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Pancreatic neuroendocrine tumor with splenic vein tumor thrombus: A case report

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ABSTRACT

INTRODUCTION: Pancreatic neuroendocrine tumors (PNET) are rare, often indolent malignancies. PNET are classified as functional or nonfunctional based on the secretion of hormones without a negative feedback loop; the latter account for up to 60% of PNET. Although PNET are associated with a better prognosis compared to pancreatic adenocarcinomas, they are often diagnosed in advanced stages, making them a significant source of morbidity for patients. Here we present a rare case of venous tumor thrombus arising from a nonfunctional PNET.

PRESENTATION OF CASE: A 44-year-old woman was referred for evaluation and treatment of a possible tail of pancreas PNET discovered during work-up for a 9 year history of intermittent subcostal pain. Previous endoscopic ultrasound with fine needle aspiration revealed a 3.5 cm × 3 cm mass, with cytological diagnosis of neuroendocrine tumor. Patient was scheduled for laparoscopic distal pancreatectomy. During surgery the mass was found to encase the splenic vein leading the surgeon to perform an en bloc distal pancreatectomy and splenectomy. Pathologic analysis revealed a 1.8 cm × 5 cm tumor thrombus lodged in the splenic vein.

DISCUSSION: Nonfunctional PNET usually present in advanced stages and can be associated with venous tumor thrombi. Preoperative imaging may not accurately predict the presence of venous tumor thrombi.

CONCLUSION: En bloc resection of primary tumor, involved organs and thrombus is the recommended treatment option and often results in long term survival. New multi-modality strategies are needed for detection of venous involvement in nonfunctional PNET to better assist with preoperative planning and counseling.

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1. Introduction

Pancreatic neuroendocrine tumors (PNETs) are rare and often indolent malignancies with an incidence lower than 1 per 100,000 persons per year. These tumors account for only 1–3% of diagnosed pancreatic neoplasms.¹ Although PNETs are generally associated with a better prognosis compared to pancreatic adenocarcinomas, many PNETs are diagnosed in advanced stages, making them a significant source of morbidity for patients with this disease.¹

Derived from cells of the endocrine pancreas, some of these tumors are able to secrete gut hormones without a normal negative feedback loop. These secreting tumors are known as functional PNETs. However, up to 60% of all PNETs do not produce any measurable hormones; thus rendering them as nonfunctional PNETs (NF PNETs). Functional PNETs are more likely to be smaller in size and symptomatic earlier in their course as opposed to NF PNETs.

Nonfunctional PNETs lead to symptoms only when their size is large enough to create a mass effect or when they invade into adjacent or distant organs. When these tumors are found at earlier stages they are generally an incidental finding noted on imaging done for another purpose such as trauma. One rarely reported feature of NF PNETs is the presence of venous tumor thrombus, which differs from the venous occlusion more commonly seen in other pancreatic malignancies, such as pancreatic adenocarcinoma.^{2–4}

We present a rare case of venous tumor thrombus arising from a NF PNET.

2. Case

A 44-year-old woman was referred to our surgical oncology department for evaluation and treatment of a possible PNET in the tail of the pancreas. The patient had reported a 9 year history of intermittent left subcostal pain which radiated to the mid epigastrium, left flank and back. This pain was associated with nausea, vomiting and diarrhea. The intermittent pain was exacerbated by drinking alcoholic beverages and, when severe, required

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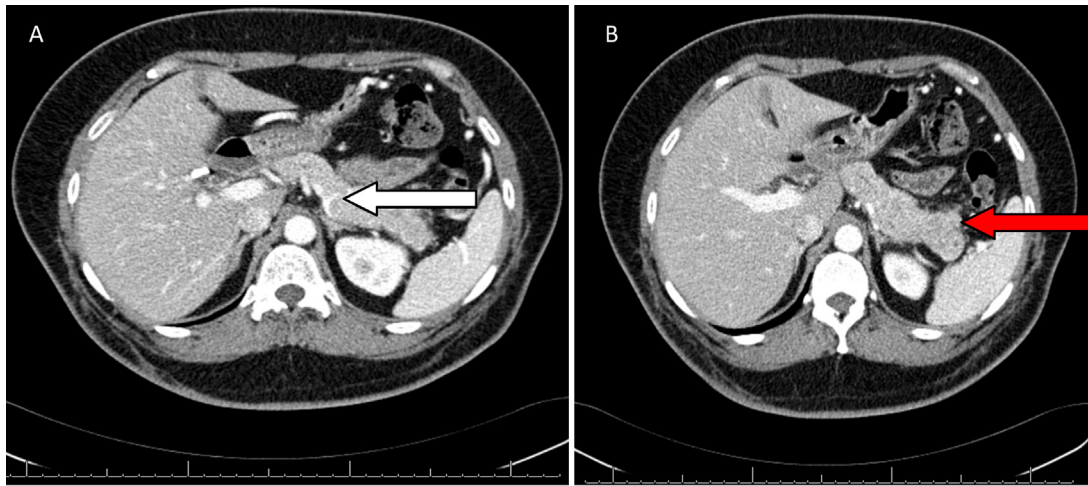


Fig. 1. (A, B) Late arterial phase CT image demonstrating beginning of splenic vein tumor thrombus (A, white arrow), and indistinct, mildly enhancing pancreatic tail lesion (B, red arrow).

admission and IV narcotics. No cross sectional imaging was performed during those encounters until six months before referral, when she developed pancreatitis. During her evaluation for this a CT was performed which reported splenic vein occlusion at the level of the mid body of the pancreas, and a 17 mm mildly enhancing mass within the tail of the pancreas (Fig. 1). After her symptoms improved, she was discharged and not seen by physicians until 3 months later when she presented with a similar episode. At that time her referring physicians requested an endoscopic ultrasound (EUS). The EUS revealed a solid pancreatic tail mass measuring 3.5×3 cm that was biopsied via ultrasound guided fine needle aspiration. Histology revealed a low-grade neuroendocrine tumor which was staged uT2 N0 Mx leading to her referral to our surgical oncology team.

The patient's past medical history was significant for hypothyroidism and diverticulosis. Her past surgical history was positive for laparoscopic cholecystectomy, incisional hernia repair and hysterectomy/bilateral salpingo-oophorectomy secondary to uterine rupture at birth of her youngest child. Family history was notable for one aunt, one uncle and 2 cousins with diagnosis of pancreatic adenocarcinoma, all on the paternal side.

Upon presentation she had mild hypertension, but an otherwise normal physical exam. Laboratory values were also within normal limits. Due to the cytology results confirming PNET she was

scheduled for a laparoscopic distal pancreatectomy and possible splenectomy. She received preoperative immunizations and then underwent surgery.

An initial laparoscopic approach was performed with conversion to a midline open laparotomy due to poor visualization of the distal pancreas secondary to adhesions. The pancreas was found to be soft with exception of the distal pancreatic tail where a firm nodular mass was felt. The mass was found to encase the splenic vein, so an en bloc distal pancreatectomy and splenectomy was performed without complications. Frozen section of the proximal margin of the pancreas was performed and shown to be negative for tumor.

Pathology evaluation revealed a $3.3 \text{ cm} \times 2.2 \text{ cm} \times 2.8 \text{ cm}$ tumor within the distal pancreas (Fig. 2). Tumor was well circumscribed and solid with a tan lobulated cut surface. The spleen was unremarkable; the splenic vein, however, had a large tumor thrombus which grossly protruded on gross sectioning (Fig. 3). The thrombus measured 1.8 cm in diameter and extended approximately 5 cm in length. Histological evaluation revealed an intermediate grade PNET with surrounding fat necrosis (Fig. 4A). Immunohistochemistry staining for synaptophysin supported the diagnosis of PNET (Fig. 4B). Peri-neural and vascular invasion were identified. None of the 5 examined lymph nodes were positive for metastasis, leading to a pathological tumor stage of T2 N0 M0.

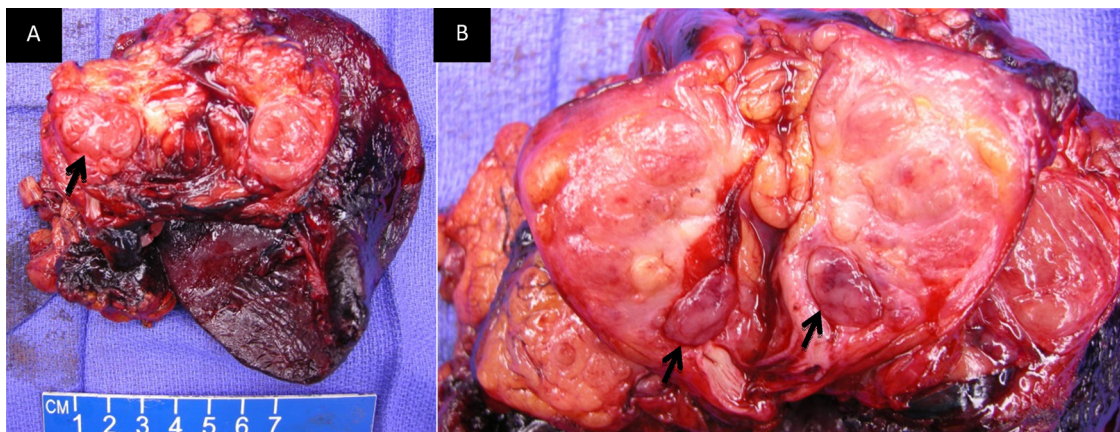


Fig. 2. (A, B) Gross photograph of a tan lobulated mass (arrows) within the pancreatic parenchyma.

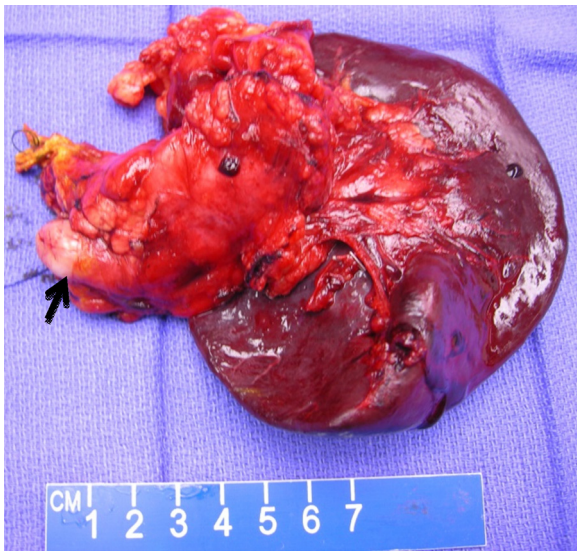


Fig. 3. Gross photograph of tumor thrombus (black arrow) protruding from the splenic vein.

3. Discussion

We present a case of a NF PNET with an associated splenic vein tumor thrombus. Although the incidence of PNETs has increased in the last 2 decades, they continue to be a rarely diagnosed malignancy of the pancreas.^{5,6} While PNETs account for only 1–3% of all diagnosed pancreatic malignancies, in more recent autopsy studies, their incidence reaches up to 10%, suggesting that these tumors frequently go unnoticed.¹

Splenic vein tumor thrombosis arising from PNETs has rarely been described in the literature. Bok and colleagues reported that from 76 patients evaluated by angiogram only one (1%) had splenic vein occlusion; unfortunately, the cause of this occlusion whether standard venous thrombosis vs tumor thrombosis was not reported.³ A larger cohort of patients reviewed by Balachandran and associates found that out of the 88 patients examined, 29 (33%) had evidence of venous tumor thrombus on computed tomography images. Of these, 15 (52%) were located in the splenic vein. Only one tumor thrombus in the splenic vein was confirmed

pathologically; leading the authors to conclude, in accordance with other investigators, that venous tumor thrombi were not accurately reported on preoperative imaging.^{2,3}

While the prognostic importance of splenic vein tumor thrombus is still to be completely understood due to its rarity, complications and changes in surgical outcomes have been reported. Splenic vein tumor thrombi arising from PNETs may lead to sinistral hypertension or even pre-sinusoidal portal hypertension if left untreated. The risk of having gastric varices and upper gastrointestinal bleed is increased in patients with sinistral hypertension; thus, increasing both morbidity and mortality of PNETs.^{10,11} The low incidence of PNETs and even lower incidence of associated splenic vein tumor thrombus, limits the possibility of prospective randomized trials to define differences in surgical treatment outcomes. In a comparison of patients with pancreatic adenocarcinoma who underwent distal pancreatectomy and splenectomy, Dedania and colleagues found that those who had a splenic vein thrombus were more likely to have pancreas-specific complications including pancreatic fistulas and delayed gastric emptying; the median survival, however, was not significantly different compared to patients who did not have a splenic vein thrombus.¹²

Surgical intervention for PNETs continues to be the recommended treatment,⁷ leading to a 10 year overall survival rate of 60% and a disease free survival rate of 30%.⁴ The benefits of surgical intervention persist regardless of PNET subtype, significantly prolonging the survival of patients whose primary tumor is removed.⁸ Distal pancreatectomy and splenectomy continue to be the standard of care for tumors arising from the body and tail of the pancreas and for those which present with invasion to the splenic vein.^{7,9}

Current literature on splenic vein tumor thrombus arising from a PNET is scarce, and the majority of previously reported cases of venous tumor thrombus from PNETs noted thrombus in the portal vein.^{13–17} Ait-Ali and colleagues reported a case of a PNET directly invading the splenic artery and vein; however, in contrast to this case, the patient had signs of isolated left-sided portal hypertension with gastric varices and there was no mention of a venous tumor thrombus in the splenic vessels.¹⁸

To our knowledge, this is one of the few reported cases of splenic vein tumor thrombus arising from a PNET, and possibly the first case report of a splenic vein tumor thrombus without invasion to adjacent organs or signs of sinistral hypertension. The

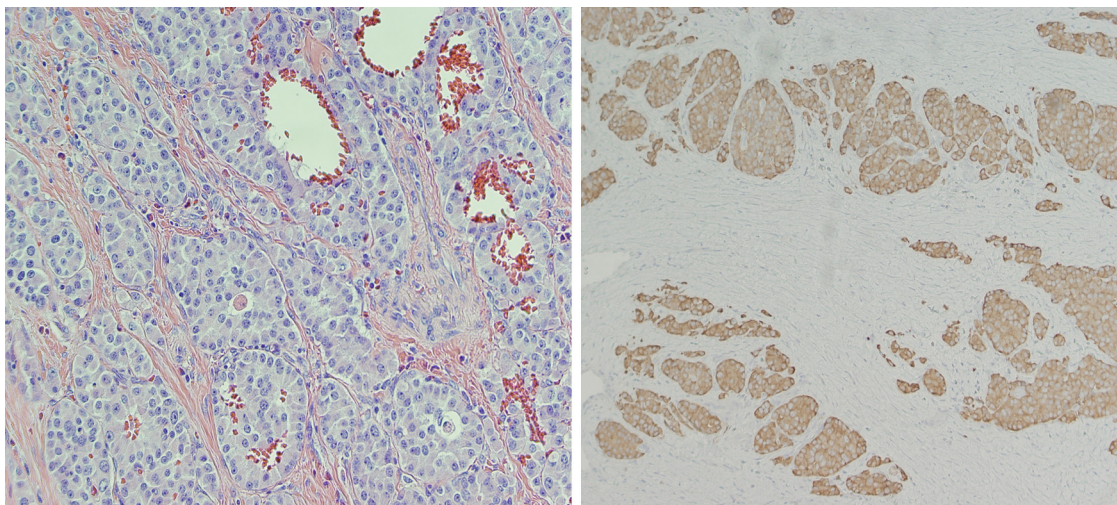


Fig. 4. (A) Hematoxylin and eosin stain at 40× demonstrating intermediate grade pancreatic neuroendocrine tumor. (B) Immunohistochemistry stain with diffusely positive synaptophysin staining.

first reported case of a splenic vein tumor thrombus arising from a PNET was published in 1992, in which Watase and colleagues reported a 16 cm × 13 cm × 12 cm PNET that directly invaded the spleen, stomach, left kidney and left colic flexure and was associated with left-sided portal hypertension.¹⁷ Other reported cases of a PNET invading into the splenic vein also document the patient presenting with sinistral hypertension, gastric varices and gastrointestinal bleeding.^{10,11}

In summary, we note that preoperative cross-sectional imaging may not always predict venous tumor thrombus arising from PNETs. Recommend treatment for patients with PNETs should be en bloc resection of tumor and thrombus with any other involved organs.

Conflict of interest

None declared.

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None.

Ethical approval

Patient has provided verbal consent for presentation of case. This informed consent was documented.

Author contributions

Data collection, writing: Rodrigo A. Rodriguez, Heidi Overton and Katherine Morris.

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