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Endosonographic and cyst fluid characteristics of cystic pancreatic neuroendocrine tumours: A multicentre case series

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ABSTRACT

Background: Pancreatic neuroendocrine tumours are uncommon neoplasms which may rarely be cystic. Differentiation from other more common cystic neoplasms may be difficult.
Aims: To describe the morphologic, cytologic, and cyst fluid characteristics of cystic pancreatic neuroendocrine tumours.
Methods: Retrospective analysis of consecutive patients referred for endosonographic evaluation of pancreatic cysts at four centres.
Results: 27 patients (12 males) with cystic pancreatic neuroendocrine tumours were identified. Prior to endosonography, this tumour was suspected in only 2 patients based on presenting symptoms (7.4%). The median cyst size was 35 mm (range 8–80 mm). Wall thickening was identified in 13 cases. The median carcinoembryonic antigen level was 1.25 (range 0.6–500). Fine needle aspiration cytology in 17 of 24 patients confirmed neuroendocrine tumour (71%). In 8 of 9 patients who had needle targeting of the cyst wall, cytology was consistent with neuroendocrine tumour (88.9%). 18 patients underwent surgical resection.
Conclusions: Cystic pancreatic neuroendocrine tumour was rarely suspected, including by cross-sectional imaging. Wall thickening was identified in approximately half of cases on endosonography. Cyst fluid was typically non-viscous with very low carcinoembryonic antigen levels. Targeting the wall during fine needle aspiration had a high diagnostic yield and should be performed.

1. Introduction

Pancreatic cysts are increasingly being recognised due to the frequent use of cross-sectional abdominal imaging. Endoscopic ultrasound (EUS) and fine needle aspiration (FNA) play an important role in the assessment of pancreatic cysts [1,2]. Pancreatic neuroendocrine tumours (pNETs) are rare, malignant lesions which may rarely be cystic with variable degrees of wall prominence. Cystic pNET may be difficult to distinguish from common cystic lesions such as pseudocysts or mucinous cystic neoplasms [3,4]. Most cystic neuroendocrine tumours are non-functional and may present a diagnostic challenge to the endosonographer. The purpose of this retrospective, multi-centre series is to evaluate the clinical presentation, EUS morphology, cyst fluid analysis, and cytology in a large cohort of cystic pNET cases.

2. Methods

A retrospective review of all patients undergoing EUS evaluation of pancreatic cysts was performed at Yale New Haven Hospital, University of Alabama Hospital, Massachusetts General Hospital, and Abbott Northwestern Hospital from July 2006 to July 2011 to identify patients with pancreatic neuroendocrine tumours. This study was approved by the respective Human Investigation committees. A search was performed at each institution of EUS and/or pathology databases for patients with a "neuroendocrine tumour." The cytology and surgical pathology were then searched to confirm a diagnosis of "islet cell tumour" or "neuroendocrine tumour." Patients identified via a surgical pathology database who did not have EUS at the study site were excluded from data analysis. From the patients identified, the study population included those with

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EUS morphology of a cystic or predominantly cystic (if mixed solid-cystic) pancreatic tumour.

Patient and cyst characteristics were retrospectively recorded including age, gender, presenting symptoms, suspicion for cystic pNET prior to and after EUS, and cross-sectional imaging findings [magnetic resonance imaging (MRI), computed tomography (CT), or trans-abdominal ultrasound (US)], if available for review. EUS findings recorded included mean cyst size, location within the pancreas, wall thickness (specifically focal or concentric), presence of mural nodule, septations, pancreatic ductal dilation or communication, and pancreatic parenchymal echogenicity. FNA data collected included needle size, number of passes, wall targeting, fluid appearance, cytology, and cyst fluid analysis. Immunocytochemistry was not specifically noted. Co-investigators at each study site completed a data sheet to compile the above information, which was collected and analysed by the lead investigator; given the expertise of each endosonographer and the unavailability of archived images, the EUS images were not re-reviewed.

Surgical pathology results were evaluated in the eighteen patients who underwent resection and the diagnosis of neuroendocrine tumour was confirmed. The degree of tumour differentiation was not specifically noted. The remaining patients who did not undergo surgical resection were either lost to follow-up, conservatively managed with serial imaging, or not operative candidates. When definitive surgical pathology was not available, the diagnosis was confirmed via cytology obtained during FNA.

All procedures were performed by experienced endosonographers. EUS was performed with Olympus (GF-UM20, GF-UM130, or GF-UM160) radial or linear (GFUC 140 or GUCT140) echo-endoscopes (Olympus America, Inc., Centre Valley, PA) or with Pentax (EG-3670URK) radial or linear (EG-3870UTK) echo-endoscopes (Pentax Medical Co., Montvale, NJ). A cytology technician or cytopathologist was available on-site for preliminary interpretation in all cases.

3. Results

During the study period between July 2006 and July 2011, 27 patients with cystic pNET were identified. Patient and clinical characteristics are summarised in Table 1. The mean age at the time of diagnosis was 60 years; median age 58 (range 34–80). Twelve patients were male (44.4%). Thirteen patients had pancreatic cysts incidentally detected on cross-sectional imaging and were asymptomatic (48.1%), 11 patients presented with abdominal pain (40.7%), 2 patients had symptoms suggestive of a neuroendocrine tumour – specifically hypoglycemia with an elevated insulin level in one patient and Cushing's-type symptoms in another patient (7.4%), and 1 patient presented with pancreatitis. Endoscopists were asked to evaluate their pre-EUS suspicion for cystic pNET based on the patient's clinical presentation. Only 2 patients were identified (7.4%). Both of the patients with pre-EUS suspicion for pNET had a clinical history suggestive of neuroendocrine tumour. One patient had a family history of MEN syndrome and presented with pancreatitis; the other patient had symptoms of hypoglycaemia. Twenty-one patients had imaging available for review prior to EUS (18 CT, 2 MRI, and 1 US) which led to a radiologist's diagnosis of cystic pNET in only 1 case (4.7%).

Table 1
Patient characteristics prior to endosonographic evaluation.

Patient characteristics	Number (%)
Total patients	27
Gender (male)	12 (44)
Median age (years) (range)	58 (34–80)
Presenting symptom	
Asymptomatic	13 (48)
Abdominal pain	11 (41)
Pancreatitis	1 (4)
"Functional"	
Hypoglycemia	1 (4)
Cushing's symptoms	1 (4)
Neuroendocrine tumour suspected per symptoms	2 (7.4)
Imaging studies (diagnosis)	
Computed tomography	18 (17 pancreatic cyst, 1 pancreatic neuroendocrine tumour) (86)
Magnetic resonance imaging	2 (1 intraductal papillary mucinous neoplasm, 1 pancreatic cyst) (9.5)
Trans-abdominal ultrasound	1 (pancreatic cyst) (4.7)
Neuroendocrine tumour suspected per imaging	1 (4.7)

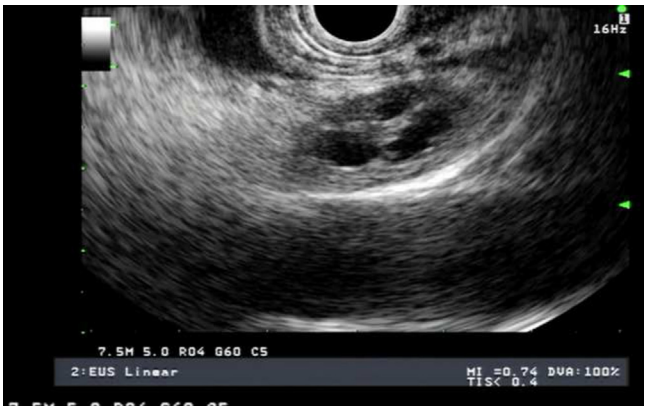

Fig. 1. Endosonographic image of thick walled cyst with central septations and anechoic spaces.

By EUS, the median cyst size was 35 mm (range 8–80 mm); 16 out of 27 patients had cysts <30 mm (59.3%). Ten were located in the head or uncinate of the pancreas (37%) and 17 were located in the body or tail (63.0%). EUS identified 2 cases with additional pancreatic cystic lesions and 1 with liver metastasis, which were not reported on prior cross-sectional imaging. Wall thickening was identified in 13 of 27 cases (48%) (focal ($n = 3$) and concentric ($n = 10$)) (Fig. 1). A nodule was identified in 7 cases (range 2.4–8 mm). Wall thickening or a nodule was seen in a total of 16 cases (59.3%). Cyst echogenicity was reported as anechoic in 15 cases (2 with debris), cystic and solid in 9 cases, hypoechoic in 3 cases. Septation was seen in 22 cases (81.5%), of which 8 were multilocular. No main pancreas ductal dilation was noted in any cases. Pancreatic ductal communication was identified in 2 cases. The pancreatic parenchyma echotexture was normal in 21 cases (77.8%), heterogeneous in 3 cases, and fatty or hyperechoic in 3 cases. A summary of the endosonographic findings is summarised in Table 2.

24 patients underwent EUS-FNA. Of the three patients who did not undergo FNA, surgical pathology confirmed neuroendocrine tumour. The endosonographers did not specifically note the reason for not performing FNA. A 22 gauge needle was used in 21 cases and a 25 gauge needle was used in 3 cases. A median of 1 pass was made (range 1–7). Nine patients had FNA with targeting of the cyst wall, specifically noted. In 8 out of those 9 patients (88.9%), cytology was consistent with neuroendocrine tumour. In those 9 cases, wall thickening was noted to be focal in 2 cases, circumferential in 4 cases, and a nodule was present in 3 cases. EUS-FNA cytology was diagnostic in 8/9 (88.9%) cases when the wall was targeted (8 NET and 1 non-diagnostic) versus 10/15 (66.7%) cases without wall targeting (9 NET, 5 benign or atypical cells, and 1 adenocarcinoma – final surgical pathology revealed well-differentiated endocrine tumour) ($p = 0.35$) (Fig. 2).