

## Pancreatic Neuroendocrine Tumor with Atypical Radiologic Presentation

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An atypical radiographic presentation of a rare non-functional pancreatic neuroendocrine tumor as seen on US, CT and MRI is described. Radiographic-pathologic correlation via gross autopsy specimens and immuno-histochemical staining demonstrates the pancreas to be markedly enlarged with extensive calcifications and numerous tiny cysts secondary to diffuse neoplastic infiltration without a focal mass.

### Introduction

Neuroendocrine tumors, also known as islet-cell tumors, are rare endocrine tumors arising within or near the pancreas with an incidence of approximately 5 cases per million persons per year. A small number may occur as part of a multiple endocrine neoplasia type-1 (MEN-1) [1]. The World Health Organization classifies neuroendocrine tumors as well-differentiated or poorly differentiated endocrine tumors, although, the traditional classification of functional and non-functional types currently referred to as “syndromic” and “non-syndromic”, still has wider acceptance [2-4].

Most neuroendocrine tumors are syndromic and secrete hormones leading to a variety of clinical syndromes. Consequently, they are small in size ranging from 0.4 to 4 cm at the time of initial diagnosis due to earlier symptomatic presentation. On CT scan, functional tumors appear as small homogeneous isodense masses that enhance. The common syndromic tumors of the pancreas include: insulinomas, gastrinomas, glucagonomas and VIPomas [4-6].

The non-syndromic neuroendocrine tumors are mostly diagnosed in patients having abdominal pain due to large focal mass or as an incidental finding on imaging studies [7]. On CT scan, non-syndromic tumors present as large discrete focal heterogeneous masses with calcifications, cysts, necrosis, vascular invasion and direct extension or metastases. Classically the pancreatic neuroendocrine tumors are hypervascular, enhancing during both arterial and venous phases [4-6, 8]. In some instances, magnetic resonance imaging (MRI) and somatostatin receptor scintigraphy are employed to further delineate local invasion and metastases.

The following case describes a highly atypical radiographic presentation of a large non-syndromic pancreatic neuroendocrine tumors with diffuse enlargement of

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Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging

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the pancreas without contour deformity or a focal mass. A multi-modality imaging approach using US, CT, and MRI with direct comparison is presented and correlated with histological findings and post-autopsy gross specimens.

### Case Report

A 46-year-old man with past medical history significant for gout presented with a one-month history of progressive weight loss of 15 pounds, weakness, lethargy, and confusion. The patient denied abdominal pain, nausea, vomiting, constipation, diarrhea, melena, or bleeding. Pertinent physical exam demonstrated mild hepatomegaly and an inflamed erythematous right great toe. Relevant laboratory values included a mildly elevated AST (51 U/L), alkaline phosphatase (198 U/L), ammonia level (208  $\mu\text{mol/L}$ ), elevated lipase (2406 U/L) and uric acid level (10.4 mg/dl). The patient was admitted with a working diagnosis of acute pancreatitis and acute exacerbation of gout.

An abdominal sonogram was performed to evaluate for gallstone pancreatitis. Marked pancreatic enlargement was found with extensive speckled calcifications and a few cystic areas (Fig.1). In addition, the portal vein was dilated and tortuous.

The contrast-enhanced CT demonstrated signs of portal hypertension with splenomegaly, portal vein engorgement, and esophageal varices. Evaluation of

the pancreas revealed it to be markedly enlarged with extensive calcifications and a few cysts (Fig.2AB), but without surrounding inflammation. Also noted was a 5 cm lobulated enhancing masses in the dome of the liver consistent with an atypical hemangioma or a metastatic lesion.

MRI of the abdomen suggested an atypical hepatic hemangioma (Fig. 3) and confirmed a massively enlarged pancreas containing multiple calcifications and tiny cysts without contour deformity or involvement

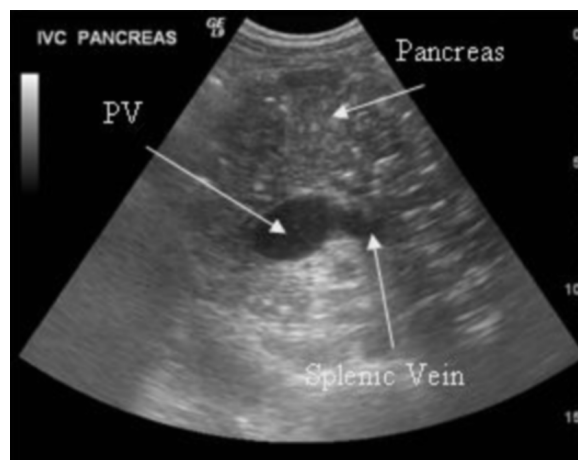


Figure 1. 46-year-old man with pancreatic neuroendocrine tumor. Transverse sonogram of the region of the pancreas shows a diffusely enlarged pancreas with extensive calcifications. PV = Portal Venous Confluence.

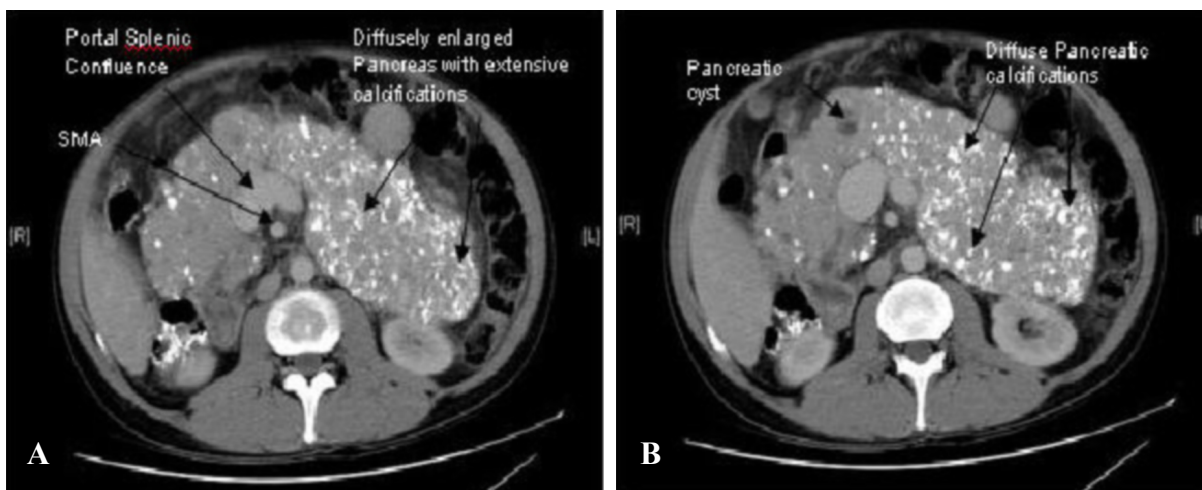


Figure 2A-B. Contrast-enhanced CT shows a markedly enlarged pancreas with extensive calcifications and cysts.

of the surrounding soft tissue structures (Fig. 4 A-D). The T1-weighted fat saturation FSPGR (TR = 120 ms; TE = 1.328 ms) images demonstrated the pancreas to be isointense to the liver (Fig. 3A). The pancreas was slightly increased in intensity with respect to the liver on T2-weighted images (TR = 991.744 ms; TE = 118.56 ms) (Fig. 3B). T1-weighted fat saturation post contrast images (TR = 120 ms; TE = 1.328 ms) demonstrated minimal enhancement in the arterial phase (Fig. 3C) and progressive enhancement in the portal venous phase (Fig. 3D). The pancreatic duct and the visualized portions of the pancreatic duct were unremarkable.

The differential diagnosis included an infiltrative pancreatic process such as an autoimmune pancreatitis, urate pancreatitis, amyloidosis, sarcoid, hemochromatosis, granulomatous diseases, or much less likely a

malignancy.

## Histology and Gross Specimens from Autopsy

The patient subsequently underwent exploratory laparotomy. The histological sample of the pancreas showed a well-differentiated Islet cell neuroendocrine tumor with positive immuno-histochemical staining for Chromogranin A, Synaptophysin, and CD 56. The liver biopsy showed fibrosis and regenerating micronodules consistent with cirrhosis, possibly due to polypeptide secretion by the pancreatic neuroendocrine tumor. The patient died two months later and a limited autopsy of the pancreas again showed a diffusely enlarged infiltrated pancreas, which measured 32 x 16 x 11 cm in size and weighed 1850 grams (Fig. 5). The entire pancreas was replaced by a micronodular neuroendocrine tumor with

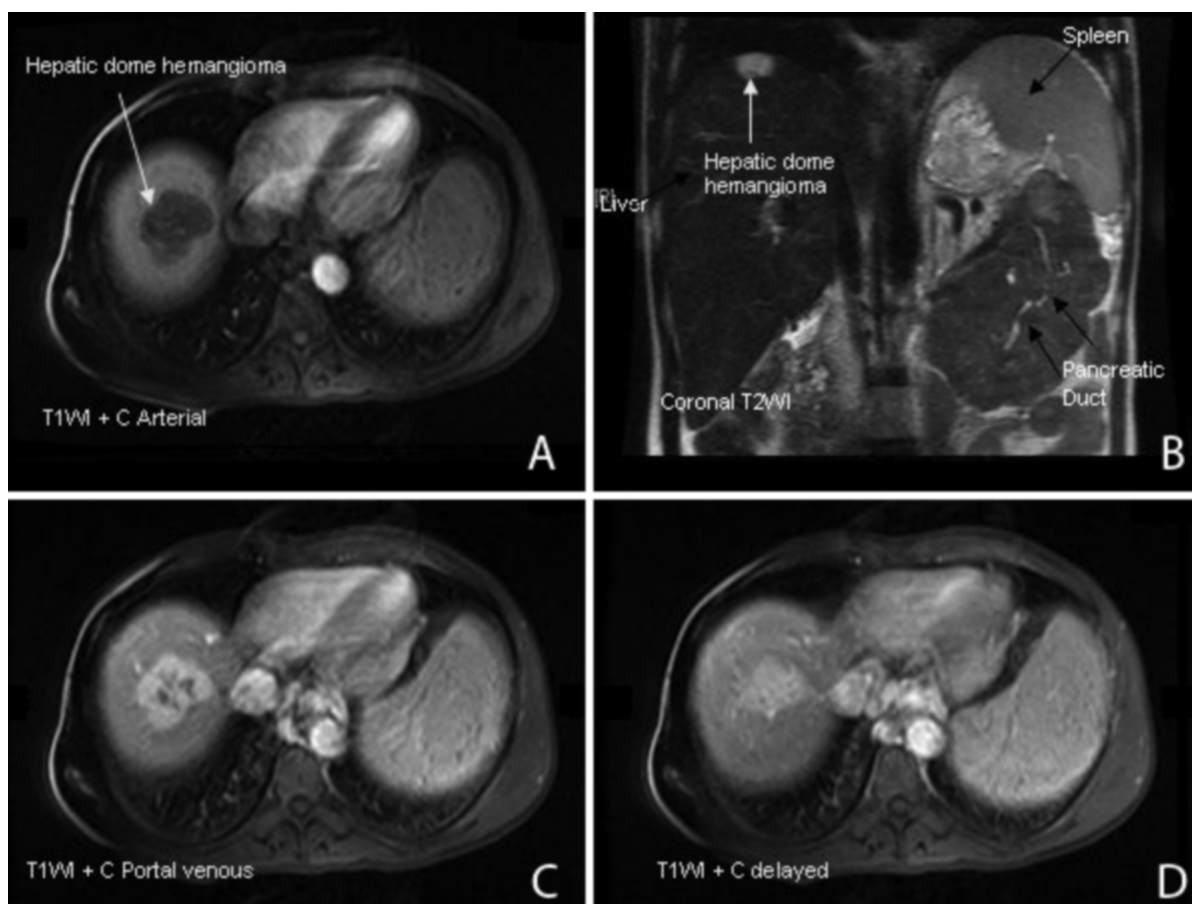


Figure 3A-D. MRI shows (A) T1 hypointense and (B) T2 hyperintense hepatic dome lesion with progressive centripetal enhancement on (C) portal venous phase and (D) delayed imaging.

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extensive calcifications. Microscopic examination of the liver revealed fibrosis and nodule formation consistent with early cirrhosis.

### Discussion

Non-syndromic neuroendocrine tumors, such as the one presented here, are generally clinically silent and consequently present late as large masses. They can grow undetected until symptoms develop only as a result of their large size, which can vary between 6 and 20 cm [7]. Nonfunctional neuroendocrine tumors may secrete polypeptides as well however, no clinical manifestations

result. On CT scan, non-syndromic tumors present as large discrete focal heterogeneous masses with calcifications, cysts, necrosis, vascular invasion and direct extension or metastases. Classically the pancreatic neuroendocrine tumors are hypervascular, enhancing during both arterial and venous phases [4-6, 8].

The pancreatic neuroendocrine tumor presented in our case was quite large, reaching a maximum dimension of 32 cm and demonstrating enhancement especially in the portal-venous phase. The intriguing aspect of the case from an imaging perspective was the diffuse massive pancreatic enlargement without a focal mass lesion or contour deformity and with extensive calcifications.

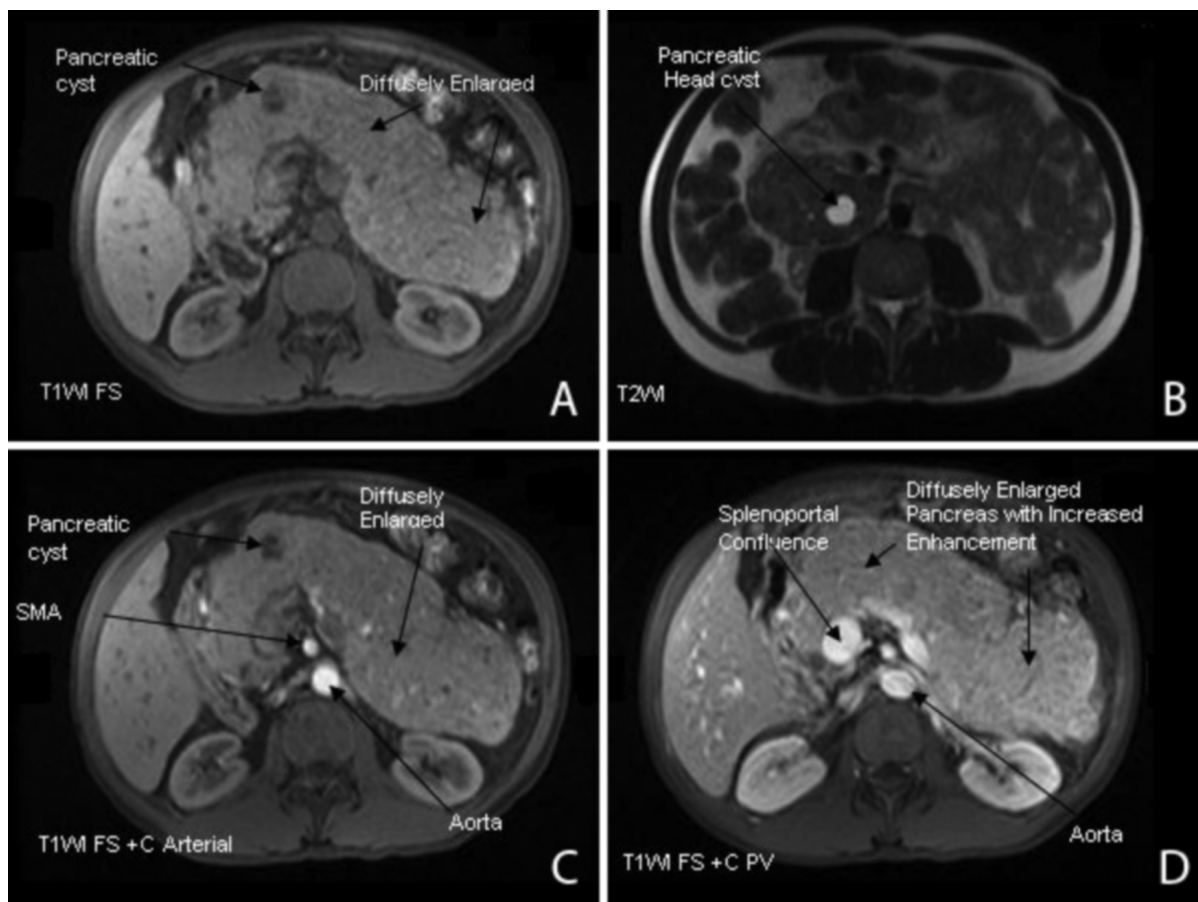


Figure 4A-D. (A) Axial T1 fat saturated MRI showing diffusely enlarged pancreas without pancreatic contour deformity or involvement of adjacent soft tissues. (B) Axial T2 MRI demonstrates one of the numerous pancreatic cysts. (C) Axial T1 MRI with contrast in arterial phase showing mild pancreatic enhancement. (D) Axial T1 MRI with contrast in portal-venous phase showing progressive pancreatic enhancement.



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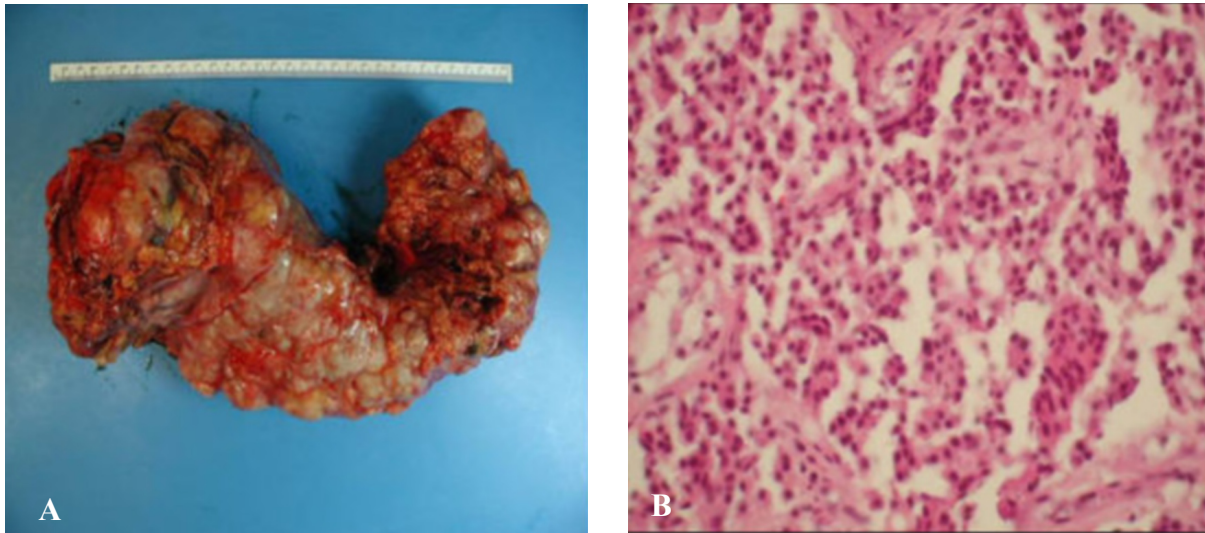


Figure 5A-B. (A) Gross specimen shows generalized enlargement of pancreas with extensive nodularity and calcifications representing diffuse tumor involvement. (B) Photomicrograph shows uniformity and cellular features typical of neuroendocrine tumor (H and E, 100x).

Regarding other possible etiologies, the biliary ducts are commonly involved in autoimmune or urate pancreatitis. Furthermore, these entities are rarely associated with pancreatic calcification thereby making them less likely. Pancreatic amyloidosis and sarcoidosis have diffuse or focal pancreatic involvement, which is predominantly hypoattenuating with or without calcifications, and may have biliary duct irregularities [9, 10]. Furthermore, involvement of other organs such as the heart, the lungs, or the kidneys is frequently encountered.

Microscopically, both benign and malignant pancreatic neuroendocrine tumors have similar appearance. Tissue sections show similar cells forming solid nests, small glandular or trabecular structures or a ribbon or gyriform pattern [5]. Approximately 10-60% of syndromic pancreatic neuroendocrine tumors are potentially malignant and up to 80% of non-syndromic tumors can be malignant [3, 5], a designation primarily determined by finding additional metastatic sites in the liver and lymph nodes.

The prognosis is generally poor for such non-functional pancreatic neuroendocrine tumors despite their indolent manifestation with a 5-year survival is reported as 60-100% for localized disease, 40% for regional, and 29% for distant metastases [3, 5, and 11]. Treatment

is surgical resection if discovered early. Given the poor prognosis it is important to recognize the various radiological presentations of the pancreatic neuroendocrine tumors, including diffuse pancreatic enlargement, which has not previously been reported.

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