

# Pancreatic islet cell tumor mimicking obstructive chronic pancreatitis: a case report

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## Abstract

Context: Pancreatic islet cell tumors are uncommon lesions, and nonfunctional islet cell tumors presenting with pancreatitis are extremely rare. Many patients with pancreatitis and islet cell tumors may initially present with acute attacks, which sometimes recur and the diagnosis of the tumors are usually delayed. Case report: We report a case of 44-year-old man who presented with a clinical impression of "calcifying chronic pancreatitis and pseudocyst" for 1 ½-year before nonfunctional islet cell tumor was diagnosed. He had a distal pancreatectomy, splenectomy and partial gastrectomy after failure of conservative management. Grossly a 1.7 cm ill-defined tumor was identified which was compressing the pancreatic duct. Histology showed nests and trabeculae of uniform endocrine cells positive for chromogranin and negative for glucagon, insulin, somatostatin and gastrin. A lymph node was positive for metastatic tumor. Conclusions: Due to this rare clinical presentation and to prevent delayed detection and complications, islet cell tumor should be considered in patients with non-remitting, persistent calcifying chronic pancreatitis. Careful pathological examination of such pancreatic resection specimen is also recommended as very small tumors can cause obstructive pancreatitis.

## INTRODUCTION

Islet cell tumors of the pancreas are uncommon with an incidence of less than 1 per 100,000.<sup>1</sup> These tumors usually present with symptoms attributable either to their endocrine hormone production or to a mass-associated pain or symptoms of obstruction. Reports in the literature have shown some association between pancreatic islet cell tumors and chronic pancreatitis, but only few were nonfunctioning islet cell tumors.<sup>2-8</sup> Many patients with pancreatitis and islet cell tumors may initially present with acute attacks, which sometimes recur and the diagnosis of the tumors are usually delayed.<sup>5</sup> The delay in the diagnosis of the tumor may result in untoward disease outcome as about 71% of tumors were malignant.<sup>5</sup> Here, we present a patient with nonfunctioning islet cell tumor that presented with features of calcifying chronic pancreatitis and pseudocyst.

## REPORT OF A CASE

A 44-year-old African-American male presented with a history of previous alcohol abuse and subsequent four months history of diffuse abdominal pain, worse in the gastric region and radiating to his back. Computed tomography (CT) imaging showed a 5.0 x 3.0 cm lobulated, fluid density located in the anterior pararenal space attached

to the pancreatic tail with abnormal punctate calcifications in the distal pancreatic parenchyma. The diagnosis of pseudocyst and chronic pancreatitis was made. The fluid was drained percutaneously over a month with symptomatic relief. However, once the drain was removed, the patient developed recurrent epigastric abdominal pain. Three months later, a repeat CT imaging showed a significant regression of the pseudocyst (less than 1.0 cm), but a 1.2 cm residual nodular focus was noted in the pancreatic body. Follow up CT imaging at 7 months showed persistence and progression of the ovoid nodular area at the body of the pancreas (1.7 cm) and dilated distal pancreatic duct. However, the changes were considered likely due to the sequelae of saponification and cicatrization. At the same time, the patient continued to experience epigastric pain. Three months later, another CT imaging showed similar findings. There was elevated serum amylase of 10538 units/dl at that time. Surgical intervention was recommended to rule out a pancreatic malignancy. As a result, the patient subsequently had distal pancreatectomy and splenectomy with partial gastrectomy.

## PATHOLOGIC FINDINGS:

The specimen consisted of the distal pancreas, spleen, and a small segment of stomach. There were extensive adhesion

and fibrosis between the pancreatic tail, stomach wall and spleen. A 1.7 × 1.5 × 1.3 cm somewhat ill defined tumor was located at the junction of pancreatic body and tail (Figure 1). The tumor had a focally hemorrhagic cut surface with tan brown appearance. The tumor compressed the pancreatic duct with completely lumen obstruction and calcification. The distal pancreatic duct was significantly dilated with associated penetrating abscess between the pancreas and gastric wall. The proximal pancreatic parenchyma was grossly unremarkable with a normal lobulated structure and yellow tan appearance. However, the pancreatic parenchyma distal to the pancreatic mass showed extensive fibrosis with white rubbery texture and loss of the normal lobulated configuration. The spleen and gastric mucosa were grossly unremarkable.

**Figure 1**

Figure 1. A 1.7 × 1.5 × 1.3 cm somewhat ill defined tumor was located at the junction of pancreatic body and tail. The tumor had a hemorrhagic cut surface showing tan brown appearance. The proximal pancreatic parenchyma was grossly unremarkable; however, the distal pancreatic parenchyma downstream the pancreatic mass showed extensive fibrosis.

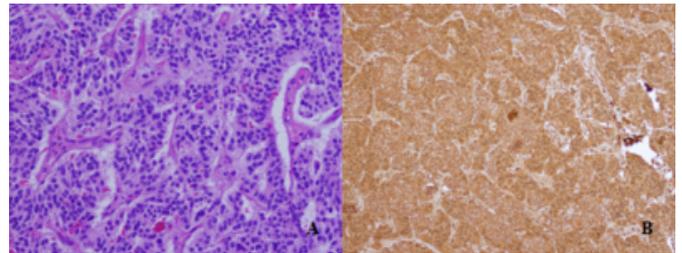


Histology showed nests and trabeculae of uniform endocrine cells, which appeared round to oval with finely stippled chromatin and inconspicuous nucleoli with cells containing scant to moderate amount of cytoplasm (Figure 2A). Few mitotic figures were noted. Tumor cells had infiltrative borders, and lymphovascular and perineural invasion was clearly visible. One parapancreatic lymph node had metastatic neuroendocrine tumor. The tumor cells were positive for chromogranin (Figure 2B), but negative for glucagon, insulin, somatostatin and gastrin. The distal pancreas showed chronic pancreatitis with extensive fibrosis,

but the proximal pancreas showed unremarkable histology (Figure 3A&B).

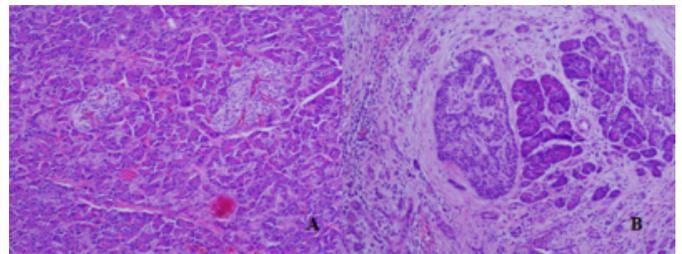
**Figure 2**

Figure 2. Nests and trabeculae of uniform endocrine cells have round to oval with finely stippled chromatin and inconspicuous nucleoli with cells containing scant to moderate amount of cytoplasm (2A, H&E, 200X). Tumor cells are positive for chromogranin (2B, IHC, 200X), but negative for glucagon, insulin, somastatin and gastrin.



**Figure 3**

>Figure 3. The proximal pancreatic parenchyma has an unremarkable histology without any inflammation or fibrosis (3A, H&E, 100X), but the distal pancreatic parenchyma has extensive fibrosis, acute and chronic inflammation, exocrine gland atrophy, and pseudohyperplasia of endocrine cells (3B, H&E, 100X).



**CONCLUSIONS**

Islet cell tumors of the pancreas represent 1% to 2% of all pancreatic tumors.<sup>9</sup> They typically occur in adults, with a peak incidence between 30 to 60 years, but cases have been described in all ages. Islet cell tumors are divided into functional and nonfunctional tumors. The majority of tumors are functional and usually produce an excess of hormone, and therefore their presence becomes evident as a result of the clinical effects of the hormone. The minority of tumors are nonfunctional and do not produce any hormone or peptide in excess. Patients with nonfunctional pancreatic endocrine neoplasms usually present with nonspecific symptoms related to the presence of the mass, although biliary obstruction and jaundice may occur with tumors in the pancreatic head. Nonfunctional tumors are more likely to be malignant and nonresectable by the time they are detected.<sup>3,10</sup> Due to delay in diagnosis, they tend to present

with a later stage and have a different clinical course from their functioning counterparts.

While the association of pancreatitis with exocrine pancreatic cancer is well recognized, its association with neuroendocrine tumors of the pancreas is uncommon with even fewer cases being reported in association with nonfunctional tumors.<sup>3,5,6,7</sup> The diagnosis of the tumor is usually delayed when an endocrine pancreatic tumor presents with acute pancreatitis. Furthermore, patients with endocrine tumors usually have multiple operations for pancreatitis or pseudocyst before the endocrine tumor is recognized. The overall incidence of pseudocyst in patients with pancreatic islet cell tumors was 33%.<sup>5</sup> The course of our case was a classic stereotype. Our patient presented with episodes of acute attack, followed by pancreatic pseudocyst formation that warranted drainage. After removing the drainage tube, he had repeated recurrences. Due to his history of heavy alcohol intake, clinicians assumed his recurring chronic pancreatitis was associated with his alcohol use. However, the radiologic findings in our case, the unremarkable pancreatic head but enlarged, abnormal pancreatic tail with dilated duct, are classic for obstructive chronic pancreatitis associated with islet cell tumors.<sup>12</sup> The consequences of delayed diagnosis for islet cell tumors may be significant, because many cases turn out to be malignant islet cell tumors.<sup>5</sup> Furthermore, the associated penetrating abscess as a long-term complication of delayed diagnosis necessitated partial gastric wall resection in our case. Radiologic identification may be difficult in small ill-defined lesions especially in a background of chronic pancreatitis with fibrosis. In the majority of reported cases of endocrine tumors presenting as pancreatitis or pancreatic duct stricture, a pancreatic mass was not detected preoperatively by abdominal ultrasound (US) or CT. On the other hand, endoscopic ultrasonography (EUS) has been shown to be very useful when a pancreatic endocrine tumor is suspected.<sup>3</sup> Endoscopic ultrasound guided-fine needle aspiration (EUS-FNA) may be helpful for obtaining a preoperative tissue diagnosis.<sup>13</sup> For pathologists, careful examination of resection specimens is very important to avoid missing small lesions, especially in the background of chronic obstructive pancreatitis.<sup>12</sup> Fortunately, despite the significant delay in the diagnosis of our case, the tumor was still resectable without distance metastasis.

Chronic pancreatitis is a risk factor for pancreatic cancer.<sup>4</sup> Ductal changes, including distortion, dilatation, and pancreatic ductal hypertension in the setting of chronic

pancreatitis, induce genomic damage and increased cell turnover. In addition, signaling mechanisms that play a role in the development of embryonic pancreas are reinstated; thus playing a role in repair, regeneration, and transformation. This, in turn, may result in dysregulation of the cell cycle and eventually leads to pancreatic cancer.<sup>14</sup> A recent publication documented that risk factors for sporadic pancreatic endocrine tumors included family history of any cancer, chronic pancreatitis, high alcohol intake, and recent-onset diabetes.<sup>16</sup> To avoid over-diagnosis of clustered islet cells in chronic pancreatitis as islet cell tumors, pathologists must be aware of neuroendocrine cell (islet cell) pseudohyperplasia due to destruction and atrophy of exocrine glands. On microscopic examination, hyperplastic endocrine cells maintain their lobulated configuration with surrounding atrophic exocrine acini and proliferation of pancreatic ducts. Also, in pseudo-hyperplastic islets, immunohistochemistry will show mixed population of neuroendocrine cells (producing mixed hormones), like in a normal Langerhans islands, rather than clonal proliferation observed in endocrine tumors.

In summary, chronic obstructive pancreatitis caused by pancreatic islet tumors is extremely rare but should be considered as a possible underlying pathology in patients that present with smoldering, unabating and/or recurrent chronic pancreatitis. When acute or recurrent pancreatitis is present without a clear cause, especially if standard imaging methods do not reveal an obvious etiology, neuroendocrine tumors should be recognized as a rare but possible cause. Clinicians need to be aware of this rare presentation to avoid delayed diagnosis and unnecessary multiple operations. During grossing examination, pathologists should carefully look for possible small endocrine tumors causing chronic obstructive pancreatitis. In addition, they need to be aware of pseudohyperplasia of endocrine cells as a mimic of endocrine tumor in order to avoid over diagnosis of the latter.

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