sheet-like fashion (Fig. 4). Necrosis, calcification, atypia, and mitotic figures were not evident. The results of an IHC analysis are shown in Table 1. These tumor cells were positive for HMB-45, Melan-A, and α-SMA (Fig. 5A-C) but negative

for a nervous system marker (S-100), epithelial markers (AE 1/AE3 and CAM5.2), and endocrine markers (synaptophysin and chromogranin A). The Ki-67 index was <5% (Fig. 5D). The above features were consistent with a PEComa.

Subsequently, the patient underwent distal pancreatectomy. The surgical specimen showed a well-circumscribed, yellowish-white mass that measured 43 mm×30 mm and was surrounded by a complete fibrous capsule with a negative surgical margin (Fig. 6A). At the microscopic level, the tumor was composed of spindle cells possessing clear to focally granular eosinophilic cytoplasm without necrosis, atypia, or frequent mitoses (Fig. 6B). The IHC findings were as follows: HMB-45 (+), α-SMA (+), Melan A (+), AE1/AE3 (−), EMA (−), S-100 (−), CD34 (−), desmin (−), and TFE (−). The Ki-67 index was <2%. This histological and IHC examination showed similar features to those of specimens obtained by EUS-FNA. We therefore achieved a definitive diagnosis of PEComa of the pancreas.
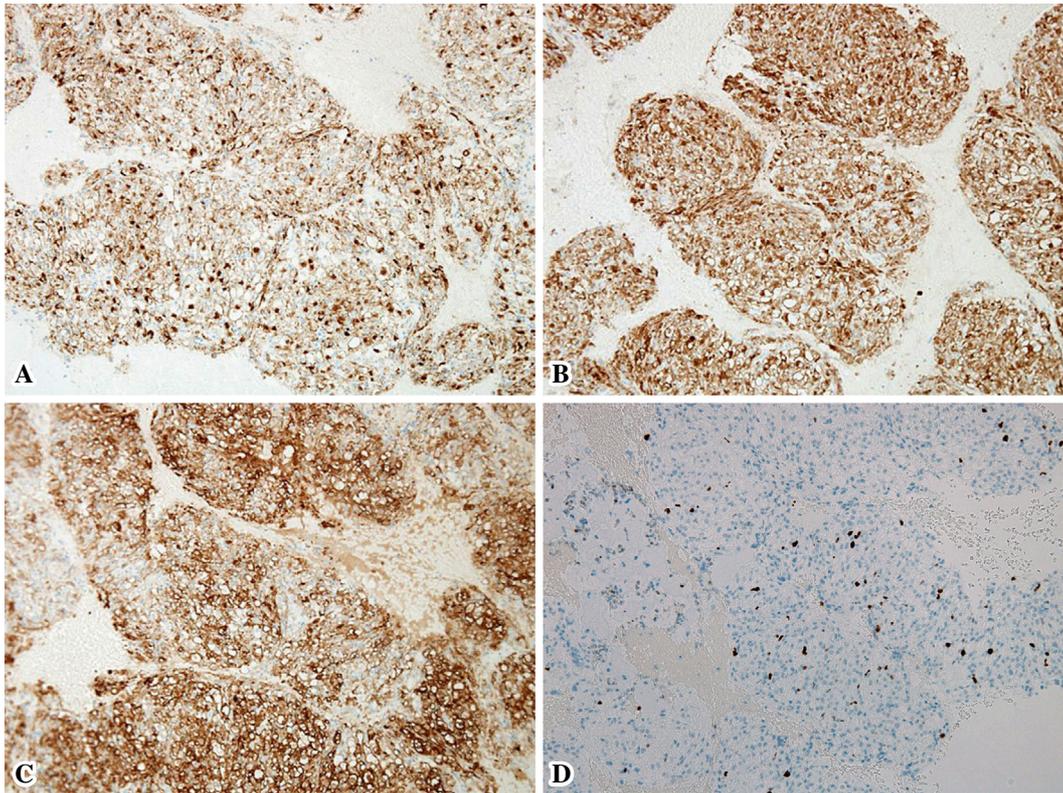
Figure 5. The results of immunohistochemical analyses. These tumor cells were positive for (A) human melanoma black 45 (HMB-45), (B) melanoma antigen (Melan-A), and (C) α-smooth muscle actin (α-SMA). (D) The Ki-67 labeling index was <5%. (×100)
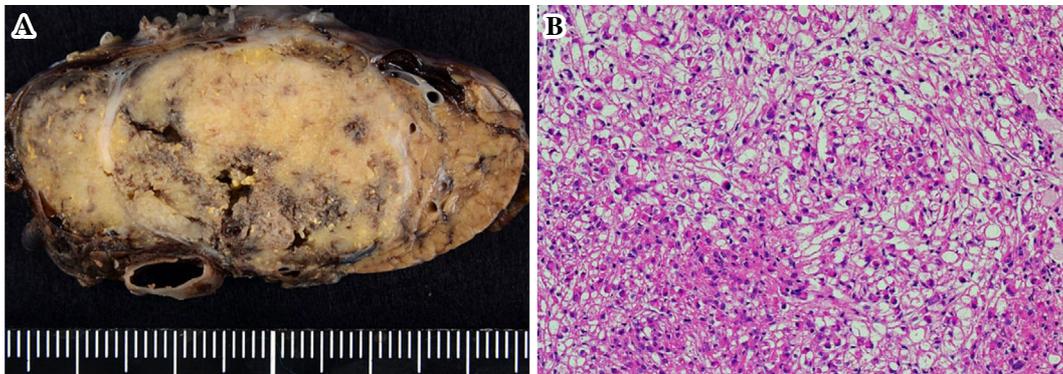
Figure 6. The surgical specimen showed a well-circumscribed, yellowish-white mass that measured 43mm×30mm and was surrounded by a complete fibrous capsule with a negative surgical margin (A). At the microscopic level, the tumor was composed of spindle-shaped cells possessing clear to focally granular eosinophilic cytoplasm without necrosis, atypia, or frequent mitoses (B) (Hematoxylin and Eosin staining ×200).

The patient was discharged on day 25 post-surgery and is currently undergoing outpatient follow-up, with no recurrence of the original tumor or distant metastasis observed at 12 months post-surgery.

Discussion

We herein report a case of PEComa of the pancreas diagnosed preoperatively by EUS-FNA. The World Health Organization defines PEComa as "a mesenchymal tumor composed of histologically and IHC distinctive PECs". PECs are characterized by an epithelioid or spindle-shaped appearance with a clear eosinophilic or granular cytoplasm, a round-to-oval centrally located nucleus, and an inconspicuous nucleolus. On IHC, PECs express melanocytic and myogenic markers but not cytokeratins or endocrine markers (12), which concurred with the findings in our case. These tumors can arise in any part of the human body and at any age but are more predominant in women than in men. PEComa of the pancreas was first reported by Zamboni et al. in

Table 2.   Previously Reported Cases of Pancreatic PEComas.

Reference No.	Age (years)	Gender	Symptoms	FNA performed	Diagnosis by	Location	Size (mm)	Recurrenece or Metastasis
13	60	Female	Abdominal pain/discomfort (upper)	Yes	Surgery	Body	20	None
15	74	Female	Abdominal pain (right upper, right flank, right paraspinal), Early satiety, Dyspepsia	No	Surgery	Head	45	None
16	31	Female	Abdominal pain (right hypochondriac)	Yes	Surgery	Body	15	None
17	46	Female	Diarrhea	No	Surgery	Body	17	None
18	47	Female	Abdominal pain (lower)	No	Surgery	Head	17	None
19	60	Female	Abdominal bulge (right upper)	Yes	Surgery	Body	32	None
20	49	Male	Fever, Cough, Malaise	Yes	FNA	Head	32	None
31	52	Male	Abdominal pain	No	Surgery	Head	40	Liver
21	58	Female	Abdominal pain (upper), Dyspepsia	No	Surgery	Head	22	None
22	62	Female	None	Yes	Surgery	Head	25	None
23	38	Female	Abdominal pain/discomfort abdominal lump (upper)	No	Surgery	Tail	140	None
24	38	Female	Abdominal pain (upper)	Yes	FNA	Uncinate process	18	N/A
3	43	Female	Abdominal pain (central upper/ left upper), Abdominal mass (central upper/left upper)	Yes	FNA	Body/ Tail	100	None
32	51	Female	Abdominal pain (right upper)/ Jaundice	Yes	FNA	Head	60	Liver
25	N/A	N/A	N/A	Yes	FNA	Head	N/A	N/A
26	31	Female	None	No	Surgery	Tail	33	None
27	17	Female	Anemia, Melena	Yes	Surgery	Head	49	None
28	58	Female	None	No	Surgery	Body	20	None
4	50	Female	None	Yes	Surgery	Head	20	None
6	61	Female	Abdominal pain (upper)	No	Surgery	Head/ Body	60	None
5	54	Female	Abdominal pain (right upper)	Yes	FNA	Head/ Body	26	None
29	31	Female	None	Yes	Surgery	Tail	6/2/1.2	N/A
30	68	Male	Abdominal pain (upper)	Yes	FNA	Head	28	None
2	43	Female	Abdominal pain (central upper)	No	Surgery	Head	115	None

FNA: Fine-Needle Aspiration, N/A: not available

1996 (13). We searched the MEDLINE database for papers in the English language from the year of database inception to May 2018 using the following terms: perivascular epithelial cell tumor, PEComa, pancreas, and pancreatic. After reviewing the titles and abstracts for eligibility, the literature search generated 24 cases from studies with available abstracts (2-6, 13-32). The clinical characteristics of previously reported pancreatic PEComas are summarized in Table 2. The prognosis of pancreatic PEComa is generally good, with no local recurrence after surgical resection and a low rate of metastasis. However, two cases showed hepatic metastases during the observation period; one had multiple hepatic metastases at 27 months (31) and the other at 6 months after pancreatic resection (32). Folpe et al. previously described features predictive of the presence of tumor recurrence or metastasis in PEComa (12). These features included a large size (>5 cm), infiltrative growth, hypercellularity, high nuclear grade, high mitotic figures (>1/50 high-

power field), and necrosis. Malignant PEComas show two or more of these worrisome features. In the present case, the tumor was approximately 40 mm in diameter, and none of the above features were identified, so this patient's prognosis is promising. As PEComa has malignant potential, surgery is considered the appropriate treatment choice, if possible. Therefore, the rapid and accurate assessment of pancreatic masses is warranted in order to direct patient management, and a correct preoperative diagnosis is crucial.

At present, the integration of CT, MRI, and ultrasound findings is the mainstay in the evaluation of pancreatic tumors. Pancreatic tumors include a heterogeneous group of primary lesions, such as adenocarcinoma, NET, SPN, pancreatoblastoma, pancreatic lymphoma, and rare miscellaneous neoplasms in general (9, 10). Tan et al. reported the imaging characteristics of PEComa in 32 cases (33). Dynamic CT and MRI showed tumors that were hypointense on T1-weighted imaging and hyperintense on T2-weighted imag-

ing, although some were isodense with fat. The tumors usually had well-defined borders and a regular shape. Most tumors were significantly enhanced heterogeneously in the arterial and venous phases. Tumors were slightly hypodense on delayed-phase CT imaging, whereas some showed delayed enhancement. Our patient showed almost the same imaging findings as those described above. However, CT imaging provides insufficient sensitivity for the diagnosis of PEComa. Two previous reports described the respective rates of a correct preoperative PEComa diagnosis as being 15.7% and 31.3% using CT and 22.7% and 40% using MRI, with almost the same sensitivity (14, 33). Therefore, imaging is not useful for differentiating pancreatic PEComa from other pancreatic mass lesions.

EUS-FNA is widely performed for the evaluation of pancreatic solid mass lesions. In the aforementioned 24 cases of pancreatic PEComa in the literature, 14 underwent EUS-FNA prior to surgery; however, 7 of these 14 cases did not obtain a clear diagnosis due to the limitations of EUS-FNA. The diagnostic accuracy of this method is affected by the availability of a rapid on-site evaluation, as a cytopathologist may not be widely available at all institutions. Furthermore, certain neoplasms, such as neuroendocrine tumors, lymphomas, and autoimmune pancreatitis, may be difficult to diagnose without IHC staining and intact histological architecture for an accurate pathological assessment. Core tissue is therefore needed in order to establish a definitive diagnosis. The Acquire® needle is a device with Franseen geometry for EUS-FNA. Several studies have assessed the utility of the Franseen needle (34-36), and when using this needle we were able to successfully obtain sufficient core samples. However, there have been concerns about the potential for tumor seeding or dissemination of tumor cells via a puncture into the peritoneal cavity. Although preoperative EUS-FNA has not been shown to be associated with an increased risk of mortality concerning tumor cell dissemination along the needle track with resected pancreatic cancer (37), only a limited number of needle punctures should be performed, using a device such as a Franseen needle to facilitate the collection of a sufficient amount of specimen.

In summary, we encountered a case of PEComa of the pancreas diagnosed preoperatively with EUS-FNA. As obtaining a definitive diagnosis of pancreatic PEComa was difficult using only imaging, preoperative EUS-FNA was useful in this case. Clinicians should consider pancreatic PEComa in their differential diagnosis of patients with a pancreatic mass. The clinical manifestations of pancreatic PEComas have not been fully clarified, so long-term regular follow-up of this patient is essential.

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

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