

A rare case of perivascular epithelioid cell tumor (PEComa) of the pancreas diagnosed by endoscopic ultrasound




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ABSTRACT

A 49-year-old woman consulted her general practitioner (GP) regarding epigastric pain that she had experienced for 2 months. Physical examination and laboratory results were unremarkable. An abdominal ultrasound indicated a solid pancreatic tumor, which was confirmed on subsequent CT and MRI. Endoscopic ultrasound (EUS) showed a well-defined heterogeneous, predominantly hypoechoic mass in the pancreatic body, so a neuroendocrine tumor (NET) was suspected. However, EUS-guided fine-needle aspiration (EUS-FNA) was performed and based on (immuno-)histochemical findings, the extremely rare diagnosis of a perivascular epithelioid cell tumor (PEComa) of the pancreas was made. Due to the malignant potential of pancreatic PEComas, laparoscopic left-sided pancreatectomy was performed. We present a case diagnosed by preoperative EUS-FNA highlighting the clinical and endosonographic features which help to distinguish it from its most important differential diagnosis, neuroendocrine tumors (NETs) of the pancreas.

Introduction

Perivascular epithelioid cell tumors (PEComas) are mesenchymal cell neoplasms that can occur in every part of the human body [1]. PEComa of the pancreas is extremely rare, and to our knowledge within the English literature, there are 21 described and only five where diagnosed preoperatively by endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA).

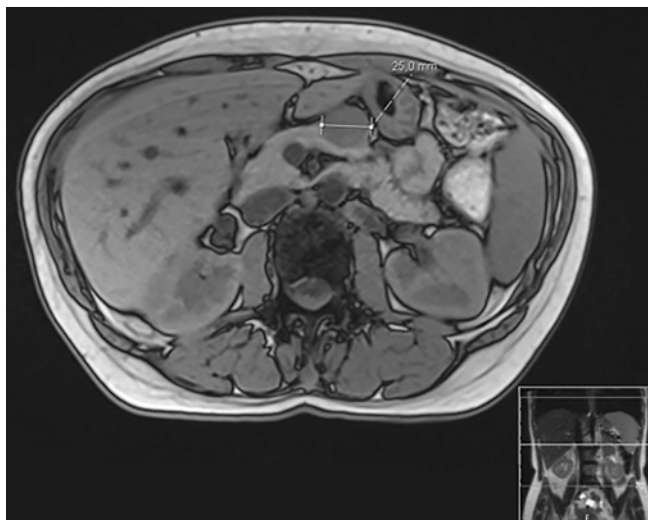
Case report

A 49-year-old woman presented to her GP with diffuse abdominal pain localized in the right and left upper quadrant and intermittent watery diarrhea for the last 2 months. Apart from uterine myomatosis with occasional menorrhagia, the patient's past medical history was unremarkable, and there was nothing

of note in her family history. She was a smoker (30 pack-years), consumed little alcohol, and took proton pump inhibitors (PPIs) when required due to the above-mentioned pain; however, she did not experience any symptom relief.

Physical examination and routine laboratory results did not show any pathological findings apart from a mild iron deficiency anemia most likely due to the hypermenorrhea. Abdominal ultrasound performed by the GP showed a round, defined, 25 mm hypoechoic mass in the pancreatic body without dilation of the pancreatic duct which was confirmed on subsequent CT and MRI (**Fig. 1**). As a pancreatic neuroendocrine tumor (NET) was suspected, Chromogranin A serum level was measured showing only a slight elevation of 145 µg/L (reference <102 µg/L).

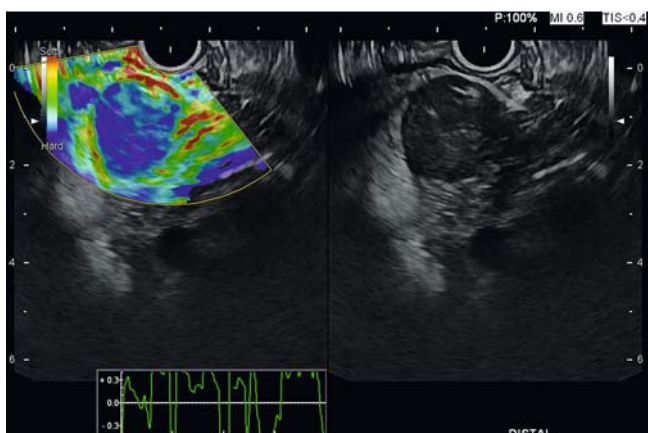
We performed endoscopic ultrasound (EUS) (with Pentax radial scanner, Pentax EG36704URK, Pentax Europe, Hamburg,



► **Fig. 1** T1-weighted MRI of the abdomen showing a hypointense mass in the body of the pancreas.



► **Fig. 2** Endoscopic ultrasound (EUS) showing a well-defined heterogeneous, predominantly hypoechoic mass with lateral shadowing in the pancreatic body measuring 25 × 20 mm without dilation of the pancreatic duct.



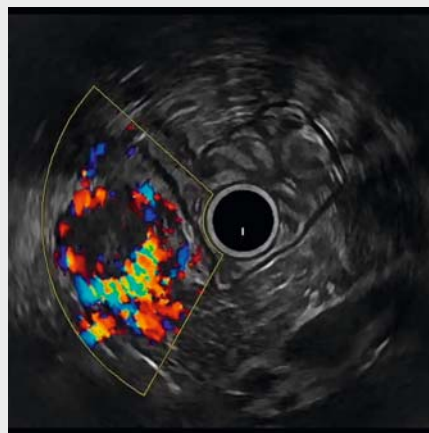
► **Fig. 3** Elastography indicated that the lesion had a rather hard (= blue) tissue appearance.

Germany) which confirmed the homogenous appearance of the pancreatic tissue but with a well-defined heterogeneous, predominantly hypoechoic mass with lateral shadowing in the pancreatic body and measuring 25 × 20 mm without dilation of the pancreatic duct (► **Fig. 2**, ► **Video 1**). EUS elastography indicated that the lesion had a rather hard (= blue) tissue appearance (► **Fig. 3**, ► **Video 1**). With B-mode (power)-Doppler, the hypervascularity of the lesion could already be suspected. Contrast Enhanced Low Mechanical Index Endosonography (CELMi-EUS) (SonoVue, Bracco, Italy) showed a clear and long-lasting hyperperfusion with late “wash-out” of the lesion (► **Video 1**).

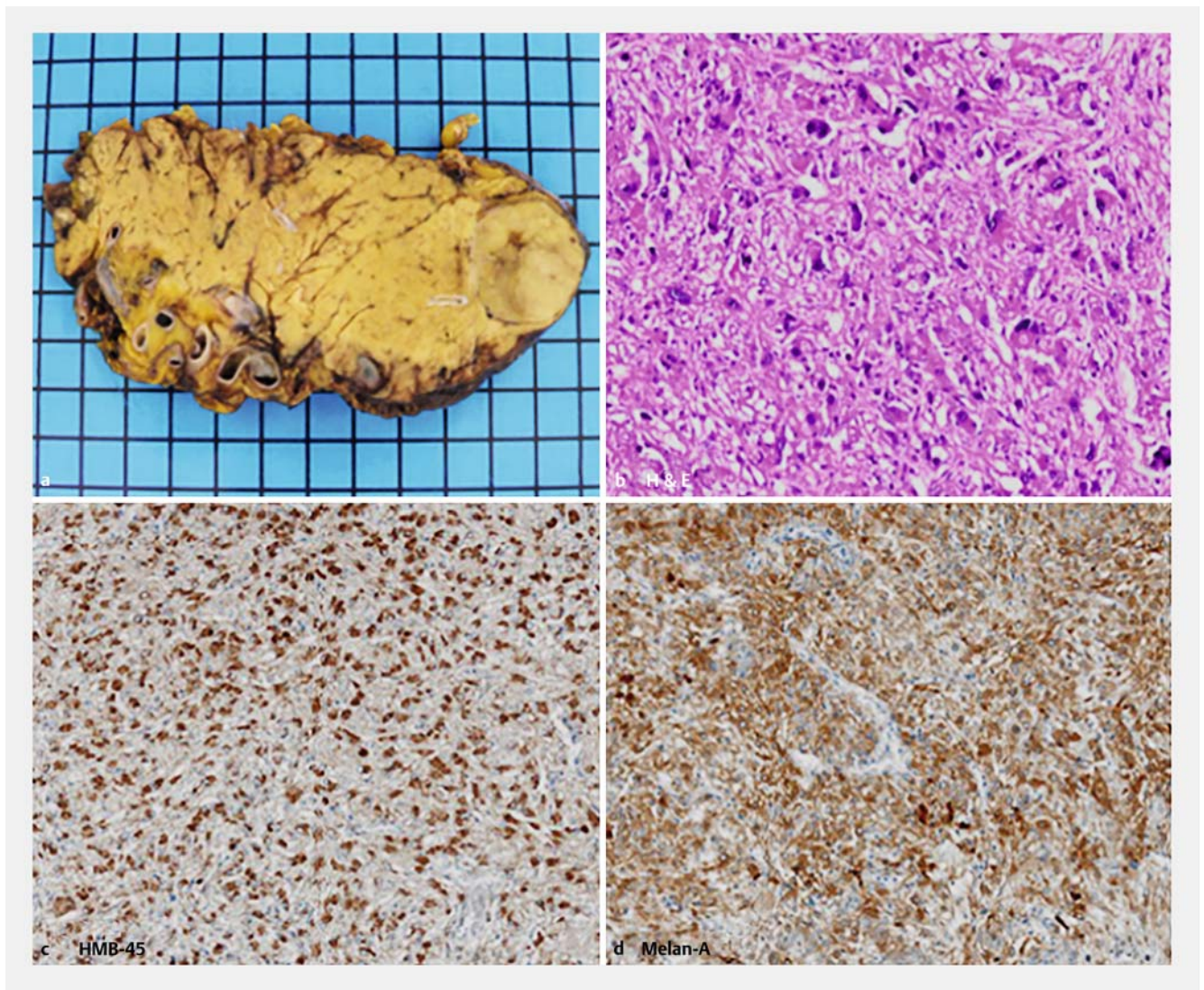
EUS-Guided fine-needle aspiration (EUS-FNA) with a 22-gauge needle (EchoTip Ultra, Cook Medical, Limerick, Ireland) was performed using the fanning technique with slow-pull of the stylet and the tissue material obtained was fixed in CytoRich Red (Fisher Scientific, Schwerte, Germany) solution for further cell block analysis.

Hematoxylin and eosin (H&E) staining revealed cells consisting of sheets of uniform, epithelioid-spindle shaped cells with abundant granular eosinophilic cytoplasm and distinct prominent nucleoli (► **Fig. 4b**). Additional immunohistochemical stains were also performed. The tumor cells showed positivity for smooth muscle markers desmin and actin as well as for melanocytic markers HMB-45 (► **Fig. 4c**) and Melan-A (► **Fig. 4d**), but negativity for synaptophysin, chromogranin A, cytokeratin (panCK, CK20, CK7), CD-117, and S-100.

Based on these findings, the diagnosis of a perivascular epithelioid cell tumor (PEComa) of the pancreas was made and other potential diagnoses such as NET, metastasis, or pancreatic cancer could be excluded. Due to the malignant potential of pancreatic PEComas, laparoscopic left-sided pancreatectomy with splenectomy was performed. The resected specimen showed a 2.5 cm × 2.5 cm × 2.3 cm well-circumscribed encapsulated spherical tumor with a homogeneous light brown cut surface, surrounded by normal lobular pancreatic parenchyma with tumor-free margins. Furthermore, spleen and resected



► **Video 1** PEComa in EUS. Doppler imaging, elastography, contrast-enhanced EUS, and contrast enhanced low mechanical index endosonography (CELMi-EUS).



► **Fig. 4** **a** Resected specimen showed a well-circumscribed encapsulated tumor, surrounded by normal lobular pancreatic parenchyma. **b** H&E staining revealed cells consisting of sheets of uniform epithelioid-spindle shaped cells with abundant granular eosinophilic cytoplasm and distinct prominent nucleoli. The tumor cells showed positivity for melanocytic markers HMB-45 (**c**) and Melan-A (**d**).

lymph nodes were free from metastases. Histological and immunohistological analysis of the resected specimen revealed the same features as already shown by previous EUS-FNA (► **Fig. 4**).

Discussion

Perivascular epithelioid cell tumors (PEComas), first described by Bonetti et al. in 1992 [1], are rare mesenchymal cell neoplasms that can occur in every part of the human body including soft tissue, bone, abdominopelvic sites, and retroperitoneal sites such as the uterus or kidney. In 1996, Zamboni et al. reported on the occurrence of PEComas in the pancreas and introduced the term “sugar tumor” due to the clear cell cytoplasm of the perivascular epithelioid cells, which are rich in glycogen in this tumor [2]. Histopathologically, these tumors are characterized by cells with a spindle or epithelioid shape typi-

cally spread around blood vessels. The characteristic immunohistochemical profile shows positivity for melanocytic markers (such as HMB-45 and Melan-A) and smooth muscle markers (such as actin and desmin) [3].

To our knowledge, at the present time, only 21 cases of primary PEComa of the pancreas have been reported since the first description in 1996 by Zamboni et al. [2], and most recently in the report by Zhang et al. [4]. These tumors can arise at any age, can affect either sex, but as in our case, seem to have a predilection for middle-aged women. Patients mostly present with fluctuant abdominal pain, swelling in the right upper quadrant, and occasionally diarrhea, though in some cases, patients are asymptomatic. There are no specific laboratory tests to screen for PEComas [4]. In our case, the mild anemia was probably caused by the hypermenorrhea, and the slightly elevated Chromogranin A most likely due to occasional intake of PPIs [5].

In all image modalities (abdominal US, EUS, CT, MRI), pancreatic PEComas are usually characterized by well-circumscribed, oval- to round-shaped masses with surrounding normal pancreatic tissue, lack of infiltration, and signs of arterial hypervascularity when color Doppler or contrast-enhanced modes are used [6]. As shown in our case, elastography demonstrated a hard tissue lesion with lateral shadowing, consistent with an encapsulated tumor. All of these imaging findings mimic pancreatic NETs but can already help to differentiate it from pancreatic adenocarcinoma, where the appearance is that of a poorly defined hypodense mass with infiltrating growth [6]. Furthermore, we observed a very long-lasting contrast enhancement in CELMI-EUS which might even help to differentiate this lesion from pancreatic NETs.

Other lesions to keep on the list of differentials include pseudopapillary neoplasm, gastrointestinal stroma tumor (GIST), acinar cell carcinoma of the pancreas, and metastasis of clear cell renal cell carcinoma or melanoma, though pancreatic NET remains the most important alternative diagnosis to exclude. European guidelines recommend enucleation at surgery for suspected NET with a solid pancreatic lesion >2 cm [7]. The present case impressively demonstrates the advantages of EUS-FNA, combining the best imaging modality with the ability to obtain a tissue diagnosis, showing that a suspected NET can be a PEComa on histopathology. Thus, exact tissue diagnosis before further treatment seems to be most reasonable as it influences clinical management.

Reviewing the literature, in 14 of 22 cases including our case a preoperative EUS-FNA was performed. In only six, the diagnosis "PEComa" was established preoperatively following the use of immunohistochemical staining for HMB-45. The other eight cases were either nondiagnostic or misinterpreted as carcinoma or neuroendocrine tumors [4, 8]. Collins et al. noticed that, in these cases, the material obtained was only used for preparing a cytological smear. The material was very scant or nondiagnostic, in their understanding most likely due to extreme cohesion of PEComa cells to each other and the matrix [8]. Thus, the benefit of smear cytology in diagnosing solid pancreatic lesions such as PEComa seems questionable. For a definitive diagnosis, microscopic examination of a H&E stained tissue cell block with the option to perform immunohistochemistry would be advised. Formalin fixed histology might be a good alternative but requires core tissue material which cannot always be obtained by EUS-guided tissue sampling.

The great majority of pancreatic PEComas are considered benign and the prognosis is relatively good with most patients remaining free from relapse and metastasis [4]. So far, to our knowledge, four primary malignant pancreatic PEComas have been reported. In two cases, liver metastases occurred, and in two cases the tumor showed malignant features such as infiltrating growth, necrosis, and size >5 cm, most recently reported by Zhang et al. In this case, adjuvant chemotherapy with a

sarcoma regimen with epirubicin and ifosfamide seems to be effective [4].

In general, PEComas might have an association with tuberous sclerosis complex (TSC). However, the association between pancreatic PEComa and TSC remains vague, since there is only one described case of a woman with TSC and pancreatic PEComa reported by Hartley et al. [9]. In our case, no signs of TSC were observed.

In conclusion, PEComa of the pancreas remains an extremely rare diagnosis of a solid pancreatic tumor with malignant potential. In EUS, which generally provides a very good image modality for diagnosing pancreatic lesions with high sensitivity and specificity, PEComas show very similar characteristics to NET, but in CELMI-EUS, a longer lasting contrast enhancement can be seen.

However, additional EUS-FNA with further adequate immunohistochemical processing seems reasonable to establish the right diagnosis to guide further therapy.

Competing interests

None

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