Isolated pancreatic tuberculosis with duodenal fistula: A case report

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Abstract

Significance: Isolated pancreatic tuberculosis (TB) is an uncommon form of gastrointestinal TB even in endemic countries.[1] It is reported in less than 5% of cases and occurs usually in disseminated TB and immunocompromised conditions. Symptoms include abdominal pain, fever, and weight loss. Its appearance on radiologic imaging can mimic pancreatic malignancy, becoming a diagnostic challenge. In this case report, we present a case of isolated pancreatic TB presenting as pancreatic mass in imaging studies, mimicking as malignancy. **Case Presentation:** Our patient is a 56-year-old Filipino male, immunocompetent, and without known comorbidities. He presented with fever and chills, epigastric pain, poor appetite, and weight loss, and epigastric tenderness on examination. **Management:** A contrast enhanced CT scan and MRI of the abdomen showed pancreatic mass with prominent lymph nodes. An EUS-guided FNA of the said mass revealed a pancreatic cystic mass at the uncinate process with noted fistulous tract to the duodenum. A re-biopsy was done at the fistulous tract in the duodenum to collect more samples for TB work-up for a more definitive diagnosis. He was then managed as isolated pancreatic TB with fistulous tract formation to the duodenum and was treated successfully with anti-tuberculous drugs. On follow up after three months, there was weight gain, resolution of fever and abdominal pain. **Recommendation:** Pancreatic tuberculosis presenting as pancreatic mass may mimic malignancy leading to misdiagnosis. Providing enough tissue samples to establish TB is warranted to guide us in managing these patients and avoid unnecessary surgery.

Keywords: case report, pancreatic tuberculosis, abdominal tuberculosis, pancreatic mass, endoscopic ultrasound

Tuberculosis is a major health concern worldwide with increasing incidence in developing countries. It usually affects the lungs but may also be found in other organ systems such as gastrointestinal tract, commonly the ileum and cecum. Intraabdominally, it can also affect the peritoneum, liver, spleen, lymph nodes, and rarely, the pancreas, especially in its isolation. Because pancreatic involvement is rare, the course of the disease is not very well studied yet. Only several case reports are being reviewed.[2] Effective treatment is a challenge because pancreatic TB is mimicked by malignancy, hence a definitive diagnosis through image-guided biopsy must be done to avoid unnecessary surgical intervention. We report a case of pancreatic tuberculosis in an immunocompetent patient diagnosed through EUS-guided biopsy and was subsequently started with anti-tuberculosis regimen.

Case Report

Our patient is J.R., a 56-year-old Filipino male, immunocompetent, presented with low back pain, non-radiating, vague in character, accompanied by fever and chills with a maximum temperature of 39°C occurring anytime of the day. Initial consideration during this time was recurrent nephrolithiasis, hence, a CT stonogram

and other work-up were initially done (see **Table 1**). He eventually experienced epigastric pain, non-radiating, accompanied with bloating, early satiety, and postprandial fullness. He also had poor appetite and unquantified weight loss. There were no cough, colds, urinary symptoms, nausea and vomiting, or changes in bowel movement.

Our patient is hypertensive. He previously underwent extracorporeal shock wave lithotripsy of the right kidney two years prior to the presentation of symptoms. He has no known allergies, no history or exposure to pulmonary TB, no history of hepatitis or pancreatitis. He has no vices, no recent travel, and works at a clothing store. He denies illicit drug use. He has no family history of gastrointestinal diseases or malignancy.

Our patient came in conscious, coherent, and not in distress. Vital signs were normal except for fever at 39°C. On physical examination, there was no jaundice, and sclerae were anicteric. There was epigastric tenderness on palpation. The rest of the systems were unremarkable.

Significant work-up done prior to this consult are shown in **Table 1**. He was advised to undergo EUS with biopsy but opted to seek consult at our institution. Tests done at our institution are shown in **Table 2.**

Table 1. Initial diagnostic work-up prior to current consult

Test	Result
CT sonogram	• No nephrolithiasis, the rest of the urinary system normal • Enlarged and inhomogenous pancreatic head with ill-defined borders (maximum diameter of 6.5 cm) with adjacent fat stranding and lymphadenopathies • Lumbar spine showed degenerative changes
Triphasic whole abdominal CT scan	• Macrocystic multiseptated cystic foci or cluster of cysts in the pancreatic head (conglomerate size of 7.8 x 8.2 x 5.4 cm; largest cystic focus in this cluster measures approximately 3.2 x 3.5 cm). The cystic foci partially encased but appears not to invade the portal vein. Primary neoplasm considered, such as a mucinous cystadenoma, an infectious process, although less likely, not entirely ruled out. With associated findings of peripancreatic fat stranding. • Hepatomegaly with multiple small cysts in both lobes • Rest of GI tract unremarkable • Multiple paraaortic lymphadenopathies with central areas of necrosis (largest at 2.1 x 1.3 cm)
Chest radiograph	Clear lungs
Serum CA 19-9	Normal

Table 2. Tests done at admitting institution

Test	Result
Magnetic resonance cholangiopancreatography; (MRCP) (see **Figures 1-3**)	Lobulated T2 hyperintense lesion measuring 3.2 x 3.6 cm arising in the head and uncinate process of the pancreas with associated necrotic retroperitoneal and periportal lymphadenopathies for which it may represent a tuberculous infection. The body and tail of the pancreas are normal with non-dilated pancreatic duct. Hepatosplenomegaly with liver span of 17.3 cm and splenic index of 816. Small hepatic and renal cysts.
EUS with FNA biopsy (see **Figure 4**)	Pancreatic cystic mass lesion, uncinate process, with perihepatic and celiac lymph nodes, sinus tract and/or fistulous communication to the descending duodenum.
CBC	Microcytic hypochromic anemia with hemoglobin at 9.5 g/dL, leukocytosis at 15,080 mm^3 (neutrophils 49%, lymphocytes 3%, stabs 40%) and platelet 340/mm^3.
Chemistries	Elevated LDH at 373 U/L, normal lipase and amylase
Blood cultures, two sites	Negative

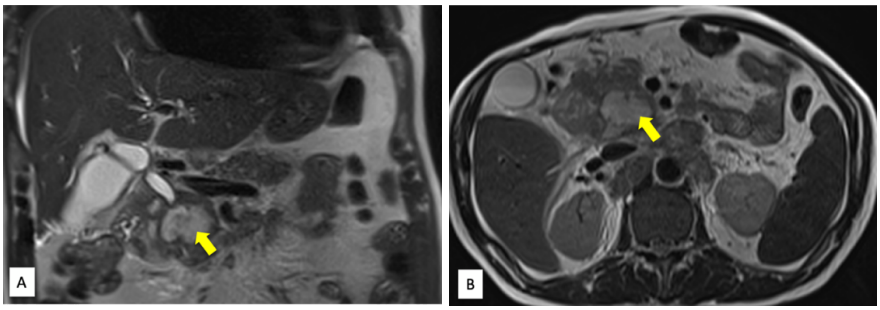

Figure 1. MRCP. (**A**) coronal and (**B**) axial views showing lobulated T2 hyperintense lesion measuring 3.2 x 3.6 cm arising in the head and uncinate process of the pancreas. It exhibits some degree of restricted diffusion as well as mild wall enhancement on post-contrast infusion.

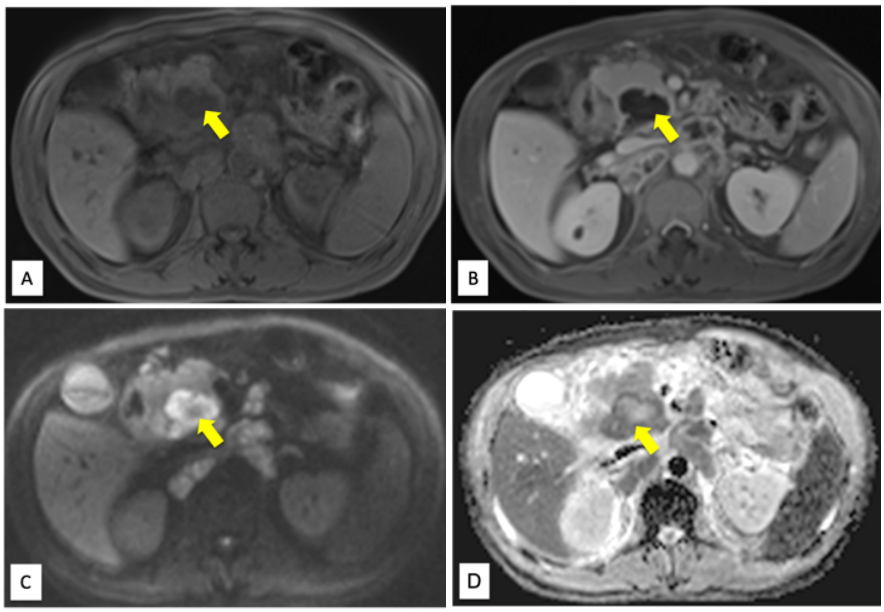

Figure 2. MRCP axial views. (**A**) Pre-contrast, (**B**) Post-contrast. The lesion shows peripheral enhancement after contrast administration. It appears bright on DWI (**C**) and dark on ADC (**D**) images reflective of restricted diffusion.

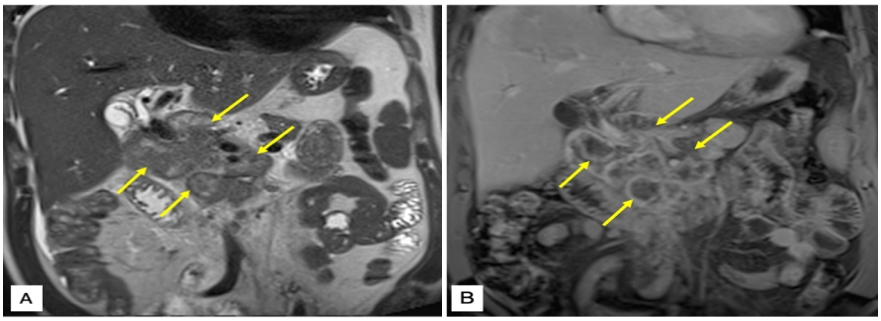

Figure 3. MRCP coronal views. (**A**) T2-weighted image. Multiple enlarged periportal and retroperitoneal lymph nodes showing peripheral enhancement and central area non-enhancing areas reflective of necrosis on post-contrast image (**B**).

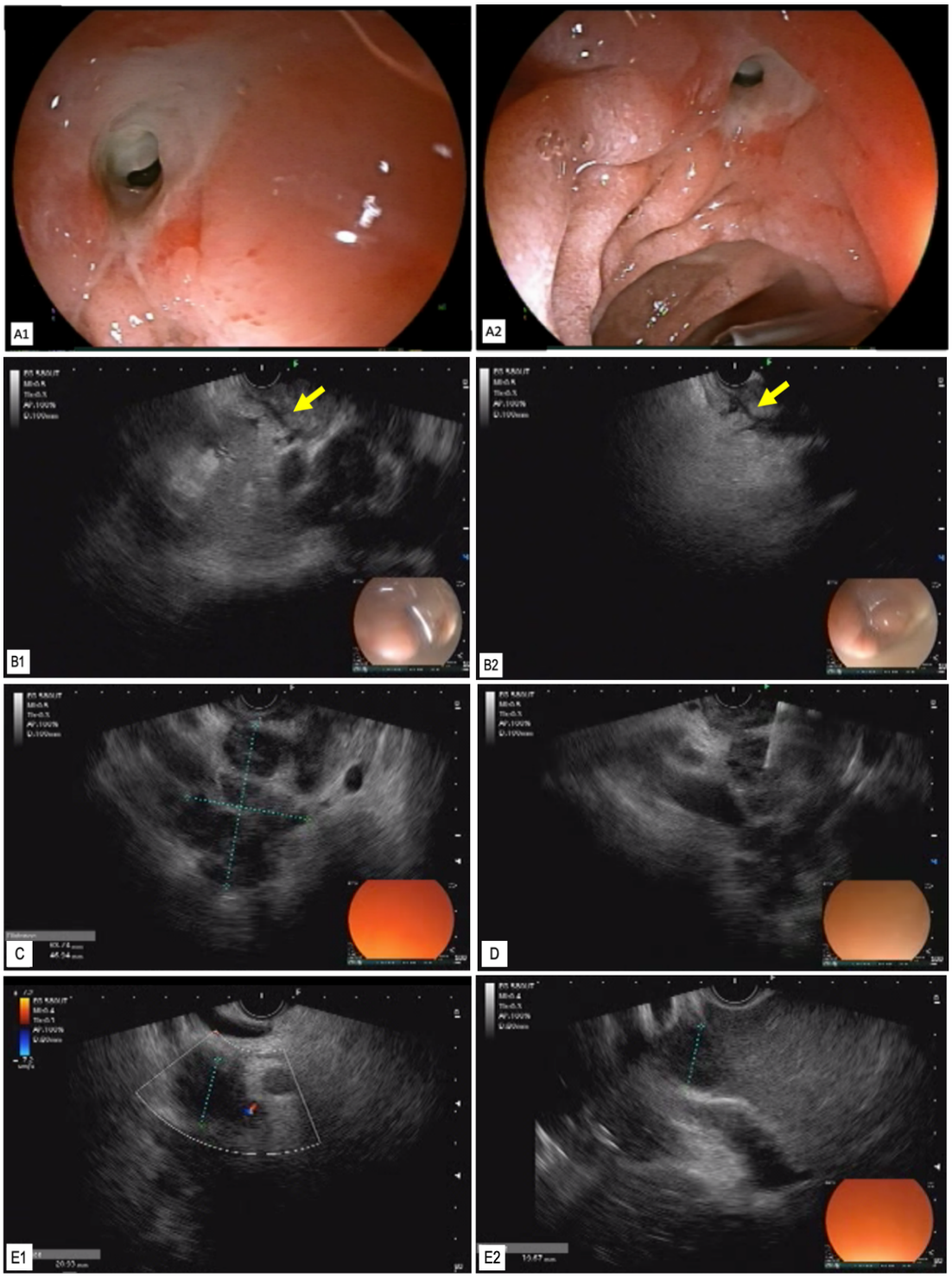

Figure 4. Endoscopic ultrasound of the pancreatic mass. **A1** & **A2**: Duodenal fistula opening seen endoscopically seems continuous with the pancreatic lesion at the uncinate process (**B1** & **B2**). **C**: Pancreatic cystic mass lesion in the uncinate process, measuring 5.6 cm in its widest diameter on EUS where (**D**) fine needle aspiration biopsy was carried out from the large cystic lesion, obtaining bloody specimen and purulent materials. **E1**: Celiac and perihepatic lymph nodes (**E2**) were also appreciated, with consistency similar to the cystic lesion of the pancreas.

Our patient was initially started on ertapenem, a broad spectrum intravenous antibiotic. Biopsy result of the pancreas revealed a chronic granulomatous inflammation with suppuration (**Figure 5**). Due to a high index of suspicion for TB, he was then started on anti-tuberculous regimen, and further evaluation for TB was done. However, due to inadequate sampling for the latter, an esophagogastroduodenoscoy (EGD) was done to re-collect specimen samples. EGD noted less amount of pus at the duodenal fistula. Additional biopsy specimens were taken at the edges and within the fistula and sent for Mycobacterium tuberculosis-polymerase chain reaction (MTB-PCR) studies and acid fast bacilli (AFB) stain. MTB-PCR result was positive, and the stain showed presence of AFB. On the third day after the initiation of anti-tuberculous therapy the patient was afebrile. He was sent home with noted improvement of symptoms and advised to continue anti-tuberculosis medications.

On follow up three months later, there was noted weight gain, resolution of fever and abdominal pain. Completion of anti-tuberculosis regimen for six months was advised.

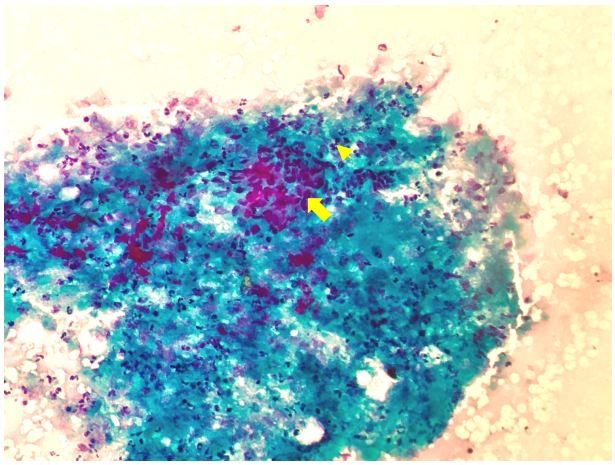

Figure 5. Histopathology of the pancreatic specimen collected shows small and large clusters of epithelioid histiocytes (arrow) admixed with polymorphous population of lymphocytes. The background shows many neutrophils (arrowhead), and necrotic debris.

Discussion

Tuberculosis is common worldwide with a higher incidence in developing countries and increasing incidence in developed countries, especially in population co-infected with HIV. The WHO estimated it to affect 10.4 million people and approximately 1.7 million deaths occurring worldwide in 2015.[3] It has a highest incidence in Asia, South America, Eastern Europe, and areas of sub-Saharan African countries.[4] It commonly affects the lungs, but may also be found in other organ systems, commonly the lymphatic, genitourinary, bone, and central nervous system. Abdominal TB, which includes the gastrointestinal tract, peritoneum, and visceral organs, may also be involved and is the sixth most frequent form of extrapulmonary TB, with peritoneal TB being the most common presentation. Along the gastrointestinal tract, the ileocecum may be more frequently involved.[5] The pancreas can also be involved; however, it is found to be rare even in highly prevalent areas. In the Philippines, TB is considered one of the major health problems. It is estimated by WHO to have 260,000 incident cases in the country in 2011.[6]

Pancreatic tuberculosis is first described by Auerbach in 1994.[7] It is extremely rare that the study of this disease entity is only found in case reports and small case studies. It is reported in less than 5% of cases occurring usually in disseminated TB and immunocompromised conditions. Furthermore, isolated pancreatic TB is even rarer with limited case reports. Only one case of pancreatic TB with duodenal fistula was reported.[8] It is hypothesized that pancreatic enzymes, including lipases and deoxyribunucleases, protect the pancreas from the colonization and proliferation of Mycobacterium tuberculosis, making the pancreas resistant to the pathogen, hence, contributing to its rarity.[4,9] Several mechanisms explain the pathophysiology of pancreatic involvement by TB – by direct extension from adjacent organs or lymph nodes, lymphatic or hematogenous dissemination, or after reactivation from a previous abdominal tuberculosis.[1,2,9] There are three forms of pancreatic TB: (1) as a part of miliary tuberculosis, a more common type; (2) spread to the pancreas from retroperitoneal lymph nodes; and (3) localized pancreatic tuberculosis, which is mostly due to M. tuberculosis secondary to primary tubercular infection of the intestinal tract.[9]

Pancreatic tuberculosis mimics pancreatic malignancy, adding a clinical dilemma to its diagnosis. Its diagnosis remains a challenge as it is rare, and its clinical presentation is slow and insidious with non-specific signs and symptoms. Symptoms may include abdominal pain, fever and malaise, night sweats, anorexia, backache, and

weight loss. Among these, abdominal pain and fever are the more common presenting symptoms. It may also present as abdominal mass and jaundice.[10] Our patient is a Filipino male who presented with back pain, abdominal pain, fever, and weight loss. The finding of pancreatic mass in initial imaging studies was suspect of a possible malignant process. Further work-up was advised.

There is no pathognomonic radiologic finding for pancreatic TB. In most reports, the pancreatic head is the most commonly involved region and pancreatic lymphadenopathies may also be seen. Imaging may reveal pancreatic masses, cystic lesions, abscesses and, in most of the cases, pancreatic carcinoma. Ultrasonographic findings may show mass with multiple hypoechoic cystic components, while CT findings include multiple hypodense cystic components with irregular borders, diffuse enlargement of the pancreas or enlarged peripancreatic lymph nodes. Magnetic resonance imaging (MRI) findings of focal pancreatic TB include a sharply delineated mass showing heterogenous enhancement where the lesions are hypointense on fat-suppressed T1-weighted images and as hypo/hyper intense on T2-weighted images.[11]

Because pancreatic TB can mimic pancreatic carcinoma and because of lack of pathognomonic findings for pancreatic TB, most cases are diagnosed after surgery.[12] Endoscopic ultrasound (EUS)-guided fine needle aspiration cytology appears to be the preferred diagnostic method for pancreatic TB, allowing sampling of pancreatic lesions for histologic and bacteriologic confirmation. Linear EUS allows high-resolution imaging that can differentiate pancreatic and peripancreatic masses and locations of lymphadenopathies. EUS-FNA has an accuracy of 76% to 95% accuracy for diagnosis of pancreatic cancer and 46% for focal inflammation.[13] In a study done by Mallery et al., they concluded that CT/US-guided sampling and surgical biopsies can also be performed and is as accurate as EUS-guided tissue sampling.[14] Our patient underwent EUS-FNA biopsy of the pancreatic mass at the uncinate process. There was also noted fistulous tract formation to the duodenum.

Histologic and microscopic features that are suggestive of TB includes the presence of caseating granulomas and presence of AFB on Ziehl Neelsen staining. Caseating granuloma is seen in 75-100% of cases, and AFB are identified in 20-40% of cases. Cultures for mycobacteria is used to confirm the diagnosis, however it takes six weeks for the bacteria to grow.[2] Polymerase chain reaction (PCR) assay is diagnostic and has been increasingly used in most patients with Mycobacterium tuberculosis with a sensitivity of 64%.[12] A TB-PCR assay in combination with histologic and microbiologic findings may be helpful in diagnosing pancreatic TB. However, drug susceptibility cannot be determined with PCR assay alone, a standard culture still needs to be performed.[9,12] The pancreatic mass biopsy samples collected in our case was sent for histopathology revealing clusters of epithelioid histiocytes admixed with lymphocytes. However, there was not enough samples for further TB work-up, hence, he underwent EGD and samples were collected from the fistulous tract opening in the duodenum. These were sent for AFB and MTB-PCR, both showing positive for TB.

The management for pancreatic TB is through medical management. Treatment is the same as the conventional pulmonary and extrapulmonary TB anti-tuberculous therapy (combination of rifampicin, isoniazid, pyrazinamide, and ethambutol). Treatment duration varies from six to twelve months depending on severity. However, the directly observed treatment short course (DOTS) recommend only six months of therapy for abdominal tuberculosis even in severe forms.[9,12] Most of these patients show symptomatic improvement after two months of treatment. According to Ray et. al., if a bacteriologic diagnosis cannot be made, an empiric treatment with anti-tuberculous therapy may be given based on clinical and imaging findings, most especially in young patients who reside in places endemic for TB. It is important to take note that an alternative diagnosis should be made if there is no improvement, or if there is deterioration after six weeks of treatment.[2] Our patient was noted to have improved on follow up after three months of anti-tuberculous regimen, with reports of weight gain, lysis of fever and resolution of abdominal pain. He was advised six months completion of anti-tuberculous regimen.

Conclusion

Isolated pancreatic TB is a rare clinical entity. The diagnosis of a pancreatic TB is challenging due to nonspecific symptoms as well as imaging findings that can mimic pancreatic malignancy. EUS-FNA with biopsy is the preferred method to aid in differentiating a benign

mass from a neoplasm. Sample specimens should be submitted for cytology, AFB staining, cultures and PCR assay for a better diagnostic yield. Most patients respond well to the anti-tuberculous therapy and achieve complete cure after completing the regimen.

It is therefore important to have a high index of suspicion especially in patients residing in endemic places for TB, like in developing countries. Furthermore, it is important to review imaging studies to prevent unnecessary surgical intervention due to high morbidity. Histopathologic with microscopic examination of a pancreatic mass through EUS-guided biopsy is recommended to establish the diagnosis. However, if collecting a specimen fails, it is advisable to do another attempt to collect a specimen sample because this will aid in the appropriate management of these patients.

Conflicts of Interest

The authors declare no conflicts of interest.

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