# PANCREATIC TUBERCULOSIS PRESENTING AS PANCREATIC MASS IN A YOUNG IMMUNOCOMPETENT PATIENT: A CASE REPORT

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Significance: Pancreatic tuberculosis is a rare clinical condition, even in endemic regions. Definitive diagnosis rests on histolopathological and bacteriological evidence of tuberculosis, either through image-guided interventions or surgery thus, making its diagnosis and management a challenge. We report here an unusual case of pancreatic tuberculosis in a young immunocompetent patient who presented with a pancreatic mass.
Clinical Presentation: A 24-year-old, Filipino gentleman with no known immunodeficiency and no history of prior tuberculosis, came in due to 3-week history of non-specific abdominal pain and a pancreatic mass noted upon work-up. Physical examination was unremarkable.
Management: Abdominal imaging revealed a heterogeneously enhancing, predominantly cystic mass in the pancreatic head and body, with encasement of common hepatic artery and multiple lymphadenopathies. Exploratory laparotomy with gastrojejunostomy, lymph node biopsy, pancreatic mass aspirate and drainage was performed with noted caseation intra-operatively. Histopathologic analysis revealed chronic granulomatous inflammation with caseation necrosis and Langhans' type multinucleated giant cells. Mycobacterium tuberculosis was detected in PCR assay and AFB staining of pancreatic mass aspirate. Antimycobacterial therapy was given for 9 months, which provided subsequent symptom relief and significant regression of pancreatic mass and lymphadenopathies.
Recommendation: There should be a growing awareness of pancreatic TB as an important differential diagnosis of pancreatic malignancy, especially in endemic areas for TB in younger patients. Although presenting and radiological features are non-specific, and without evidence of tuberculosis elsewhere, high index of suspicion is warranted to make an appropriate diagnostic approach and avoid unnecessary surgery.

Keywords: *case report, isolated pancreatic tuberculosis, pancreatic TB, pancreatic mass*

# Isolated pancreatic tuberculosis presenting as pancreatic mass in a young immunocompetent patient: A Case Report

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### *Introduction*

Tuberculosis (TB) caused by Mycobacterium tuberculosis is a serious health problem worldwide, occuring in nearly 9.7 million people and claims about 2 million lives each year worldwide[1], with highest incidence among developing countries, such as the Philippines. Although the lung is most commonly affected, extrapulmonary TB accounts for one-fifth of cases in immunocompetent hosts. Pancreatic involvement is reported in less than 5% of cases and it often occurs in the setting of disseminated TB and immunodeficiency states.[2] Isolated tuberculosis of the pancreas, in the absence of involvement of any other organ or previously identified TB, nonetheless, is an extremely rare condition with most published literature in the form of case reports or small case series.[3] Clinical features are quite variable and non-specific, often mimicking characteristics of a pancreatic malignancy and subsequently misdiagnosed.[4] Radiographic imaging studies of the abdomen can suggest pancreatic tuberculosis, but cytological or histological confirmation is required to establish the diagnosis,[5] either through percutaneous ultrasonography or computed tomography (CT)-guided biopsy, open or laparoscopic surgical biopsy or Endoscopic ultrasonography (EUS) biopsy[2]. This paper presents a case of an isolated pancreatic tuberculosis in a 24-year-old male patient who presented with a pancreatic mass encasing the common hepatic artery.

### *Case presentation*

A 24-year-old, Filipino gentleman was admitted at our institution under surgery service due to abdominal mass on imaging studies. He had 3 weeks history of vague abdominal pain, prompting consult with a local physician. He had no previous history of steroids or immunosuppressant medication intake. There was no fever, nausea, vomiting, anorexia, weight loss, jaundice nor any urinary or bowel complaints. Initial laboratory tests included CBC, urinalysis, serum electrolytes, liver and pancreatic enzymes were unremarkable but abdominal ultrasound showed a hypoechoic mass lesion at the epigastric/pancreatic region, measuring about 4.01 x 2.93 x 2.75cm with enlarged upper abdominal lymph nodes. HIV screen was done with negative results. An intravenous (IV) contrast enhanced computed tomography (CT) was then performed, which revealed a partially well-defined epigastric mass lesion, measuring 5.1 x 4.2 x 2.4cm, resting on the upper aspect of the head and body of the pancreas with no continuous cleavage, showing a faint hypodense CT texture with heterogenous enhancement and multiple central non-enhancing areas. Multiple enlarged lymph nodes were also noted, showing mainly similar pattern of enhancement thus, a pancreatic neoplasm versus other retroperitoneal neoplastic lesion with upper abdominal nodal metastasis was considered at that time. Patient sought consult with another physician, wherein a triple phase contrast enhanced whole abdominal CT scan was again requested. Repeat scan described a fairly-defined, predominantly cystic mass in the pancreatic head and body region, measuring approximately 5.1 x 5.6 x 6.1cm with minimal perilesional fat stranding and multiple lymphadenopathies (Figure 1). Posteriorly, it was noted to encase the common hepatic artery from its take-

off site from the celiac trunk up to its left hepatic artery and was intimately related to the splenic artery, with no significant encasement of the latter. The right hepatic artery, superior mesenteric artery and vein, splenic vein, and portal vein were not involved, as well as the pancreatic nor the common bile duct (Figure 2).

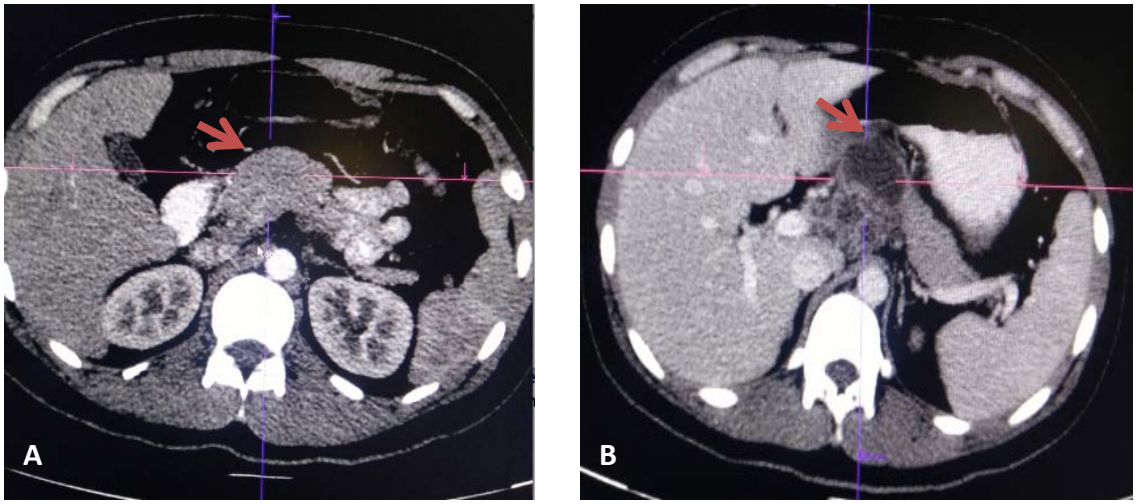



**Figure 1.** Contrast enhanced abdominal computed tomography scan showing a fairly-defined, predominantly cystic mass in the pancreatic head and body region (red arrow) in arterial phase **(A)** and venous phase **(B),** with minimal perilesional fat stranding and multiple lymphadenopathies.

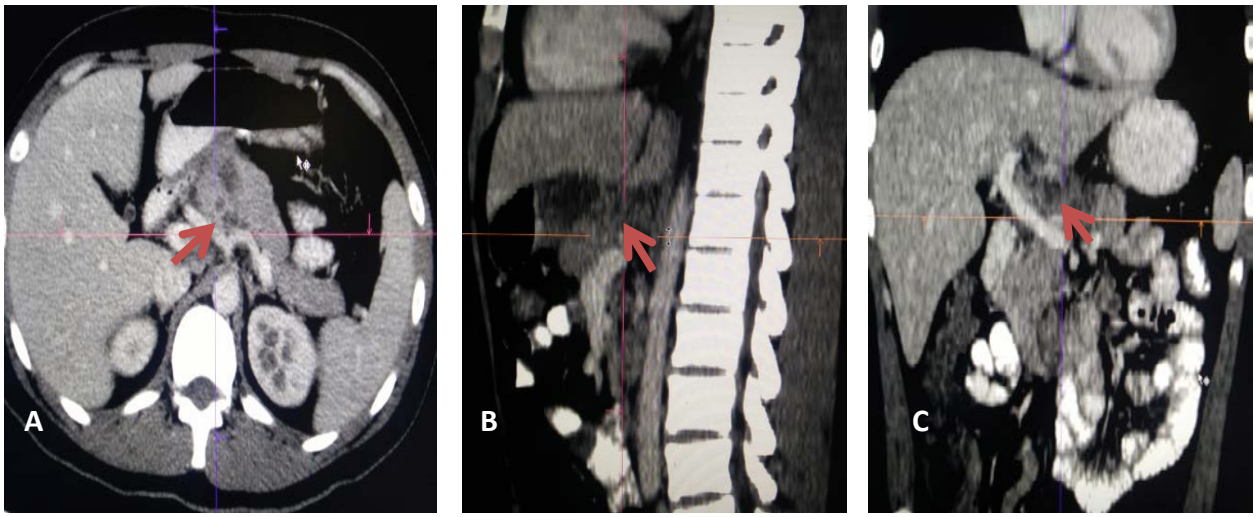
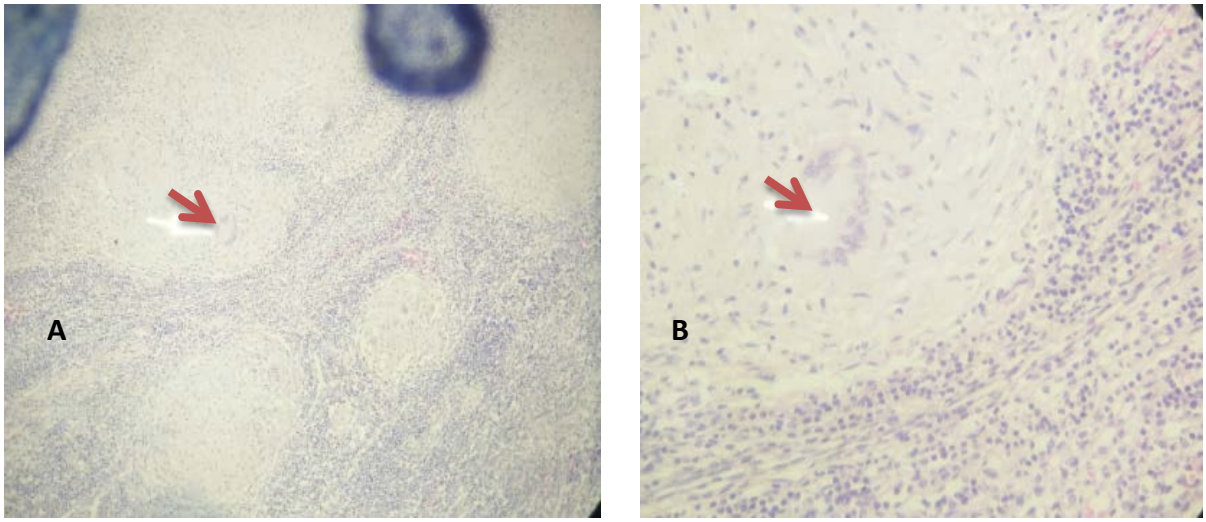



**Figure 2.** Abdominal computed tomography scan showing a fairly-defined, predominantly cystic mass mass in the pancreatic head and body region with encasement of common hepatic artery in axial **(A)**, sagittal **(B)** and coronal view **(C)**.

Patient was a non-smoker, with no significant alcohol intake or history of illicit drug use. He no prior illnesses, such as previous gallstone disease or tuberculosis, nor any previous surgeries or hospitalization. There was also no history of tuberculosis in the family nor any malignancy. Physical examination findings were generally unremarkable upon admission, and pre-operative laboratory tests were within normal limits, including liver function tests, pancreatic enzymes and tumor marker CA 19-9 of 6.59 U/mL (reference range: 0-37.0 U/mL). Chest radiography also did not show any abnormality. Because of suspicion for a pancreatic malignancy, patient was scheduled for a Whipples procedure. However intraoperatively, patient was noted to have a mass at the pancreatic body encasing the celiac trunk, compressing on the gastric antrum with enlarged para-aortic and retroduodenal lymph nodes with caseation. Rest of the

abdomen showed no obvious pathology, there were no tubercles in the peritoneum or omentum and the small and large bowel appeared normal. Pancreatic tuberculosis was then considered hence, an exploratory laparotomy with gastrojejunostomy, lymph node biopsy, pancreatic mass aspirate and drainage was performed instead, and patient was subsequently referred to a gastroenterologist. Biopsy results revealed presence of chronic granulomatous inflammation with caseation necrosis and Langhans' type multinucleated giant cells (Figure 3).

**Figure 3.** Histopathology sections examined under low power (A) and high power field (B) revealed presence of chronic granulomatous inflammation with caseation necrosis and Langhans' type multinucleated giant cells (white arrow).




Acid fast bacilli was detected (AFB +1) on Ziehl-Nielsen staining of the pancreatic mass aspirate and presence of Mycobacterium tuberculosis complex through MTB PCR assay was confirmed. Patient was immediately started on anti-mycobacterial fixed dose combination, consisting of Rifampicin 450 mg (R), Isoniazid (H) 300 mg, Ethambutol (E) 800mg and Pyrizinamide (Z) 1500mg; 4 tablets once a day with Vitamin B complex for 2 months. Upon start of treatment, patient had dyspepsia while taking anti-mycobacterial medications thus, was treated with proton pump inhibitor (PPI) and prokinetics. This is an expected side-effect of the medication seen in 10.3% of cases from studies[6]. Repeat CT with Pancreatic Protocol revealed reduction in the size of the pancreatic mass (2.3 x 4.2 x 3.8cm from 5.1 x 5.6 x 6.1cm) and retroperitoneal lymph nodes. Clinically, there was improvement of patient's appetite and weight. Quadruple anti-TB medications were then shifted to Isoniazid and Rifampicin for the next 7 months. He had hyperuricemia with occasional joint pains during his sixth month of treatment, for which he was given Feboxustat. Patient's liver and kidney status were monitored through measurement of serum ALT and Creatinine levels which remained stable throughout treatment and patient subsequently reported significant symptom relief. Repeat contrast enhanced CT scans during the course of antimycobacterial therapy showed interval regression of lymphadenopathies and significant decrease in size of previously noted pancreatic mass, now only measuring 1.8 x 1.6 x 1.7cm with good cleavage planes with the adjacent stomach and liver, though still encasing the common hepatic artery (Figure 4).

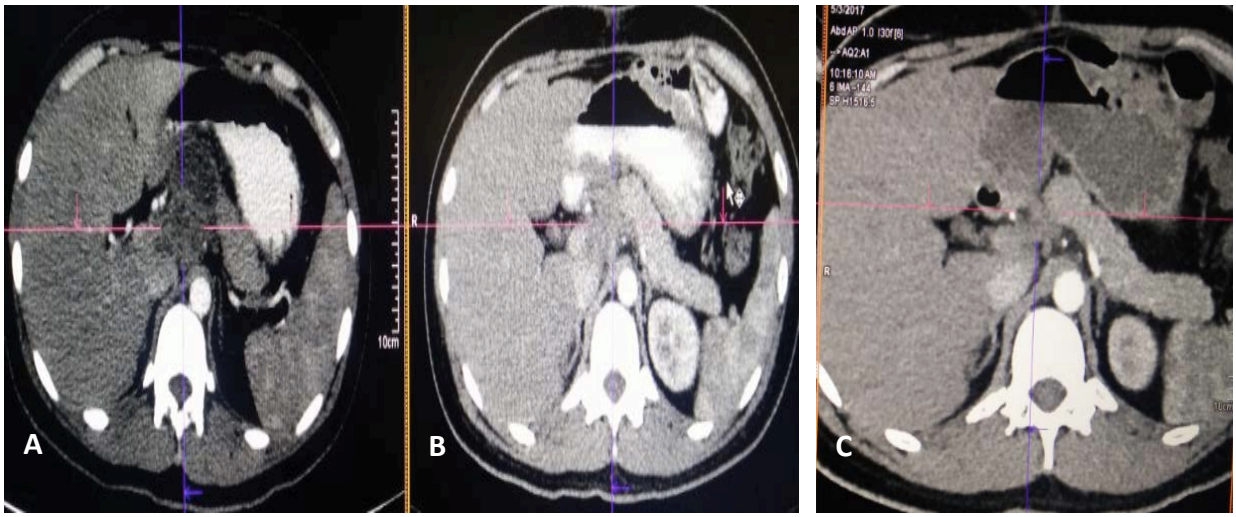



**Figure 4.** Repeat contrast enhanced abdominal computed tomography scans during the course of antimycobacterial therapy (A→B→C), showed interval regression of pancreatic mass (red arrow) and lymphadenopathies, with good cleavage planes with the adjacent stomach and liver, and still encasing the common hepatic artery.

### *Discussion*

Extrapulmonary TB is a diagnostic problem, especially when an unusual organ such as the pancreas is involved. It is biologically protected from infection by Mycobacterium tuberculosis, probably due to the presence of pancreatic enzymes such as lipases and deoxyribonucleases that interfere with colonization, seeding and proliferation of the Mycobacterium. Isolated pancreatic involvement is predominantly observed among patients who reside in endemic tuberculose zones, in the setting of miliary or widely disseminated tuberculosis and often in immunocompromised hosts.[1] More than half of patients with pancreas tuberculosis in the world literature are young adults, less than 30 years old, as was our patient and proposed mechanisms of spread to the pancreas may be through any of the following: hematogenous or direct lymphatic contiguous spread via respiratory or gastrointestinal tract; toxic-allergic reaction of the pancreas in response to generalized tuberculosis; or reactivation of dormant bacilli in an old lesion, particularly intra-abdominal or during an immunosuppressed state.[3] According to series of cases reported in China, the disease often emerges insidiously with non-specific constitutional symptoms, such as abdominal pain (75%), anorexia or weight loss (69%), malaise or weakness (64%), fever or night sweats (50%) and jaundice (31%).[7] Other unusual presentations were obstructive jaundice, gastrointestinal bleeding, pancreatic abscess, chronic pancreatitis, diabetes and splenic vein thrombosis.[7] Patients may or may not have had other forms of tuberculosis in the past and clinical examination is usually non-contributory. Laboratory abnormalities include anemia, lymphocytopenia, hypertransaminasemia and elevated alkaline phosphatase in approximately 50%[7] of cases and non-invasive imaging studies may suggest the possibility of tuberculosis. Ultrasonographic features include a diffusely enlarged pancreas with focal hypoechoic lesions or cystic lesions of the pancreas and associated findings include mesenteric lymphadenopathy, bowel wall thickening, usually in the ileocaecal region, focal hepatic or splenic lesions and ascites.[9] CT scan most commonly reveals a hypodense mass lesion, typically located in the pancreatic body or head,[10] and provides data about the structure of the lesion and its relation with the vessels. Tuberculous lesions may be solid, cystic, or mixed, may present calcifications, may dilate the biliary tract or the main pancreatic duct, and

may be associated with multiple peripancreatic lymphadenopaties. However, none of the methods mentioned above are specific enough nor pathognomonic to confirm the diagnosis.[11] Moreover, according to some reports, pancreatic tuberculosis may exhibit local vascular invasion, such as involvement of the portal vein, superior mesenteric vein and hepatic artery, thereby causing further diagnostic confusion with locally advanced or metastatic pancreatic malignancy.[1] From clinical reviews, between 60–100% cases of pancreatic tuberculosis were initially diagnosed as having pancreatic cancer and between 45–86% required surgery to confirm the diagnosis.[3] However, improvement in radiological investigations and image-guided interventions helped in the diagnosis and prevention of unnecessary laparotomy.[2] Currently, endoscopic ultrasonography (EUS) biopsy is considered the gold standard for diagnostic modality for pancreatic mass.[2] The crucial microscopic features are those of caseating granulomatous inflammation, while acid- fast bacilli (AFB) are rarely seen[9], with sensitivity of Ziehl Neelsen staining of about 50% compared to culture.[12] However, establishing diagnosis by culture for mycobacteria may take up to 6 weeks to grow though a positive culture is highly specific. Emergence of new technology such as, polymerase chain reaction (PCR)-based assay provides a positive result earlier, often obtained within a day, detecting Mycobacterium tuberculosis DNA in specimens with high specificity, even when special staining techniques and cultures of these tissues are negative.[9] Nevertheless, it must be remembered that bacteriological confirmation has been reported in only half of cases with extrapulmonary TB[8] and may not be possible in many patients.

A serum tumor marker called Cancer antigen 19-9 (CA 19-9) has been used widely as a tool for the investigation and management of patients with pancreatic mass. CA 19-9 is a sialylated Lewis (Le) blood group antigen synthesized by the normal human pancreatic and biliary ductular cells, as well as by the gastric, colonic, endometrial and salivary epithelia, thus explaining elevated levels in many different kinds of malignancies[13], especially in cases of pancreatic cancers with reference range of less than 37 U/mL. Sensitivity of the CA 19-9 assay was 83.7% and specificity was 90.4%. However, despite the fact that elevated serum level of CA 19-9 in the presence of pancreatic lesions usually suggests malignant nature of the lesion[14], it may occasionally be elevated in non-neoplastic diseases including benign pulmonary diseases, renal failure and hepatobiliary disease such as liver cirrhosis and cholecystitis with gallstones, thereby emphasizing that interpretation of its result must be in conjunction with clinical findings and other ancillary investigations.[13]

Once diagnosis of pancreatic tuberculosis is established, standard anti-mycobacterial therapy appears to be successful in the management of pancreatic TB. Majority of patients respond well to 6–12 months of treatment with excellent long term outcome, but if diagnosis is delayed, pancreatic tuberculosis can be fatal.[1] Follow-up CT imaging after treatment may show complete resolution of pancreatic lesions secondary to tuberculosis and may guide clinicians regarding duration of therapy.[15] Although, according to several studies, a 6-month treatment for abdominal tuberculosis is as effective as 9 months of treatment in terms of achieving complete response to treatments[16] with the benefits of increased compliance and reduced cost[17], and there is also no difference in the success rate of 6 months (99%) vs 12 months (94%) of antituberculous drugs reported in a randomized controlled trial by Balasubramaniam et al.

Our patient initially presented with non-specific abdominal pain and constitutional

features consistent with the published literature to date on pancreatic TB. Non-specific markers for chronic inflammatory disease such as TB, in the form of anemia, lymphocytopenia and hypertransaminasemia were not present in this case. There were no features of TB elsewhere and the patient was not immunocompromised with normal CA 19-9. Abdominal imaging revealed a predominantly cystic mass lesion in the pancreatic head and body region, encasing the common hepatic artery, with multiple lymphadenopathies but no noted calcifications, peritoneal or mesenteric masses nor splenic and hepatic lesions. In this case with the appropriate clinical (lack of any evidence of disseminated tuberculosis, immunocompromised status) and CT findings of potentially resectable tumors, the inability to definitely differentiate the lesion from a pancreatic malignancy by doing EUS with fine-needle aspiration due to its absence in our institution, prompted to pursue a surgical intervention, in the hands of experienced surgeons. Specimen obtained intra-operatively revealing a chronic granulomatous inflammation with caseation necrosis and Langhans' type multinucleated giant cells, in conjunction with a positive result for both TB PCR and AFB staining, established the diagnosis of a pancreatic tuberculosis and justifies initiation of anti-mycobacterial therapy. Still, a pancreatic neoplasm was a close differential diagnosis but the patient's excellent symptom and imaging response to antimycobacterial therapy, tumor marker CA 19-9 negativity, no malignant cells seen on pathology and lack of disease progression over the last few months of follow-up argues against this.

***Conclusion***

Isolated pancreatic TB is an extremely rare clinical entity but should always be included in the differential diagnoses of a pancreatic malignancy, especially in a younger patients with constitutional symptoms coming from developing countries, where the infection is endemic[3]. Diagnosis poses a great challenge, requiring high level of suspicion, because it closely mimics pancreatic carcinoma both in clinical presentation and radiological appearance. Nevertheless, every effort should be made for a histopathological or microbiological evidence of tuberculosis to avoid unnecessary interventions, including laparotomy[9]. Directly observed therapy with standard multiple anti-mycobacterial regimen for 6-12 months is usually effective, and symptomatic response and repeat abdominal imaging studies guides the clinician regarding treatment response and duration[2.] Patients still need to be followed up carefully since anti-mycobacterial drugs may have hepatotoxic effects, thereby requiring modification of treatment dosing or duration.

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***Conflicts Of Interest***

The author(s) declare that there are no conflicts of interest.

***References***

1. Shahrokh S, Miri MB, Safari MT, Alizadeh AH. Pancreatic Tuberculosis: An Overview. JOP. J Pancreas (Online) 2015 May 20; 16(3):232-238.

2. Zacharia GS, Antony R, Kolassery S and Ramachandran TM. Case report Isolated pancreatic tuberculosis masquerading as pancreatic cancer. Gastroenterology Report 2 (2014) 154–157.

3. Wijaya R, Koo CH, Chiow AKH, Tan SS, Tan Su-Ming. Isolated tuberculosis of the pancreas mimicking a pancreatic tumor with concomitant choledocholithiasis. Int J Hepatobiliary Pancreat Dis 2014; 4:26–31.

4. Faria HP, Alves JT, Villela OCC, Filho RM and Romeiro MA. Pancreatic Tuberculosis: A Case Report And Literature Review. Radiol Bras 2007; 40(2):143–145.

5. Jethwani U, Singh G, Mohil RS, Kandwal V, Chouhan J, Saroha R, et al. Pancreatic tuberculosis: a Case report. OA Case Reports 2013 Jun 05;2(5):41.

6. Jacobs TQ and Ross A. Adverse effects profile of multidrug-resistant tuberculosis treatment in a South African outpatient clinic, South African Family Practice, 54:6, 531-539, DOI: 10.1080/20786204.2012.10874288

7. Saluja SS, Ray S, Pal S, Kukeraja M, Srivastava DN, Sahni P and Chattopadhyay TK. Hepatobiliary and pancreatic tuberculosis: A two decade experience. BMC Surgery 2007, 7:10.

8. Taher MT, Hashemi SMH, Mohammadi M and Hashemi F. Tuberculosis of pancreas and peripancreatic lymph nodes: a case report. Eastern Mediterranean Health Journal, Vol. 15, No. 6, (2009) 1617-1620.

9. Pramesh CS, Heroor AA, Gupta SG, Krishnamurthy S, Shukla PJ, Jagannath P and DeSouza LJ. Case report Pancreatic tuberculosis: an elusive diagnosis. HPB 2003 Volume 5, Number 1 43±45.

10. Falkowski AL, Graber J, Haack HG, Tarr PE and Rasch H. Isolated pancreatic tuberculosis: A case report and radiological comparison with cystic pancreatic lesions. Journal of Radiology Case Reports. Radiology Case. 2013 Jan; 7(1):1-11.

11. Kohan G, Ditulio OA, Klappenbach RF, Faerberg A and Imventarza O. Primary Pancreatic Tuberculosis: A Diagnosis and Therapeutic Dilemma. A Case Report. Journal of the Pancreas (Online) 2017 Mar 17; 18(2):216.

12. Kaur M, Dalal V, Bhatnagar A, Siraj F. Pancreatic Tuberculosis with Markedly Elevated CA 19-9 Levels: A Diagnostic Pitfall. Oman Medical Journal. 2016;31(6):446-449. doi:10.5001/omj.2016.89.

13. Pavai S and Yap SF. The Clinical Significance of Elevated Levels of Serum CA 19-9. Med J Malaysia Vol 58 No 5. December 2003.

14. Cwik G, Wallner G, Skoczylas T, Krzyzanowski M, Ciechainski A, and Madro P. Elevated tumor marker CA 19-9 in the differential diagnosis of pancreatic mass lesions. Ann Univ Mariae Curie Sklodowska Med. 2004;59(2):213-8.

15. Raghavan P and Rajan D. Case Report Isolated Pancreatic Tuberculosis Mimicking Malignancy in an Immunocompetent Host. Case Reports in Medicine Volume 2012, Article ID 501246.

16. Esguerra DC, Subedi KR, Abola LE. Six Months Versus 9 Months Of Anti-Tb Therapy For Abdominal Tuberculosis: A Meta-Analysis.

17. Sang Hyoung Park, Suk-Kyun Yang,* Dong-Hoon Yang, Kyung Jo Kim, Soon Man Yoon, Jae Won Choe, Byong Duk Ye, Jeong-Sik Byeon, Seung-Jae Myung, and Jin-Ho Kim. Six-month versus 9-month therapy for intestinal tuberculosis: A prospective randomized trial. Antimicrob. Agents Chemother. doi:10.1128/AAC.00874-09. 2009

18. Feldman M, Friedman L and Brandt L. Pancretic Cancer, Cystic Pancreatic Neoplasm and other Non endocrine pancreatic tumors. Sleisinger and Fordtran's Gastrointestinal and Liver Disease 10th edition Chapter 60 p1027-1043.

19. Rao RN, Pandey R, Rana MK, Rai P, Gupta A. Pancreatic and peripancreatic tuberculosis presenting as hypoechoic mass and malignancy diagnosed by ultrasound-guided fine-needle aspiration cytology. Journal of Cytology / Indian Academy of Cytologists. 2013;30(2):130-135.

20. Waintraub DJ, D'Souza LS, Madrigal E, Harshan M, and Ascunce, GI. A Rare Case of Isolated Pancreatic Tuberculosis. ACG Case Reports Journal Volume 3, Issue 4. July 2016.

21. Mohan A, and Sharma SK. Extrapulmonary tuberculosis. Review Article Indian J Med Res 120, October 2004, pp 316-353.