EUS diagnosis of cystic pancreatic neuroendocrine tumors

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EUS-guided FNA (EUS-FNA) is an important technique for the assessment of pancreatic cysts.<sup>1</sup> Pancreatic neuroendocrine tumors (pNETs) are rare lesions that can be solid or cystic. Cystic pNETs account for 10% to 18% of resected pNETs<sup>2,3</sup> and 7% to 10% of all pancreatic neoplasms.<sup>4-6</sup> Most cystic pNETs are nonfunctional and can present a diagnostic challenge to the radiologist and endosonographer.

Endosonographically, cystic pNETs often have thickened walls and septations.<sup>7,8</sup> Wall thickening, low carcinoembryonic antigen (CEA) levels, and diagnostic cytologic features are found significantly more frequently in patients with cystic pNETs than in patients with mucinous cysts.<sup>8</sup> Targeted cyst wall puncture and aspiration during EUS-FNA increases the diagnostic yield.<sup>7,8</sup> Other notable characteristics of pNET are described in Table 1.<sup>9,10</sup>

The aim of this video case series is to demonstrate the endosonographic appearances of cystic pNET and EUS-FNA techniques to optimize the diagnosis of cystic pNET (Video 1, available online at www.VideoGIE.org). A thickened cyst wall and septations should raise suspicion for a cystic neuroendocrine tumor. Cyst fluid may have low cellularity, and CEA levels are typically low. The cyst wall and septations should be targeted with FNA to maximize cytologic diagnosis.

# CASES

## Patient 1

A 60-year-old man presented for elective outpatient upper EUS. The patient had a history of hepatitis C and was referred for abdominal CT scan (Fig. 1A) to evaluate abnormal liver function test results and abdominal pain. A cystic and solid mass was detected in the body of the pancreas. On EUS, a 2.8-cm  $\times$  2.5-cm cystic and solid mass with a few small vessels in the superior portion was

identified in the body of the pancreas. After a Doppler study confirmed the absence of flow in the needle path, 2 passes were made with a 25-gauge needle to sample the cyst wall (Fig. 2A). On-site cytologic analysis identified single and dyscohesive groups of tumor cells with eccentrically located nuclei in a bloody background, suggestive of cystic pNET (Figs. 3A and B).

## Patient 2

A 75-year-old man presented for elective outpatient EUS. The patient had a left lower lobe infiltrate and a history of tobacco use and chronic obstructive pulmonary disease and was referred for magnetic resonance imaging (MRI) of the chest (Fig. 1B). A pancreas cyst was incidentally detected, and MRI of the abdomen was performed. A 1.2-cm cyst was identified on the tail of the pancreas. On EUS, the 1.6-cm  $\times$  1.1-cm cyst was thick-walled with central anechoic areas, a few septations, and a 0.3- to 0.5-cm hypoechoic rim around the lesion. After Doppler study, sampling of the cyst wall was performed with a 25-gauge needle (Fig. 2B). On-site cytologic analysis identified cells suggestive of cystic pNET. A second pass was made with a 25-gauge needle for cell block.

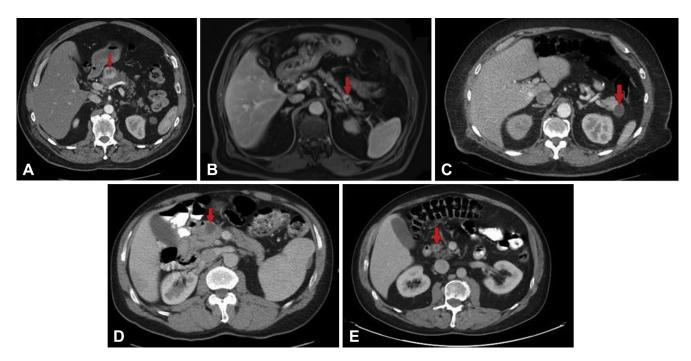
# Patient 3

A 61-year-old man who had previously undergone a gastrectomy presented for elective outpatient EUS. The patient had right flank pain and hematuria and was referred for CT scan of the abdomen for renal stones. A 3-cm cyst in the tail of the pancreas was incidentally detected (Fig. 1C). On EUS, there was a 2.5-cm unilocular cyst in the pancreas tail, with a 1.5-cm  $\times$  2-cm cystic and solid lesion with thick central components (Fig. 2C). Small vessels coursed superior to the lesion. One pass was made with a 25-gauge needle into the superior solid portion (Fig. 2C). On-site cytologic

TABLE 1. Findings on EUS-FNA characteristics of cystic pNETs						
Study	Location	Diameter (range)	Wall thickening (>2 mm thick)	Septation	Cyst fluid CEA level (range)	Cytologic diagnosis of NET
Ho et al, 2013 <sup>9</sup>	63.0% body/tail	Median 35 mm (8-80)	48.1% of cases reported	81.5% of cases	Median 1.25 ng/mL (0.6-500)	71.0%
Yoon et al, 2013 <sup>10</sup>	73.7% body/tail	Median 24 mm (13-70)	57.9% of cases reported	42.1% of cases	Median 1.1 ng/mL (0.3-500)	68.4%

CEA, Carcinoembryonic antigen; pNETs, pancreatic neuroendocrine tumors.

Written transcript of the video audio is available online at www.VideoGIE.org.



**Figure 1. A,** Patient 1: abdominal CT with a 2.8-cm cystic and solid pancreas mass. **B,** Patient 2: abdominal MRI with a 1.2-cm pancreas cyst. **C,** Patient 3: abdominal CT with a 3-cm pancreas cyst. **D,** Patient 4: abdominal CT with a 2-cm pancreas cyst. **E,** Patient 5: abdominal CT with a 1.2-cm pancreas cyst. *MRI*, magnetic resonance imaging.

analysis identified cells suggestive of cystic pNET. A second pass was made with a 22-gauge needle for cell block.

### Patient 4

A 60-year-old man presented for EUS. The patient had low back pain and was referred for abdominal CT (Fig. 1D). An abnormal, hyperenhancing, multiseptated 2-cm cystic lesion was incidentally detected in the body of the pancreas. On EUS, a 2-cm cyst with thick septations was seen adjacent to an elongated pancreas side-branch that extended to the cyst. One pass of the thickened septations (Fig. 2D) was made with a 25-gauge needle. Onsite cytologic analysis identified cells suggestive of cystic pNET. A second pass was made with a 22-gauge needle, yielding nonviscous, blood-tinged fluid.

#### Patient 5

A 63-year-old man with a history of melanoma presented for EUS. A 1.2-cm cyst was incidentally detected in the head of the pancreas on CT of the abdomen (Fig. 1E) for

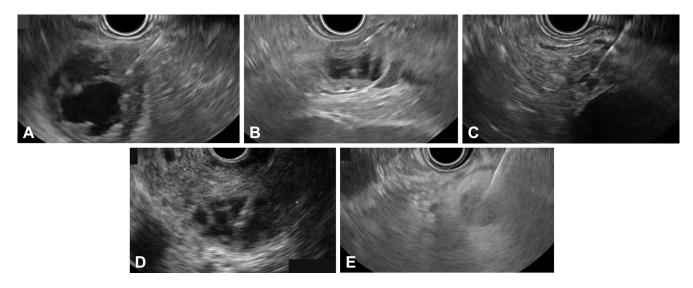


Figure 2. A, Patient 1: FNA targeting thickened cyst wall. B, Patient 2: FNA targeting thickened cyst wall and septations. C, Patient 3: FNA targeting thickened portion of cystic/solid lesion. D, Patient 4: FNA targeting septations of multi-septated cyst. E, Patient 5: second-pass FNA targeting thickened wall of cyst with self-limited hemorrhage.

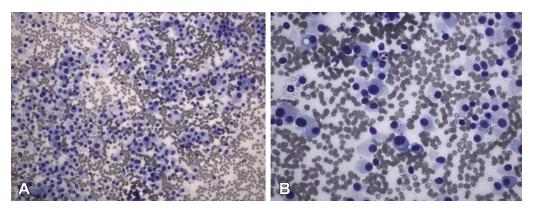


Figure 3. On-site cytologic view of sample from patient 1 showing dyscohesive groups of tumor cells and eccentrically located nuclei in a bloody background. Some tumor cells have fine cytoplasmic vacuoles. A few histiocytes are also present (Diff-Quik stain, orig. mag. ×200 and ×400).

restaging of melanoma. On EUS, a unilocular 1.4-cm  $\times$  1.1-cm cyst with a 1.7-mm-thick wall and small debris within was seen in the head and neck of the pancreas. One pass was made with a 25-gauge needle of the cyst wall (Fig. 2E). On-site cytologic analysis identified cells suggestive of cystic pNET. After FNA, there was a self-limited hemorrhage within the cyst, seen as hyperechoic material. A second pass was made with a 22-gauge needle, yielding scant, blood-tinged aspirate that was placed in wash.

## **CONCLUSIONS AND LEARNING OBJECTIVES**

Prophylactic intravenous (IV) antibiotics (such as 400 mg IV ciprofloxacin) are given before EUS-FNA of cystic lesions.<sup>11</sup> On EUS, thickened pancreas cyst walls and septations should raise a suspicion of cystic pNET. Doppler study can be used to identify and avoid blood vessels and the pancreas duct at the time of EUS-FNA, and thickened walls and septations should be targeted to maximize cytologic diagnosis. FNA with 25-gauge or 22-gauge needles provides a cellular sample of thickened walls for onsite review, which can confirm a suspicion of cystic pNET. Full (10 mL) suction or capillary technique, which consists of slowly removing the stylet while moving the needle at the target site, can be used to sample thickened cyst walls or septations. If the cellularity of the aspirate is low, 10 mL of suction may be used. Twentytwo-gauge needles with suction applied may be used to aspirate the cyst fluid in combination with targeting the wall. Cystic pNETs typically have low cyst fluid CEA levels.

### DISCLOSURE

All authors disclosed no financial relationships relevant to this publication.

Abbreviations: CEA, carcinoembryonic antigen; IV, intravenous; MRI, magnetic resonance imaging; pNETs, pancreatic neuroendocrine tumors.

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