Received: 14 June 2023 | Revised: 26 August 2023 | Accepted: 25 September 2023

DOI: 10.1002/ccr3.8023

CASE REPORT

Clinical Case Reports Open Access WILEY

Pancreatic tail cancer in the setting of pancreatitis with a review of the literature: A case report

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Key Clinical Message

Environmental risk factors for pancreatic cancer include acute and chronic pancreatitis, obesity, and tobacco use. Differentiating a pancreatic neoplasm in a patient with pancreatitis can be challenging due to their similar presentations. A 57-year-old African American man with a history of congestive heart failure, pancreatitis, and incomplete pancreas divisum presented with an epigastric abdominal pain that radiated to his back. Imaging showed necrotizing pancreatitis, a developing splenic infarct, and a mass at the pancreas tail. The patient was discharged with pain medications and was recommended follow-up imaging after resolution of his pancreatitis. He was readmitted to the emergency department 2 weeks later with recurrent acute abdominal pain. Computed tomography scan of abdomen and pelvis followed by magnetic resonance imaging and endoscopic ultrasound revealed an infiltrative pancreatic tail mass. Biopsy of the mass confirmed a locally advanced pancreatic tail adenocarcinoma. Chronic pancreatitis is associated with pancreatic cancer. Practitioners should be aware of the coexistence of chronic pancreatitis and pancreatic cancer, and the initial steps to evaluate a malignancy in chronic pancreatitis.

KEYWORDS

chronic pancreatitis, imaging, pancreatic ductal adenocarcinoma, pancreatic neoplasm

1 | INTRODUCTION

Pancreatic ductal adenocarcinoma (PDAC) is the fourth leading cause of cancer-related death in the US. While medical advancements have increased the 5-year survival for a subset of surgically resected patients from 1.5% in 1975 to 17.4% in 2011, the overall 5-year survival still remains below 5%.[1] Given the high morbidity and mortality rate of pancreatic cancer, early detection, and treatment are crucial in improving survival rates.

Both acute and chronic pancreatitis are significant risk factors for pancreatic cancer. Patients with acute pancreatitis have been reported to have double the risk of developing pancreatic cancer over the course of a 5-year follow-up period.[2] The International Pancreatitis Study Group followed 2015 patients with chronic pancreatitis in six countries for a mean of 7.4 years.[3,4] They found that the standardized incidence ratio (the ratio of observed to expected cases) was 26.3 (95% confidence interval, 19.9–34.2). Differentiating pancreatitis from pancreatic cancer

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in a patient, however; can be challenging due to their similar presentations. Here we report a case of a patient diagnosed with pancreatic cancer in the setting of acute on chronic pancreatitis and diagnostic strategies to distinguish between the two clinical entities.

2 | CASE PRESENTATION

A 57-year-old African American man presented to our institution following 6 weeks of intermittent epigastric pain. He characterized the pain as stabbing, burning, and radiating towards his back. Initial imaging conducted at an outside hospital indicated necrotizing pancreatitis, raising concerns about splenic vein thrombosis, a progressing splenic infarct, and a mass located at the tail of the pancreas. To further evaluate the mass, the patient was transferred to our facility for a potential necrosectomy and endoscopic ultrasound (EUS).

Upon arrival at our institution, the patient exhibited minimal abdominal pain. He reported symptoms of constipation, abdominal bloating, and a recent weight loss of 15 pounds. His basic laboratory tests showed stable results, with a slightly low hemoglobin level of 12.2 g/dL (reference range: 13 g/dL–17.5 g/dL), normal platelet count of 275 K/mm^3 (reference range: 150–400 K/mm^3), normal white blood cell count of 4.7 K/mm^3 (reference range: 3.8–9.9 K/mm^3), and a normal serum lipase level of 97 units/L (reference range: 10–99 units/L).

The patient's medical history was notable for congestive heart failure, chronic pancreatitis, and incomplete pancreas divisum. He endorsed consuming a pint of liquor and 5–6 cans of beer every weekend. Additionally, he reported smoking 4–5 cigarettes per day and having a history of cocaine use. His acute on chronic pancreatitis was treated with supportive care. The patient was recommended follow-up imaging after resolution of his acute inflammatory process and was discharged on acetaminophen, naproxen, and oxycodone for pain management.

After 2 weeks, the patient was readmitted due to recurring abdominal pain, nausea, persistent poor appetite, and a weight loss of 10 pounds. A contrast-enhanced computed tomography (CT) scan of the abdomen and pelvis revealed an infiltrative mass in the pancreatic tail that extended into the medial spleen, raising concerns for pancreatic adenocarcinoma or a neuroendocrine tumor (Figure 1). The scan also identified additional findings, including non-visualization of the splenic artery and narrowing of the splenic vein, likely caused by occlusion from the mass in the pancreatic tail. Magnetic resonance imaging (MRI) of the patient's abdomen exhibited a pancreatic tail process with walled off necrosis (Figure 2).

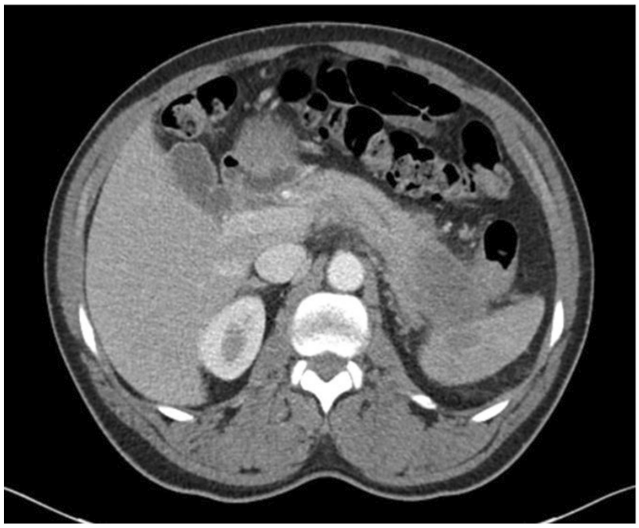


FIGURE 1 CT with IV contrast demonstrates diffusively infiltrative lesion within pancreatic tail with medial spleen involvement.

An endoscopic ultrasound (EUS) was performed to conduct a more detailed evaluation of the pancreatic tail mass (Figure 3). A fine-needle biopsy was then performed, and subsequent pathology results confirmed the presence of invasive moderately differentiated adenocarcinoma. The patient received a diagnosis of locally advanced pancreatic tail adenocarcinoma and commenced neoadjuvant chemotherapy with mFOLFIRINOX.

3 | DISCUSSION

Pancreatitis is a major risk factor for developing PDAC.[5,6] The risk of developing pancreatic cancer has been reported to be at least 50-fold greater than that of the general population among patients with hereditary pancreatitis or tropical pancreatitis.[7] While the exact causal relationship between pancreatitis and PDAC has not yet been established, Guo et al. conducted an integrated bioinformatic analysis of genetic data to identify genes and pathways associated with both.[8] These pathways included copper ion detoxification, metabolism of cysteine and methionine, hyperoxia response, digestion and absorption of protein, immune response, and transport of fatty acids. Additionally, they identified CEL (carboxyl ester lipase; responsible for cholesterol and lipid absorption) as a hub gene that may be implicated in the transformation from chronic inflammation to PDAC.

Previous studies have also shown that chronic inflammation of the pancreas may lead to oncogenic mutations.[9] In multiple studies, a significant proportion of patients with chronic pancreatitis were found to have several downregulating mutations of tumor suppressing

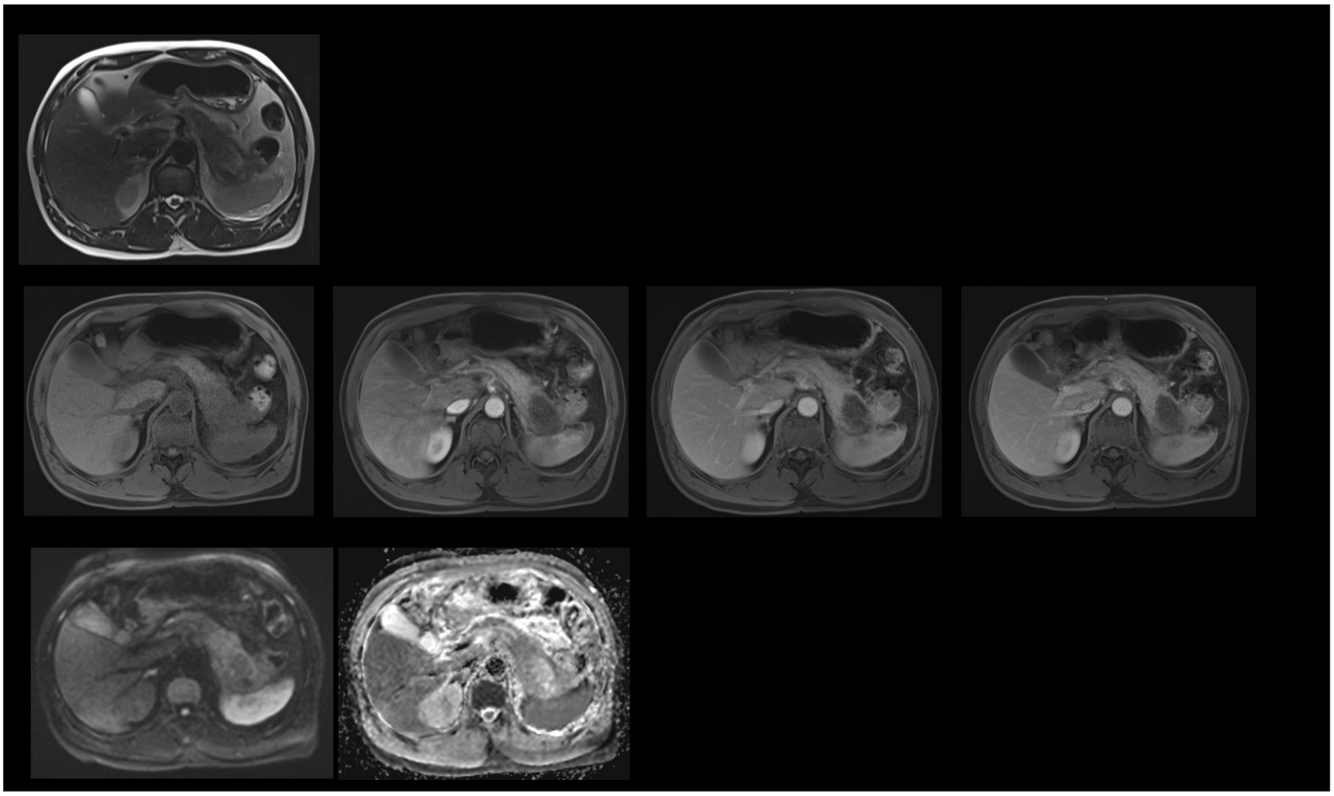
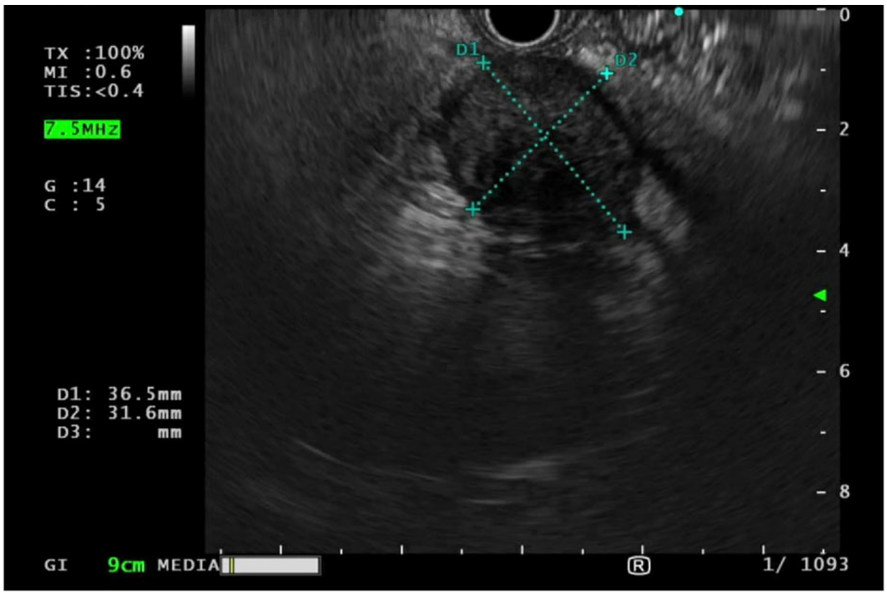


FIGURE 2 MRI of abdomen and pelvis demonstrating a predominantly T2 hyperintense fluid collection (top left image, T2 HASTE). Dynamic contrast enhanced images show progressive peripheral enhancement and central nonenhancement (middle images, T1 VIBE precontrast on the left, arterial phase, portal venous phase, and delayed phase images post IV Gadolinium contrast from left to right). There are additional areas of peripheral diffusion restriction (bottom left = ADC map, bottom right = B800 DWI). These findings are consistent with walled off necrosis.

FIGURE 3 EUS of hypoechoic pancreatic tail mass measuring at least 3.5 cm.



genes, such as p16 and p53, and upregulating mutations of oncogenic genes, such as K-ras.[5,9–12] In addition to these possible genetic factors, the strong association between chronic pancreatitis and PDAC may also be attributed to their shared environmental risk factors, such as alcohol and nicotine usage.[9]

Differences in clinical presentations, image findings, laboratory results, and biopsy results can all help

practitioners distinguish between PDAC and chronic pancreatitis. While PDAC and chronic pancreatitis have overlapping clinical presentations, the appearance of certain new signs and symptoms in a patient with pancreatitis should raise a suspicion for PDAC. In particular, new onset diabetes or worsening diabetes, pain refractory to pain relief, and unexplained weight loss may indicate a malignant transformation.[13] Development of obstructive jaundice also hints at PDAC, since malignant biliary stricture tends to present as a complete obstruction.[13] In addition, a pre-existing diagnosis of hereditary or tropical pancreatitis may warrant surveillance for pancreatic cancer.[13]

Image findings also provide helpful clues for distinguishing between PDAC and pancreatitis. CT with contrast, EUS, and MRI are among the common imaging modalities for assessing the pancreas.[14–17] On CT, PDAC is classically described as a hypoattenuating hypoenhancing pancreatic mass with ill-defined margins.[15] Other common findings include dilated upstream pancreatic duct, atrophied upstream pancreatic parenchyma, hypoenhancing distal pancreatic parenchyma, and abrupt pancreatic duct cutoff.[15,18] On fat-suppressed MRI, PDAC appears as a hypointense mass on T1-weighted sequence and a mass with variable signal intensity on T2-weighted sequence.[15,19] Both the American Gastroenterological Association and American Society for Gastrointestinal Endoscopy guidelines recommend MRI and EUS as preferred modalities for pancreas cancer screening due to their high sensitivity for the detection of pancreas lesions.[16,17]

Detecting PDAC in the setting of chronic pancreatitis can be challenging even on biopsy. A study by Fritscher-Ravens et al. demonstrated that endoscopic US-guided fine-needle aspiration has a sensitivity of 89% and a specificity of 100% for patients with a focal pancreatic mass and otherwise normal pancreatic parenchyma.[14,20] However, in the setting of chronic pancreatitis, the same study measured a sensitivity of 54% and a specificity of 100%. The markedly decreased sensitivity poses a significant limitation to prompt diagnosis of PDAC in the presence of chronic pancreatitis.

While interpreting CT image findings, practitioners should be aware of the three inflammatory processes that mimic PDAC on imaging: mass-forming chronic pancreatitis (MFP), autoimmune pancreatitis (AIP), and paraduodenal pancreatitis (PDP).[15] There are subtle features on imaging that can be used to distinguish between PDAC from these inflammatory diseases. For instance, a study by Ren et al. identified tumor size and delayed contrast enhancement as predictors in differentiating MFP from PDAC, with cutoff values of >3.285 cm (100% sensitivity and 50.9% specificity) and > 70.5 HU (84.2% sensitivity and 84.7% specificity), respectively.[21] Moreover, analyzing the textural features of the pancreatic lesion on contrast-enhanced CT scans in both arterial and portal phases presents an additional valuable tool for distinguishing between these clinical entities.[22] Other findings that favor MFP over PDAC include the presence of pseudocysts, dilated collateral branch duct in uninvolved pancreas, and low pancreatic duct-to-parenchyma ratio (<0.34).[15,23–27] The duct-penetrating sign, which is when the main pancreatic duct in the mass is seen without an obstruction, also suggests inflammation.[15,28] Accurate preoperative differentiation between MFP and PDAC is crucial, as it informs appropriate treatment choices. Considering that PDAC may necessitate resection whereas MFP is managed conservatively, precise differentiation becomes paramount for enhanced patient outcomes. Incorrectly resecting MFP could unnecessarily increase the risk of pancreatic insufficiency.

Similar to MFP, AIP can also mimic PDAC on imaging. In the case of AIP, a low-attenuation capsule-like rim of the mass is pathognomonic for Type I AIP.[15,29,30] Without this rim, Type II AIP can more closely resemble PDAC. Still, the presence of multiple pancreatic and biliary strictures and the duct penetrating sign may suggest AIP over PDAC.[15,31,32] The third PDAC mimic, PDP, appears as a mass at the pancreaticoduodenal groove.[33] A duct-penetrating sign, a lack of biliary dilatation, a thickened medial duodenal wall, and a wide distance between the duodenal lumen and the ampulla suggest PDP over PDAC.[15,34,35]

Laboratory findings are also a crucial part of detecting PDAC in the presence of acute on chronic pancreatitis. Carbohydrate antigen 19-9 (CA 19-9) is a sialylated Lewis blood group antigen commonly used as a biomarker for disease prognosis in PDAC. However, CA 19-9 levels are also elevated in nonmalignant conditions including chronic pancreatitis, cirrhosis, and obstructive jaundice.[36] A subset of patients with PDAC are Lewis antigen A and B negative (Le^{a-b-}) and do not secrete CA 19-9. An alternate biomarker combination may be CA 19-9 with MUC5AC, a mucin produced by both well-differentiated and poorly-differentiated PDAC.[14,37–39] Kaur et al reported that the combination of CA 19-9 with MUC5AC improved the sensitivity and specificity for differentiating between chronic pancreatitis and PDAC compared to CA 19-9 alone.[14,37]

Detecting PDAC in the setting of pancreatitis is challenging given their similar risk factors, clinical presentations, image findings, and laboratory findings. However, a thorough evaluation of new clinical symptoms, distinguishing imaging signs, and biomarker combinations can allow for a more prompt diagnosis of PDAC in patients with pancreatitis.

AUTHOR CONTRIBUTIONS

Shinji Rho: Investigation; methodology; writing – original draft. **Sooyoung Martin:** Resources; writing – review and editing. **Zack Nigogosyan:** Resources; writing – review and editing. **Vladimir Kushnir:** Resources; writing – review and editing. **Aaron J Mintz:** Resources; writing – review and editing. **Zishuo Ian Hu:** Conceptualization; supervision; writing – review and editing.

FUNDING INFORMATION

No funding was received to assist with the preparation of this manuscript.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

CONSENT

Written informed consent was obtained from the patient.

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How to cite this article: Rho S, Martin S, Nigogosyan Z, Kushnir V, Mintz AJ, Hu ZI. Pancreatic tail cancer in the setting of pancreatitis with a review of the literature: A case report. *Clin Case Rep*. 2023;11:e8023. doi:10.1002/ccr3.8023