Cystic Neuroendocrine Tumor of the Pancreas: A Rare Type of Pancreatic Cystic Lesion Accurately Diagnosed and Staged by EUS-FNA

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Cystic neuroendocrine tumors of the pancreas are extremely rare. The tumors are solitary, solid or cystic and occur predominately in the pancreatic head. The exception is in the setting of MEN-1 (multiple endocrine neoplasia type 1) where multiple tumors occur. We present the case of a 42 year-old male with multiple cystic lesions of the pancreas, diagnosed as a cystic neuroendocrine tumor on endoscopic ultrasound fine needle biopsy, and the diffuse nature of involvement resulting in the first reported total pancreatectomy.

INTRODUCTION

Pancreatic neuroendocrine tumors (NETs) represent about 2% of all pancreatic neoplasms. Although pancreatic NETs have been considered to classically present with clinical syndromes related to hormone hypersecretion, up to 40% of all pancreatic NETs are nonfunctioning (i.e. inactive, clinically silent or nonsyndromic). Nonfunctioning neuroendocrine tumors present with symptoms secondary to mass effects of the tumor or may present with features of pancreatitis. The most common symptoms include abdominal pain, usually epigastric or left upper quadrant radiating to the back, and jaundice. While not adequately specific to be diagnostic, as they can be secreted by other tumors, NETs can secrete chromogranin A and B (90-100%), pancreatic polypeptide (58%), alpha-HCG (human chorionic gonadotropin) (40%) and Beta-HCG (20%). NETs usually present late with an average time to diagnosis from onset of symptoms of five years; 72% of the lesions are greater than 5cm and hepatic metastasis are present in 64-92% of cases at the time of diagnosis. Sporadic pancreatic NETs are almost always solitary and well demarcated. Their texture varies from fleshy to fibrotic and they are rarely cystic. Multiple tumors or diffuse pancreatic involvement usually occurs in a setting of familial syndromes that occur at an early age such as multiple endocrine neoplasia-1 (MEN-1), Von Hippel Lindau syndrome (VHL), neurofibromatosis type 1 and tuberous sclerosis. We present a unique case of multifocal cystic pancreatic NET.

Case Description

A 42 year-old white male presented with crampy epigastric pain that had waxed and waned for one year; this was associated with cough, nausea and mild weight loss. His medical and family histories were significant only for an 18 pack-year history of smoking and the use of omeprazole (40mg daily) for pain control. An upper GI series was significant only for prominent mucosal folds in the duodenal bulb with a possible ulcer in the distal inferior duodenal bulb. His serum amylase was 217 U/L and serum lipase was 170 U/L. A right upper quadrant abdominal ultrasound showed a dilated common bile duct (5.5mm), gallbladder polyp (7.7mm x 6.5mm x 8.8mm) and a cyst in the head of the pancreas measuring 1.25cm x 1.29cm x 1.37cm. Computed tomography (CT) scan and MRCP (magnetic resonance cholangiopancreatography) of the abdomen revealed multiple cystic lesions throughout the pancreas, the largest of which (2.9cm) was present in the tail (Figure 1). The pancreatic duct was dilated to 8mm with the common bile duct dilated to 1cm. A splenic cyst was also noted with a diameter of 8mm.

The patient was scheduled for endoscopic ultrasound and fine needle aspiration (EUS-FNA). Multiple cysts were noted throughout the head, body...
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and tail of the pancreas. Additional characteristics were multiple septations in some cysts and an irregular pancreatic duct that measured 6mm in the head and neck without filling defects. The largest lesion in the tail was aspirated with a 22g FNA needle and sent for analysis of carcioembryonic antigen (CEA), amylase and cytology (Figure 2). A second cyst in the body was drained and was targeted for additional testing due to the presence of a mural nodule (Figure 3). The cystic fluid analysis revealed amylase levels of greater than 12,000, indicating ductal communication, and CEA levels of <5, excluding mucinous-type lesions. The cytology was positive for neoplastic cells consistent with a pancreatic neuroendocrine tumor. Further clinical evaluation excluded multiple endocrine neoplasia syndromes. Laboratory values were significant for a pancreatic polypeptide level greater than 1600, parathyroid hormone level of 43, corrected calcium was 9.32, prolactin level was 8.0 and chromogranin A was 31.6. CT scan of the chest, abdomen and pelvis, evaluating for other lesions, was negative except for the noted pancreatic cystic lesions.

The patient subsequently underwent exploratory laparotomy, appendectomy, total pancreatectomy with splenectomy, hepaticojejunostomy, gastrojejunostomy and Braun enterointerostomy (Figure 4). During surgery, he had multiple small intussusceptions and an intraoperative enteroscopy was performed to look for lesions contributing to the intussusceptions. Examination to the mid-jejunum showed healthy mucosa except for duodenitis and multiple small duodenal ulcers. Postoperatively, his course was complicated by a chyle leak, which required drain placement. This resolved within one month with conservative management and the drain was removed without problems. Final

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Figure 5. A low power view of one of the lesions shows a cyst with a solid component in the wall

Figure 6. Higher magnification shows the characteristic trabecular and acinar architecture of a neuroendocrine tumor. The nuclei are relatively uniform with stippled (so-called “salt and pepper”) chromatin

pathologic evaluation of removed tissue displayed well-differentiated pancreatic neuroendocrine neoplasm (stage IB; pT2N0) with less than 2 mitoses per high-powered field and Ki-67 index less than 2% (Figures 5 and 6). The tumor was confined to the pancreas and all 37 regional lymph nodes were negative for metastasis and the microscopic margins were clear.

At present, one year later, the patient has well managed insulin-dependent diabetes, feels well and is being monitored closely by surgical oncology and hematology/oncology. He has not received any oncologic treatment as it was felt that his tumor had favorable characteristics and the entire tumor was removed with clear margins.

CONCLUSION/DISCUSSION

The differential diagnosis of pancreatic cystic neoplasms includes pseudocysts, mucinous cystic neoplasm, intraductal papillary mucinous neoplasm, serous cystadenoma and solid pseudopapillary tumor. Cystic neuroendocrine tumors are very rare with the first case reported by Thigpen in 1940. Nonfunctioning cystic neuroendocrine tumors have a typical radiologic appearance 80% of the time. On ultrasound, the lesions are well-circumscribed, hypoechoic masses with smooth margins. On CT scan, the lesions are well circumscribed and in 90% of cystic lesions the rim is hypervascular. Multiple cystic lesions occur in a very small subset of patients and require close investigation to make an accurate diagnosis as they closely resemble other pancreatic neoplasms.

Pancreatic cystic neuroendocrine lesions should be considered when there are solid areas within the cyst as well as when multiple cysts are present. Abdominal ultrasound has a reported sensitivity of <20% to 80% depending on the location of the lesion. Therefore, historically, the only definitive way to differentiate these cystic lesions was through open biopsy of the cyst wall due to the inability of ultrasound and CT to differentiate these lesions definitively. As demonstrated by our case however, EUS-FNA effectively evaluates these cystic lesions and offers a minimally invasive option to obtain an accurate tissue diagnosis thus allowing appropriate medical and surgical intervention.

References