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Pancreatic masses clinically diagnosed as tuberculosis: Case reports

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Abstract

Pancreatic masses are commonly encountered in clinical practice, with concern for the possibility of cancer. Tissue sampling or outright surgical resection may be offered in this setting. However, surgery has been unnecessarily performed in patients with pancreatic masses that proved to be benign. Less invasive options for pancreatic masses that may be benign like tuberculosis should thus be explored. Three adult Filipino patients less than 60 years old presented with symptomatic pancreatic masses suspected of cancer on abdominal imaging studies. Two were smokers without a history of prior tuberculosis. Without any tissue sampling, anti-tuberculosis treatment was eventually given to all three patients due to concomitant diagnoses of extrapancreatic tuberculosis. Endoscopic ultrasound documentation of post-treatment resolution of pancreatic masses was noted in all cases. In endemic regions, although clinical diagnosis of tuberculosis may be possible for pancreatic masses, empiric treatment should still be a last-line option in cases where tissue sampling cannot be done.

Keywords

Pancreatic mass, tuberculosis, clinical diagnosis, EUS

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Introduction

Adult patients with pancreatic masses are not unusually encountered in clinical practice, be it as an incidental finding or symptomatic manifestations. Regardless, a pressing concern for these cases is the possibility of malignancy such as pancreatic ductal adenocarcinoma, which may herald a poor prognosis. On the other hand, one should also keep in mind the possibility of benign pancreatic lesions that may be very treatable. For instance, tuberculosis, which has been called a "great masquerader," is still a significant problem in low-income countries and may present as a pancreatic mass, albeit uncommonly, that would warrant anti-tuberculosis therapy. Hence, the determination of the etiology of pancreatic lesions is of paramount importance. Commonly, tissue sampling via endoscopic ultrasound (EUS)-guided or percutaneous biopsy is done. Occasionally, in patients with a high degree of suspicion of cancer, outright pancreaticoduodenectomy (Whipple procedure) is done for resectable masses. However, these procedures may be cost-prohibitive in some regions. Furthermore, there have been reports of pancreaticoduodenectomy being performed on patients with pancreatic masses that turned out to be benign on histopathology.[1–3]

Here, we present three cases of patients in whom pancreatic masses were detected on workup and were subsequently treated with anti-tuberculosis medications without any evidence from pancreatic tissue sampling.

Presentation of cases

Case 1

A 55-year-old male, known hypertensive and a 10 pack-year smoker, presented with 3-year occasional mild epigastric pains unrelated to food intake, associated with episodes of intermittent jaundice. Subsequent worsening epigastric pains with radiation to the back, associated with weight loss and decreased appetite prompted consults at local clinics, with

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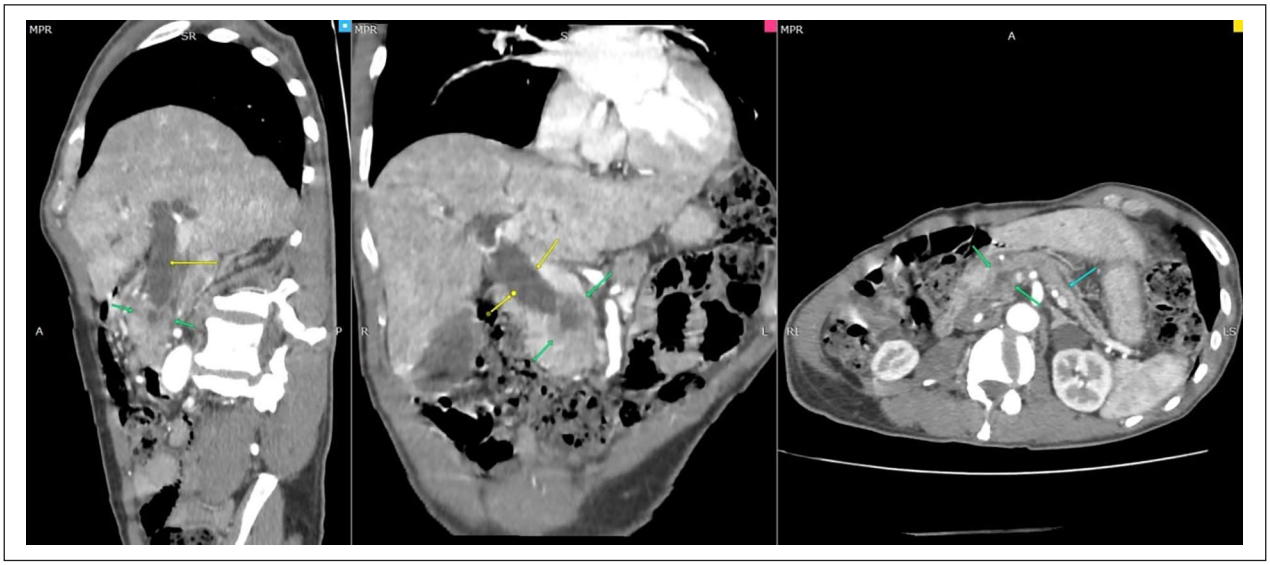

Figure 1. Arterial phase multi-planar reconstruction of initial abdominal computed tomography scans with pancreatic protocol for Case 1. The full length of the pancreas is demonstrated in these sagittal (leftmost), coronal (middle), and axial oblique (rightmost) images. Shown are the pancreatic head mass (green arrows) seen as an irregular, complex, heterogeneous focus with central non-enhancing components; dilated common bile duct (yellow arrows); and dilated pancreatic duct (cyan arrow). The pancreatic mass visualized here was no longer seen on endoscopic ultrasound done after anti-tuberculosis treatment was started.

abdominal imaging studies showing pancreatic masses. The patient eventually consulted our institution for further management. On physical examination, he was anicteric but with bitemporal wasting. The abdomen was soft, flat, and nondistended, with direct right upper quadrant-to-epigastric tenderness but without palpable masses. Pertinent laboratory results showed microcytic anemia with hemoglobin (Hgb) 85 g/L, prothrombin time with international normalized ratio (PT-INR) 1.33, alkaline phosphatase (ALP) 1032 U/L, aspartate aminotransferase (AST) 32 U/L, alanine aminotransferase (ALT) 26 U/L, total bilirubin (TB) 0.7 mg/dL, albumin (Alb) 38 g/L, and lipase 191 U/L. CA 19-9 level was normal at 19.43 U/mL. Abdominal computed tomography (CT) scan with triple contrast enhancement (Figure 1) showed an irregular, complex, heterogeneous focus with central non-enhancing components centered in the pancreatic head, appearing to be hypoenhancing relative to the rest of the pancreatic parenchyma. There was also upstream dilatation of the pancreatic duct and the rest of the hepatobiliary tree. The gallbladder was markedly distended with intraluminal sludge, whereas the liver and spleen were unremarkable. No enlarged lymph nodes were seen. Initially, EUS was planned but did not immediately push through due to institutional scheduling issues. In the interim, the patient was managed with pain medications while awaiting EUS to be done. As part of the workup for the weight loss, he was found to have bacteriologically confirmed pulmonary tuberculosis with a positive polymerase chain reaction (PCR) on sputum testing and was thus started on anti-tuberculosis treatment with World Health Organization (WHO) Category I treatment. He subsequently had good weight gain with decreased abdominal pain. EUS was finally done, which showed lobularities without honeycombing and hyperechoic foci without shadowing in the pancreatic parenchyma, with a dilated main pancreatic duct, but no masses were seen in the pancreas and ampullary area. On further follow-up, the patient had a good appetite and no longer had abdominal pain.

Case 2

A 44-year-old male, 12.5 pack-year smoker without any family history of cancer, presented with painless jaundice and weight loss in the year 2020 and was later worked up to have pancreatic mass on imaging. He was newly diagnosed with type 2 diabetes mellitus at that time and was maintained on sitagliptin/metformin. Biliary decompression was done with percutaneous transhepatic biliary drainage (PTBD) after a failed endoscopic retrograde cholangiopancreatography (ERCP) in another hospital. Around this time, as part of the workup of weight loss, the patient was also clinically diagnosed with pulmonary tuberculosis based on chest X-ray and was thus started on anti-tuberculosis medications (WHO Category I treatment). The PTBD was later inadvertently removed, with a recurrence of jaundice, and the patient subsequently consulted our institution for further management. Initial laboratory results showed ALP 253 U/L, AST 29 U/L, ALT 22 U/L, TB 5.24 mg/dL, DB 4.05 mg/dL, Alb 34 g/L, and elevated CA 19-9 at 1147.86 U/mL. Abdominal CT scan with pancreatic protocol showed an ill-defined focus in the pancreatic head and neck region, with consequent pancreatic duct and biliary ectasia (Figure 2). EUS was performed, with findings of a pancreatic head mass that was unresectable

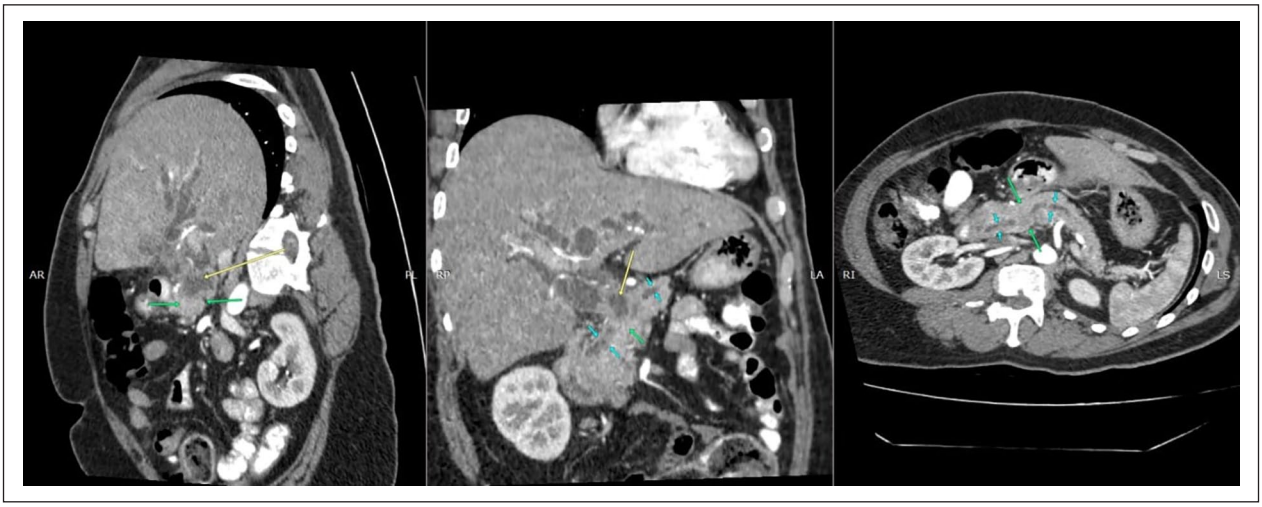

Figure 2. Initial abdominal computed tomography scan with pancreatic protocol for Case 2. Shown is an ill-defined, iso- to slightly hypoenhancing focus (green arrows) in the region of the pancreatic head and neck. This causes cutoff and upstream dilatation of the common bile duct (yellow arrows) as well as the pancreatic duct (cyan arrows). This focus appears isodense and isoenhancing to the pancreatic parenchyma in the rest of the contrast phases.

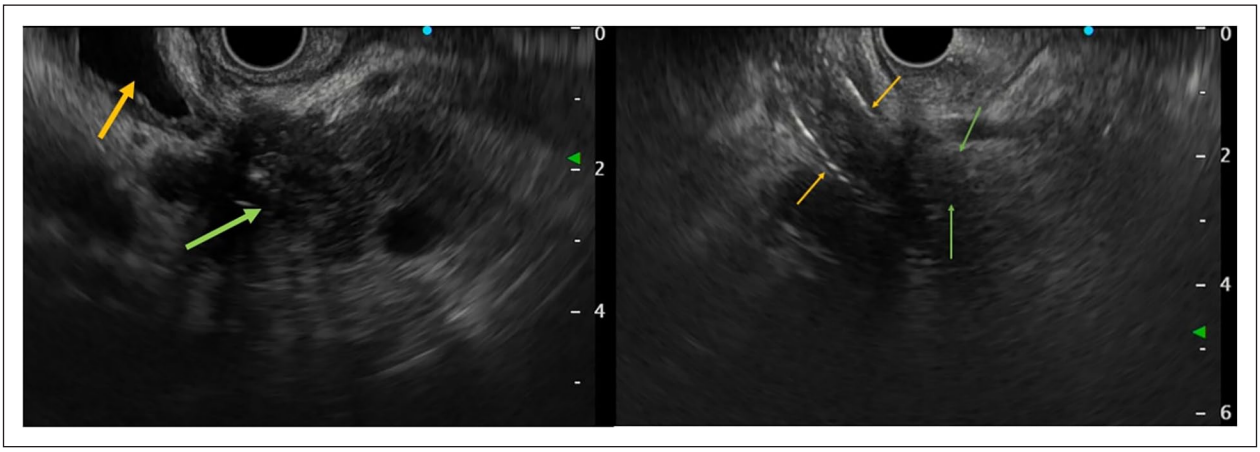

Figure 3. Endoscopic ultrasound (EUS) images for Case 2. The left image shows the initial EUS visualizing the pancreatic head mass (green arrow) and common bile duct (orange arrow) as indicated by the labels. The right image shows the EUS after anti-tuberculosis treatment, with the previously seen pancreatic head mass no longer visualized (green arrows). The metal biliary stent (orange arrows) can also be appreciated in the right image, with bile sludge within it.

based on EUS features (Figure 3). With high suspicion of malignancy, an uncovered biliary self-expanding metallic stent was inserted via ERCP as a palliative measure, and the jaundice was subsequently resolved. Fine-needle biopsy of the mass only yielded fibrocollagenous tissue without a definite neoplastic process identified. The patient continued and completed the 6-month course of anti-tuberculosis treatment, with good weight gain. A few months later, the patient was readmitted due to 10-day mild abdominal pains with febrile episodes and a recurrence of jaundice. A repeat EUS was done, which no longer showed any pancreatic mass but rather a common bile duct sludge seen as an intraductal hyperechoic focus without posterior shadowing (Figure 3). Other findings included cholecystolithiases and multiple lymphadenopathy in the paraceliac, periportal, and perihepatic areas. ERCP was then done to clear the bile ducts of sludge, with bile specimens also collected for a tuberculosis PCR test, which yielded a negative result. On follow-up, the patient had resolved jaundice, no abdominal pain, with a good appetite. Further surveillance abdominal imaging studies also showed regression of abdominal lymphadenopathy.

Case 3

A 29-year-old female with a history of pulmonary tuberculosis treatment during childhood presented with a 1-year

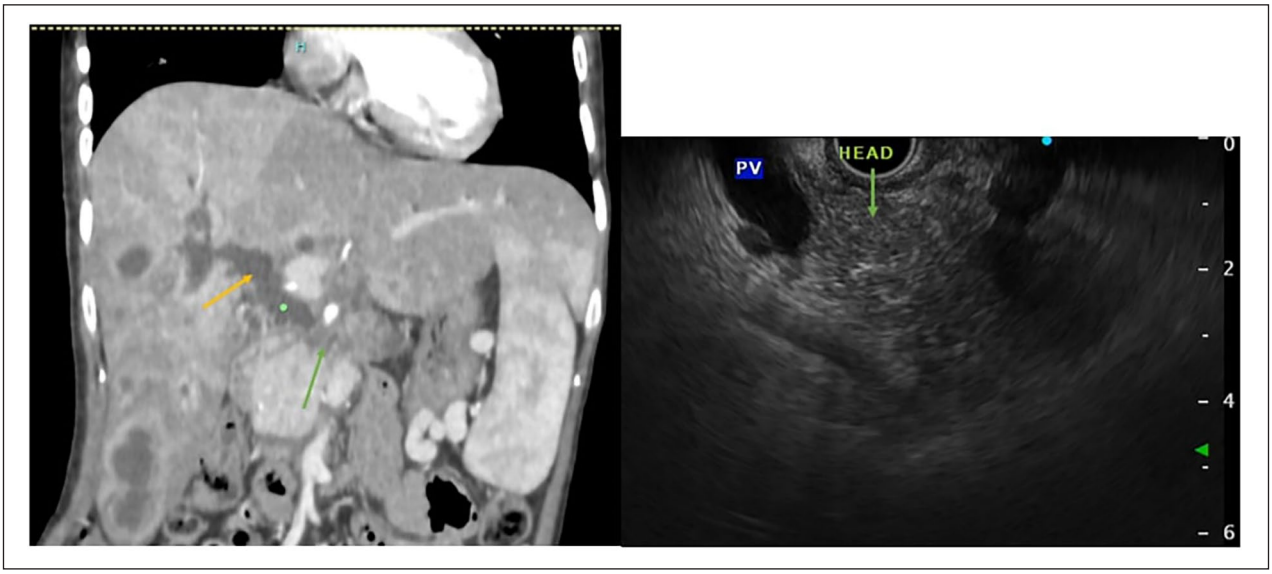

Figure 4. Imaging studies for Case 3. The pancreatic head mass (green arrow) with resultant common bile duct dilatation (yellow arrow) is shown in the coronal view of the abdominal computed tomography scan image on the left. The right image shows a normal-looking pancreatic head (green arrow) with a characteristic "salt-and-pepper" appearance without any masses visualized on endoscopic ultrasound after anti-tuberculosis treatment. The portal vein is also visualized in the right image.

history of intermittent non-radiating epigastric pains with associated fever episodes, weight loss, jaundice, tea-colored urine, and itching. Workup at a local hospital showed pancreatic and liver lesions on imaging. An eventual consult was made in our institution for further management, with an abdominal CT scan (Figure 4) showing an ill-marginated, lobulated, hypoenhancing pancreatic head mass sized $3.5 \times 5.4 \times 2.6$ cm, involving the pancreatic body as well as encasing the common hepatic artery and portal vein. An abrupt cutoff was seen at the distal common bile duct, with upstream biliary tree dilatation. PTBD was performed with subsequent resolution of jaundice and itching. Later on, the development of progressive generalized weakness with bipedal edema prompted readmission. On physical examination, she was coherent but weak-looking, with anicteric sclerae, no palpable cervical lymphadenopathy, bipedal edema without palpable inguinal lymph nodes, and soft nondistended abdomen with intact PTBD draining turbid greenish output. Pertinent laboratory results include PT-INR 2.19, ALP 638 U/L, AST 20 U/L, ALT 17 U/L, TB 1.4 mg/dL, DB 1.1 mg/dL, and elevated CA 19-9 at 138.05 U/mL. All viral hepatitis serologies were non-reactive. A repeat abdominal CT scan showed an increase in the size of the pancreatic mass but with regression of biliary ectasia (status post-PTBD). In addition, other features that may be consistent with disseminated tuberculosis were found, like thickening of the terminal ileum and cecum with ileocecal mesenteric lymph nodes, as well as pulmonary findings suggestive of possible miliary spread. A colonoscopy with ileal intubation was done, revealing multiple varisized irregular ulcers with heaped-up edges in the terminal ileum, ileocecal valve, cecum, and proximal ascending colon. Histopathology of the ileocolic ulcers showed chronic active inflammation, granulation tissue formation, and foci suspicious for granuloma, and acid-fast bacilli were detected on tissue staining via fluorescence method. The patient was then eventually started on anti-tuberculosis medications (WHO Category I treatment), with subsequent clinical improvement manifested as good weight gain, good appetite, and resolved abdominal pain. The PTBD tube was later removed, with no recurrence of jaundice. Repeat EUS already showed unremarkable findings without any note of pancreatic masses (Figure 4). Surveillance colonoscopy also showed resolution of previously seen ileocolic ulcers.

Table 1 summarizes and compares the key clinical and diagnostic features of the three patients presented in the cases above.

Discussion

Pancreatic tumors are generally classified as benign, borderline, and malignant. These masses can present with similar symptoms, making them difficult to differentiate based on clinical grounds.[4] Ductal adenocarcinoma is the most common malignancy arising from the pancreas, accounting for >90% of pancreatic cancers.[4,5] While it is currently the seventh leading cause of cancer mortality globally, it is expected to become the second leading cause of cancer death by 2030.[4,6] It carries a similar poor 5-year survival rate among high-income, middle-income, and low-income countries.[9] The dismal prognosis has a heavy implication in the workup and management of patients with pancreatic masses, highlighting

Table 1. Summary of clinical and diagnostic findings of the three cases presented.

Parameter	Case 1	Case 2	Case 3
Age	55	44	29
Smoking history	10 pack-year	12.5 pack-year	Non-smoker
Prior treatment for tuberculosis	None	None	Yes (pulmonary)
Family history of cancer	None	None	Yes (breast cancer)
CA 19-9 level	Normal	Elevated	Elevated
Acquisition of pancreatic tissue sample	None	Yes	None
Diagnosis of extrapancreatic tuberculosis	Yes	Yes	Yes
Regression/resolution of pancreatic masses with anti-tuberculosis treatment	Yes	Yes	Yes

the importance of an accurate diagnosis. Fine-needle aspiration (FNA) biopsy, whether CT-guided or EUS-guided, is usually indicated for unresectable or metastatic disease for histological confirmation. On the other hand, outright surgical resection without prior tissue diagnosis may be offered to most patients with potentially resectable pancreatic masses suspected to be malignant based on clinical and imaging findings. A potential disadvantage of this approach is the possibility of unnecessarily performing major surgical operations for pancreatic masses that may prove to be a benign entity. For instance, pancreaticoduodenectomy (Whipple procedure) has been performed on patients with suspected pancreatic cancer that turned out to be tuberculosis on histopathology.[1–3] Therefore, in endemic areas, it may be helpful to keep in mind the possibility of pancreatic tuberculosis mimicking cancer to avoid overtreatment of patients.

Cases of tuberculosis may be defined as pulmonary or extrapulmonary, with the former involving the lung parenchyma or tracheobronchial tree and the latter involving organs other than the lungs such as the pancreas.[7] The diagnostic terms for both pulmonary and extrapulmonary tuberculosis are presumptive, bacteriologically confirmed, or clinically diagnosed. Presumptive tuberculosis refers to any patient with signs and symptoms suggestive of tuberculosis, specific to the suspected site. Bacteriologically confirmed tuberculosis refers to cases where a biological specimen is positive by smear microscopy, culture, or a WHO-approved rapid diagnostic test. Clinically diagnosed tuberculosis refers to cases that do not satisfy the criteria for bacteriologically confirmed tuberculosis but have been diagnosed by a clinician with active disease based on imaging studies and histology but without laboratory confirmation.[7,8]

While tuberculosis cases are usually pulmonary, around 12.5% are extrapulmonary, with abdominal tuberculosis comprising 11%–16%. The pancreas has been considered one of the rarely affected locations by abdominal tuberculosis, with a large autopsy series on tuberculosis patients reporting pancreatic involvement in only 4.7% of cases. An important clinical significance is pancreatic tuberculosis masquerading as pancreatic mass. A systematic review by Panic et al.[9] of 166 patients diagnosed with pancreatic tuberculosis showed that most presented with weight loss, pain, and a pancreatic mass. Most of the patients underwent abdominal CT scan and ultrasound, with a substantial portion also undergoing EUS-guided FNA biopsy. More than half were also subjected to laparotomy. Identification of tuberculosis was made via histology in the majority of cases, with several cases also involving staining and culture. In a retrospective study by Song et al.[10] where 21 consecutive patients with pancreatic/peripancreatic tuberculosis who underwent EUS-FNA were reviewed, it was found that correct diagnosis with EUS-FNA was made in 76.2% of cases, thus sparing these patients from unnecessary surgery.

Some studies looked into the utility of imaging features in differentiating between pancreatic tuberculosis and malignancy, short of tissue sampling. In a study by Dong et al., it was noted that on EUS, patients with pancreatic tuberculosis had normal-sized common bile ducts, with multiple retroperitoneal lymphadenopathies seen in 75% of cases. Contrast-enhanced ultrasound showed that 3 of the 12 cases demonstrated hyperenhancement. Finally, on elastography, all pancreatic tuberculosis lesions were markedly stiffer than surrounding pancreatic parenchyma. This may help aid in the differentiation from pancreatic adenocarcinoma where the duct is almost always dilated if the lesion is located in the head and lesions may be less stiff than the pancreatic parenchyma.[11] Nonetheless, another review by Sharma et al. reported that there are no distinctive features of pancreatic tuberculosis on CT scans that differentiate it from carcinoma.[12] A case series by Rana et al.[13] suggested that vascular invasion does not distinguish pancreatic tuberculosis from malignancy. From the findings in these studies, it would seem that distinguishing pancreatic tuberculosis from pancreatic cancer based on clinical grounds and imaging alone is not straightforward. Therefore, tissue sampling still appears to be invaluable in arriving at an accurate diagnosis and eventually leading to appropriate treatment.

The three cases presented all had symptomatic patients in whom pancreatic masses were detected, with suspicion of malignancy. Two of the patients were less than 50 years of age; it should be noted that pancreatic cancer is typically a disease of the elderly, with 90% of newly diagnosed patients

over age 55 with a median age at diagnosis of 70 years. All three of them were also eventually diagnosed with tuberculosis in an extrapancreatic organ, whether clinically or bacteriologically, and treated accordingly. It should be noted though that cases of isolated pancreatic tuberculosis have been reported.[3,14] Although anti-tuberculosis treatment was not directly intended as therapy for the pancreatic lesions in all three cases, the presented patients all had clinical improvement, with documentation of resolution of the pancreatic masses on surveillance imaging studies. Hence, the relatively young age, the presence of extrapancreatic tuberculosis, and good response to anti-tuberculosis treatment served as the basis for the presumed diagnosis of pancreatic tuberculosis despite the absence of direct histologic or microbiological confirmation. While these cases demonstrate that clinical diagnosis of pancreatic masses as tuberculosis may be possible, foregoing tissue sampling and proceeding with empiric treatment still cannot be routinely recommended at this time given the potential cases of missed or delayed diagnoses of true pancreatic malignancies that would undoubtedly be detrimental.

Conclusion

While tissue biopsy or outright surgery for resectable lesions may be planned for patients with solid pancreatic masses wherein malignancy is highly suspected, the possibility of tuberculosis should be kept in mind in endemic regions. Although tissue sampling for definitive diagnostic testing is still preferably pursued, empiric anti-tuberculosis treatment with clinical and imaging surveillance may be an alternative management option, with the benefit of potentially avoiding overtreatment such as unnecessary surgical resection. However, to minimize the risk of missed or delayed diagnosis of actual pancreatic malignancies, this approach may only be justified as a last-line measure, particularly for younger patients with concomitant evidence of tuberculosis in other organs, as well as in areas where interventions like EUS may be unavailable or inaccessible.

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Author contributions

V.C. conceptualized the research project, recorded all pertinent medical data, obtained pertinent radiologic images, wrote the manuscript, and proofread the manuscript. J.B., A.O., and M.T. III made minor additions to the discussion and approved the final submitted manuscript. R.M. guided the conceptualization of the report, supervised manuscript writing, and approved the final submitted manuscript.

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Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

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