Pancreatic Tuberculosis: Current Update on Clinical Manifestation and Diagnostic Modalities

Samudra Andi Yusuf, Hasan Maulahela**, Anjar Raraswati***, Maureen Irawati Koesnadi**

*Abdi Waluyo General Hospital, Jakarta

**Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia/Dr. Cipto Mangunkusumo General National Hospital, Jakarta

***Faculty of Medicine, Universitas Padjajaran, Bandung

Corresponding author:

Hasan Maulahela. Division of Gastroenterology, Department of Internal Medicine, Dr. Cipto Mangunkusumo General National Hospital. Jl. Diponegoro No. 71 Jakarta. Phone: +62-21-3153957; facsimile: +62-21-3142454. E-mail: hasan.maulahela@yahoo.com

ABSTRACT

Background: *Pancreatic tuberculosis is a very rare disease in either immunocompetent or immunocompromised hosts. The incidence of pancreatic tuberculosis (TB) was reported to be less than 4.7% in an autopsy series on tuberculosis patients in 1944 and 2% in another autopsy series in 1966. Despite that, in recent times, an increase in the number of reports of pancreatic TB has been noted. This condition is possibly caused by an improvement in diagnostic imaging tools, the development of different techniques that make obtaining specimens from the pancreas possible, and an increase in human immunodeficiency virus (HIV) prevalence worldwide. Therefore, this review article discusses the current update in the clinical manifestations and diagnostic modalities of pancreatic tuberculosis.*

Results: *Signs and symptoms of patients with pancreatic TB most frequently were abdominal pain (74.8%), weight loss (51.6%), fever (46.5%), and jaundice (20.0%). Pancreatic TB usually presented as an abscess or cystic mass localized mainly in the pancreatic head (59.0%). Several diagnostic modalities can be used to aids the diagnosis of pancreatic tuberculosis such as ultrasonography (USG), computerized tomography (CT) scan, magnetic resonance imaging (MRI), polymerase chain reaction (PCR), and histopathology. However, recently endoscopic ultrasound-guided fine-needle aspiration (EUS FNA) has emerged as an excellent tool for the cytological diagnosis of pancreatic and peripancreatic masses in 80-95% of cases. Once diagnosis of pancreatic tuberculosis is established, most patients respond well to anti-tuberculosis medication. Surgical intervention is indicated where a diagnosis is not established with percutaneous or EUS guided approaches.*

Conclusion: *Pancreatic tuberculosis is a very rare condition with a various range of non-specific clinical presentation and image features overlapping with those seen in pancreatic neoplasia. A combination of diagnostic modalities should be done to establish a diagnosis of pancreatic tuberculosis. Currently, direct histopathological examination is the best way of diagnosing tuberculosis. US/CT/EUS-guided biopsy is the recommended diagnostic technique. Most patients with pancreatic tuberculosis respond well to anti-tuberculosis drugs.*

Keywords: *pancreatic tuberculosis, diagnosis, clinical manifestation, ultrasonography (USG), computerized tomography (CT) Scan, magnetic resonance imaging (MRI), polymerase chain reaction (PCR), histopathology, endoscopic ultrasound-guided fine-needle aspiration (EUS FNA)*

ABSTRAK

Latar belakang: *Tuberkulosis (TB) pancreas merupakan penyakit yang sangat jarang baik pada pasien yang imunokompeten maupun immunocompromised. Angka kejadian dari TB pancreas berdasarkan data laporan sekitar kurang dari 4.7% pada otopsi serial yang dilakukan terhadap pasien TB tahun 1944 dan 2% pada otopsi serial lainnya di tahaun 1966. Akan tetapi, dewasa kini, didapatkan peningkatan laporan kasus TB pancreas yang dilaporkan. Kondisi ini kemungkinan disebabkan oleh kemajuan alat pencitraan diagnostic, perkembangan tehnik-tehnik yang membuat pengambilan specimen dari pancreas menjadi memungkinkan, dan peningkatan prevalensi HIV di dunia. Oleh karena itu, review artikel ini akan membahas mengenai perkembangan terkini dari manifestasi klinis dan metode diagnostik untuk tuberculosis pancreas.*

Hasil: *Tanda dan gejala pasien dengan TB pankreas paling sering adalah nyeri perut (74,8%), penurunan berat badan (51,6%), demam (46,5%) dan ikterik (20%). TB pancreas biasanya dipresentasikan sebagai abses atau massa kistik yang terlokalisasi biasanya pada kepala pankreas (59%). Beberapa modalitas diagnostik dapat digunakan untuk membantu penegakan diagnosis tuberculosis pankreas seperti ultrasonography (USG), computerized tomography (CT) Scan, magnetic resonance imaging (MRI), polymerase chain reaction (PCR), dan histopatologi. Akan tetapi, baru-baru ini penggunakan endoscopic ultrasound-guided fine-needle aspiration (EUS FNA) sedang berkembang menjadi alat uji diagnostic yang sangat baik untuk diagnosis sitologi dari massa pankreas dan peripankreas pada 80-95% kasus. Setelah diagnosis tuberculosis pankreas dapat di tegakkan, sebagian besar pasien berespon baik dengan pemberian obat-obatan anti tuberculosis. Intervensi bedah di indikasikan apabila diagnosis tidak dapat di tegakkan dengan pendekatan percutaneous/EUS guided.*

Simpulan: *Tuberkulosis pankreas merupakan kondisi yang sangat jarang dengan berbagai macam presentasi klinis yang tidak spesifik dan gambaran radiologis yang mirip dengan tumor pankreas. Kombinasi dari beberapa modalitas diagnostik harus digunakan untuk penegakan diagnosis tuberculosis pankreas. Dewasa kini, pemeriksaan histopatologi merupakan modalitas utama untuk menegakkan diagnosis tuberculosis pankreas. US/CT/EUS-guided biopsy merupakan tehnik diagnosis yang direkomendasikan. Sebagian besar pasien memberikan respon yang baik terhadap obat-obatan anti tuberculosis.*

Kata kunci: *Tuberkulosis pankreas, diagnosis, manifestasi klinis, ultrasonography (USG), computerized tomography (CT) scan, magnetic resonance imaging (MRI), polymerase chain reaction (PCR), Histopatologik, endoscopic ultrasound-guided fine-needle aspiration (EUS FNA)*

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by mycobacterium tuberculosis. It affects nearly 9.7 million people and claims about 2 million lives each year worldwide with the highest incidence being in Asia, South America, Eastern Europe, and most sub-Saharan African countries.[1] Tuberculosis usually infects the lungs, however; it can also infect other sites than the lung called extra-pulmonary TB. Extra-pulmonary TB (EPTB) accounts for nearly 10-30% (approximately 15-20%) of all cases of TB in immunocompetent hosts.[1] It can develop in almost any organ system; most commonly in the lymph nodes, pleura, abdominal, genitourinary system, and bone. One of the most common sites for EPTB is abdominal TB. It accounts for 5-12% of patients with tuberculosis (with the highest prevalence in developing countries) and almost 11-16% of patients with EPTB have abdominal involvement.[1] The most common site of abdominal TB is in the ileocecal region. Though, abdominal TB can also affect another region of the gastrointestinal tract and intra-abdominal organs such as the spleen, liver, and pancreas.[1]

Pancreatic tuberculosis is a very rare disease in either immunocompetent or immunocompromised hosts.[2] The incidence of pancreatic tuberculosis was reported to be less than 4.7% (14/297 cases) in an autopsy series on tuberculosis patients in 1944 and 2% (11/256 cases) in another autopsy series in 1966.[1,2,3] Despite that, in recent times, an increase in the number of reports of pancreatic TB has been noted.[3] This condition is possibly caused by an improvement in diagnostic imaging tools, the development of different techniques that make obtaining specimens from the pancreas possible, and an increase in HIV prevalence worldwide.[2,3] Frequently, pancreatic TB afflicts the region of the head and uncinate process of the pancreas.[1] It is often misdiagnosed because in most cases the symptoms mimic pancreatic carcinoma.[1,2,3] Nevertheless, it is important to be able to diagnose pancreatic TB in time to initiate an adequate treatment and also to prevent costly and risky surgical procedures. Therefore, this review article will talk about the current

update on clinical manifestation and diagnosis of pancreatic tuberculosis.

Epidemiology

Tuberculosis (TB) is one of the most important infectious diseases in the world which caused an estimated 1.6 million deaths in 2017.[1-3] The incidence rate of tuberculosis in South East Asia is 181 per population.1 Indonesia ranks third in the world in the number of TB cases, after China and India with the total TB incidence were 842,000 and the prevalence rate was 297 per 100,000 population.[4-6] TB usually occurs in the lung, but nearly 10-30% occurs extra-pulmonary TB, and abdominal TB was the most common accounting for 11-16%.[1,3] TB affects various intra-abdominal organs, including the intestines, gastroduodenal, liver, biliary tract spleen, and pancreas.[3,7] The most common site of abdominal TB is in the ileocecal region.[1]

Tuberculosis of the pancreas is extremely rare cases in immunocompromised as well as immunocompetent patients.[2,3,7,8] In large autopsy series on TB patients, Auerbach et al and Bhansali et al reported pancreatic involvement in only 4.7% and 0% of patients.[3,8] Paraf et al study about autopsy series in 1966 reported an incidence on pancreatic TB is 2%.[2] Despite that, in recent times, an increase in the number of reports of pancreatic TB has been noted.[3] It has been reported that the incidence of pancreatic TB is only 0.46% among patients with TB and typically occurs in patients who reside in endemic tuberculous zones.[9]

Pathogenesis

Over the last few decades, the pathogenesis of tuberculosis has been thoroughly researched, and many aspects have been well explained, but a few questions remain unanswered. The majority of adult cases of pulmonary tuberculosis are caused by the reactivation of a latent tuberculosis infection developed earlier in life. *M. tuberculosis* is thought to be present in one-third of the world's population, providing a vast reservoir for the pathogenic organism's propagation. Diabetes, chronic kidney disease, AIDS, immunosuppressive drugs, and hematologic malignancies, that weaken the immune system may all cause the reactivation of latent tuberculosis infection.[10]

Invasion of pathogenic bacteria causes granulomatous inflammation, which leads to abdominal tuberculosis. Ulceration, bleeding, and perforation may result from such invasion and inflammation. Pathogenic bacteria enter the gastrointestinal tract through the mouth by contaminated food, hematogenous spread from active pulmonary infection, contiguous dissemination from neighboring affected viscera or lymph nodes, and in a rare circumstance, dairy items that haven't been pasteurized.[11]

Due to the degradation of tuberculosis by pancreatic enzymes, the pancreas is relatively tuberculosis tolerant.[2] Some literature hypothesized that pancreatic enzymes (such as lipase and deoxyribonuclease) inhibit the growth of mycobacteria, which may explain the disease's low prevalence (even in endemic areas)[10]

Abdominal tuberculosis may manifest in the pancreas, albeit uncommonly. It may be isolated, associated with adscititious enteric involution, or occur in the setting of disseminated tuberculosis.[11] There are three forms of pancreatic tuberculosis: (a) as part of miliary tuberculosis, (b) transmitted to the pancreas from retroperitoneal lymph nodes, and (c) localized pancreatic tuberculosis, which is caused primarily by *Mycobacterium tuberculosis* and occurs as a result of primary tuberculosis of the intestine. Pancreatic involvement in tuberculosis is most often associated with military tuberculosis (type (a)).[2]

Clinical Manifestation

Clinical presentation of pancreatic tuberculosis more often than not is insidious and non-specific. A systematic review conducted by Panic et al shows demographics and risk factors among 166 patients diagnosed with pancreatic TB.[3] The majority of the patients were male (62.1%) diagnosed at a mean age of 41.61 ±13.95 years.[3] Furthermore, HIV-positive was one of the most important risk factors since 22 out of 166 (22.3%) patients were previously or simultaneously diagnosed with HIV.[3] Other risk factors for pancreatic TB include alcohol abuse (10.5%), intravenous drug abuse (8.1%), and smoking (6.9%).[3] Previous TB infection was present in only 7.3% of patients.[3] Table 1 below shows demographics and risk factors among patients diagnosed with pancreatic TB.

According to study Panic et al and Saluja et al, the signs and symptoms of patients with pancreatic TB most frequently were abdominal pain (74.8%), weight loss (51.6%), fever (46.5%), and jaundice (20.0%).[3,7] Pancreatic TB usually presented as an abscess or cystic mass localized mainly in the pancreatic head (59.0%), and less frequently in the body (18.2%), tail (13.4%), or neck (1.8%).[2,3,12,13] From the physical examination, the most important findings on abdominal examination included hepatomegaly (n = 9), palpable gallbladder (*n* = 4), gallbladder mass (n =1), and abdominal

mass (n = 1).[7] Table 2 and 3 below reports clinical characteristics of patients diagnosed with pancreatic TB.[3,7]

Table 1.Demographics and risk factors in 166 patients diagnosed with pancreatic tuberculosis[3]

Age (years)	41.61 ± 13.95
Age range (years)	16-82
Sex	
Male	103 (62.1%)
Female	63 (38.0%)
Origin	
North America, Australia and New Zealand	38 (22.8%)
Europe	34 (20.5%)
Asia	83 (50.0%)
Africa	7 (4.2%)
South America	4 (2.4%)
Risk Factors	
Drugs	7 (8.1%)
Alcohol	9 (10.4%)
Smoking	6 (6.9%)
HIV-positive	22 (22.3%)
Previous tuberculosis	7 (7.3%)

Table 2.Clinical characteristics in 166 patients diagnosed with pancreatic tuberculosis[3]

Symptoms	
Fever	74 (46.5%)
Pain	119 (74.8%)
Weight loss	82 (51.6%)
Jaundice	31 (20.0%)
Diarrhoea	5 (3.1%)
Clinical presentation	
Pancreatic mass	132 (79.5%)
Pancreatic head mass	98 (59.0%)
Pancreatic neck mass	3 (1.8%)
Pancreatic body mass	30 (18.2%)
Pancreatic tail mass	22 (13.4%)
Acute pancreatitis	10 (6.0%)
Chronic pancreatitis	11 (6.6%)
Pancreatic abscess	20 (12.1%)
Pseudocyst	3 (1.8%)
Extrapancreatic involvement	
Peripancreatic lymph nodes	69 (47.3%)
Pulmonary	9 (6.3%)
Intestine	12 (8.2%)
Liver	10 (6.9%)
Spleen	12 (8.3%)

Diagnostic Modalities of Pancreatic Tuberculosis

Solitary pancreatic TB may have a variety of radiological manifestations. It can mimic carcinoma, lymphoma, cystic neoplasia, retroperitoneal tumors, pancreatitis, or pseudocysts.[14] There are no pathognomonic radiological features of pancreatic TB thus an accurate preoperative diagnosis of PTB is clinically challenging.[14-16]

Ultrasonography

Ultrasonography (USG) is often used as the first imaging modality in abdominal pain or obstructive jaundice assessment because it is non-invasive, simple, readily available, and cost-effective.[1,16,17] Pancreatic TB USG shows bulky inhomogeneous pancreas or a cystic lesion or one or more focal hypoechoic masses in the pancreatic parenchyma that may sometimes show central liquefaction, diffuse enlargement of the pancreas, and enlarged peripancreatic and other abdominal lymph nodes (Figure 1).[2,14,16]

CT Scan

The CT findings of pancreatic TB in the literature provide a wide spectrum, including a low-attenuation focal mass, a cystic mass, small nodular lesions, pancreatic calcification, and focal and diffuse pancreas enlargement.[1,18] The majority of CT findings show a hypodense, hypovascular well-defined mass with irregular borders and peripheral enhancement, typically in the pancreas head, diffuse pancreas enlargement, or enlarged peri-pancreatic lymph nodes (Figure 2).[2,15,16,18,19] The common bile duct and the pancreatic duct are reported to be normal in patients with pancreatic TB, even if the mass is positioned centrally in the head of the pancreas while the pancreatic duct and common bile duct are usually dilated in centrally located adenocarcinomas of the pancreatic head.[2,15,19]

Table 3. Clinical features of patients based on the organ involved[7]

Symptoms and signs	Liver (n = 2)	Gallbladder (n = 3)	Biliary (n = 6)	Pancreatic (n = 7)	Overall Incidence (n = 18)
Abdominal pain	1	2	5	5	13
Jaundice	1	0	6	3	10
Fever	2	1	4	2	9
Anorexia	2	1	3	2	9
Weight loss	2	1	3	3	9
Melena	1	1	0	0	2
Enlarged Supraclavicular lymph nodes	0	0	0	2	2
Hepatomegaly	1	1	4	3	9
Palpable gallbladder	1	0	1	2	4
Gallbladder mass	0	1	0	0	1
Abdominal mass	0	0	0	1	1

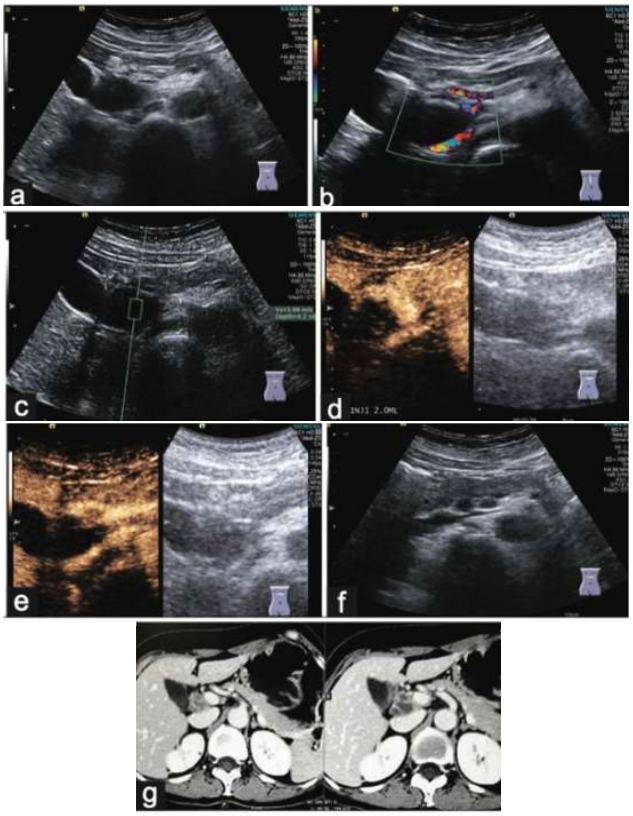

Figure 1. Pancreatic tuberculosis pictures in (a) USG B_mode, (b) color Doppler flow imaging and (c) ultrasound elastography with Virtual TouchTM Quantification measurement, (d) on contrast-enhanced ultrasound arterial phase, and (e) portal venous phase, Lymphadenopathies were detected both on (f) B-mode ultrasound and (g) computed tomography.[14]

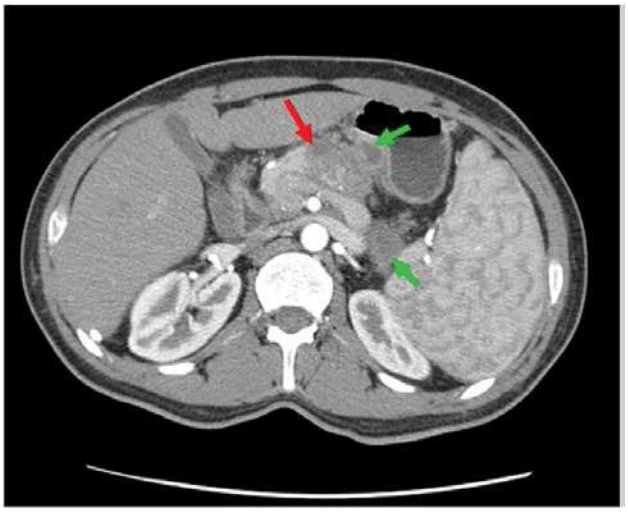

Figure 2. on A 48-year-old man with pancreatic tuberculosis. Arterial phase axial computed tomography showed an ill-defined hypodense mass lesion at the body of the pancreas (red arrow); adjacent hypodense lymph nodes, with a peripheral rim of enhancement; 1 node is seen compressing the gastric lesser curvature (green arrows).[18]

Magnetic Resonance Imaging (MRI)

A sharply delineated mass usually located in the pancreatic head, with heterogeneous enhancement, is one of the MRI findings of focal pancreatic TB.[2,15,16] These lesions are multinodular masses that appear hypointense on fat-suppressed T1-weighted images and have a combination of hypo/hyper strength on T2-weighted images.[2,14,15,16]

Polymerase Chain Reaction

Since traditional approaches often fail to diagnose extrapulmonary tuberculosis, polymerase chain reaction (PCR) assays are diagnostic in most patients presenting with unusual manifestations of tuberculosis, such as pancreatic and hepatobiliary tuberculosis.[2,20] Based on a study conducted by Makeshkumar in the review article written by Poras Chaudhary, PCR was found to be more effective than traditional methods in detecting extrapulmonary tuberculosis patients in a study of 178 patients. In the detection of Mycobacterium tuberculosis, PCR assays are superior to smear and culture. It has a 64 percent sensitivity.[20] Another study by Ganavilli et al shows that the overall positivity for EPTB was 12.1% (22/182) in the tested samples using PCR, as shown in table 4. Furthermore, the PCR positivity was highest if it is taken in the pus samples as shown in table 5.[22] Data from those research shows that PCR assay combines with other non-invasive methods, can help in diagnosing pancreatic tuberculosis and prevent the need to do laparotomy procedure.[2,22]

Table 4.Tests detecting *M.Tuberculosis* in clinical samples[22]

Tests	Numbers	Percentage
PCR only	10	45.5
PCR & Culture	6	27.3
All Positive	3	13.6
ZN only	2	9.1
PCR & ZN	1	4.5

PCR: polymerase chain reaction, ZN: Zieh-neelseen

Table 5.Distribution of Extrapulmonary samples and PCR Positivity[22]

Sample	Total tested	PCR	Positivity rate
Tissue	46	6	13.0
Pus	31	8	25.8
CSF	30	2	6.7
Pleural fluid	19	1	5.3
Urine	19	1	5.3
Synovial fluid	13	1	7.7
Blood	12	0	0.0
Other fluid	7	0	0.0
Peritoneal fluid	5	1	20.0
Total	**182**	**20**	**11.0**

PCR: polymerase chain reaction, SCF: cerebrospinal fluid

Histopathology

Pathological confirmation is an indispensable method for establishing the ultimate diagnosis of tuberculosis.[2,11,23,24] If imaging tests and FNAC fail to validate the diagnosis, a direct histopathological test by

laparotomy should be performed.[2,11] The success rate of identifying acid-fast bacilli from the biopsy specimen has been between 20 and 40% while cultures were found to be positive in about 77% of cases.[24]

A biopsy is usually taken from a pancreatic lesion and/or peripancreatic lymph node.[2] The pathologic feature of tuberculosis is a granulomatous inflammation with signs of necrosis.[2,11,23,24] Tuberculosis caused by Mtb is the most common disease in the formation of caseous granuloma. Granuloma, the central part, is caseous necrosis in which mycobacteria DNA can be found with numbers ranging from 0 to 9%, the peripheral part is clusters of immune cells including macrophages, epithelioid cells, multinucleated giant cells, Langerhans cells, and lymphocyte.[23] However, granulomas may also be caused by a variety of diseases, including Chron's, sarcoidosis, and histoplasmosis, so diagnostic caution is needed.[2,22] Figures 3 below shows the histopathological feature of pancreatic tuberculosis.[23]

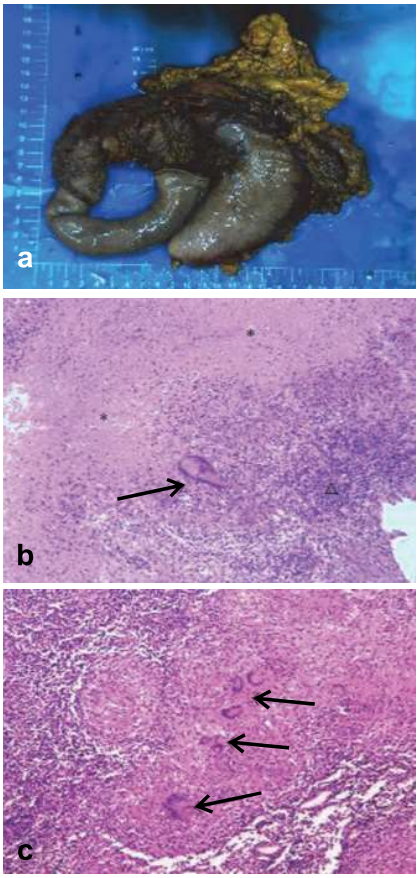

Figure 3. The histopathological pictures. (a) Whipple surgical specimens contained the pancreas, duodenum, partial stomach, and omentum. The lesion was located on the pancreatic head. ((b) and (c)) HE staining. Granulomatous nodules consisting of lymphocytes, epithelioid cells, and multinucleated giant cells can be seen at the site of the lesion. Necrosis can be seen in the middle of nodules which were marked with an asterisk. The triangle marked the lymphocytes around the nodules. The arrow indicated the multinucleated giant cells reaction. These pathological features suggested tuberculous lesions.[23]

Endoscopic Ultrasound-Guided Fine Needle Aspiration (EUS FNA)

Endoscopic ultrasound (EUS) is a type of endoscopic procedure. It involves the insertion of a thin tube into the mouth and down into the stomach and the first part of the small intestine.[25] Then, using the guidance of the high-frequency ultrasound transducer on the tip of the echoendoscope, a small gauge needle is passed through the wall of the gastrointestinal tract and into the pancreas.[25] Endoscopic ultrasound-guided fine-needle aspiration (EUS FNA) has emerged as an excellent tool for the cytological diagnosis of pancreatic and peripancreatic masses in 80-95% of cases.[2,3,26,27] EUS is more effective than CT or US in differentiating between malignant and non-malignant lesions of the pancreas.[2,3,26,27,28] In addition, the advantage of using EUS-guided sampling is its ability to target small pancreatic lesions that are not detectable with ultrasound or CT scan.[26,27]

In pancreatic TB, the diagnostic accuracy of EUS-FNA is difficult to determine due to the rarity of the disease. However, in a case series reported by Song et al, EUS-FNA was able to diagnose pancreatic/peri-pancreatic TB in 76.2% of patients.[26,27] Thus, it can prevent unnecessary surgery for these patients. Figure 4 dan 5 below shows EUS finding in pancreatic TB and cytologic examination after FNA.[26]

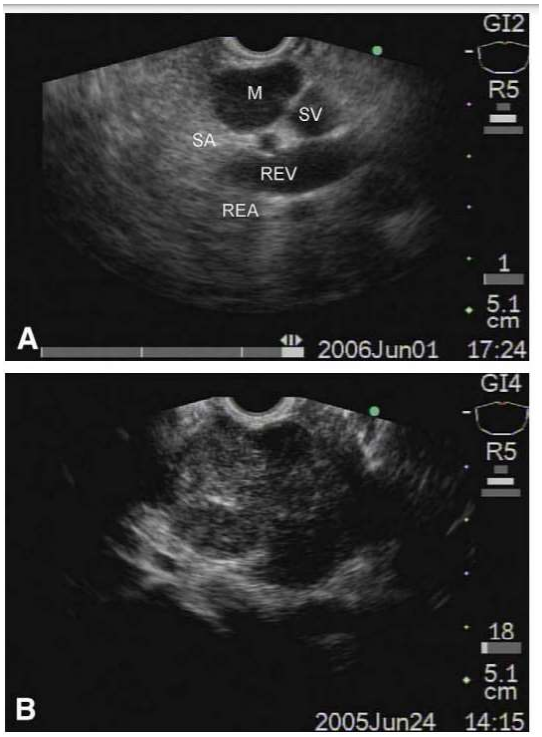

Figure 4. EUS findings in pancreatic TB. A, A well-demarcated hypoechoic and homogeneous mass (15 12 mm) in the tail of the pancreas. M, mass; SA, splenic artery; REV, renal vein; REA, renal artery. B, A well-demarcated hypoechoic, heterogeneous mass (39 x 32 mm)[26]

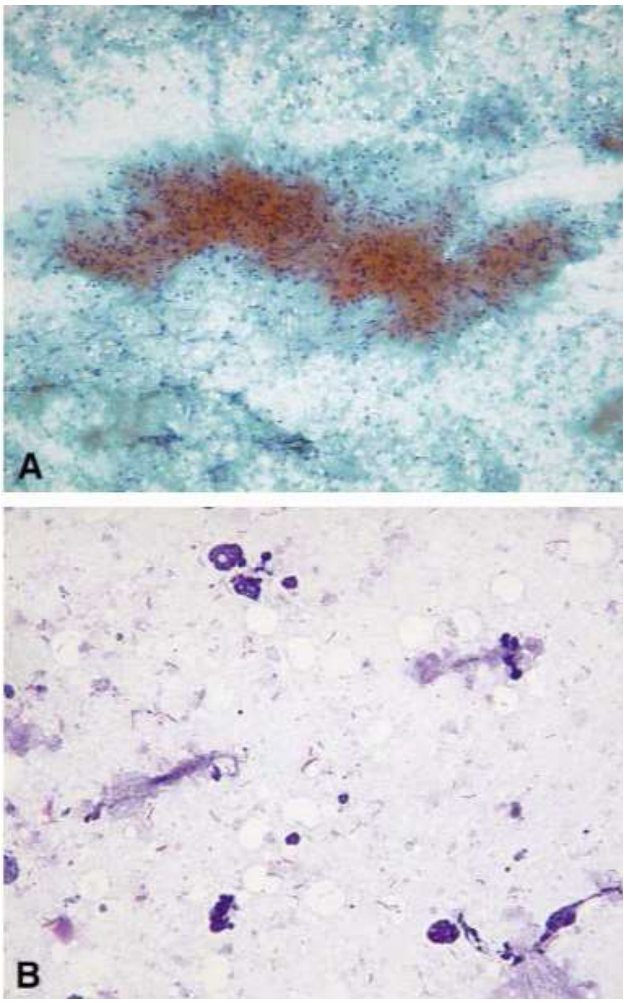

Figure 5. Cytologic examination after FNA. A Smear, showing caseating granulomas (Papanicolaou's stain, Orig. mag. 200). B, Smear, showing numerous beaded AFB. (Ziehl-Neelsen stain, orig. mag. 1000)[26]

Treatment of Pancreatic Tuberculosis

Anti-tuberculosis Drugs

Pancreatic tuberculosis is generally hard to diagnose, but once discovered, it can be treated with anti-tuberculosis treatments. Pancreatic tuberculosis is treated in the same way as any other type of extrapulmonary tuberculosis. The foundation of therapy for tuberculosis remains standard antituberculosis treatments involving at least four regiments. Antituberculosis medications should be taken for 6 to 12 months. Table 6 below shows regimens, dose, and duration for anti-tuberculosis treatment.[2]

The treatment procedure consists of the initiation and continuation phases. The initiation phase of treatment consists of intensive therapy with multi-drug combination therapy (isoniazid, rifampicin, pyrazinamide, and ethambutol) for at least two months, followed by a four-month continuation phase with rifampicin and isoniazid).[29]

Table 6. Antituberculosis drugs for extrapulmonary tuberculosis[2,29]

Regimens	Dose	Duration
Inisiation phase		for 2-4 months
Pyrazinamide	25(25-30 mg mg/kgBW/ day)	
Ethambutol	15 (15-20) mg/kgBW/day	for 4-12 months
Continuation phase		
Isoniazide	5 (4-6 mg/kgBW/day)	
Rifampicin	10 (8-12mg/kgBW/day)	

The World Health Organization (WHO)-Collaborating Centre for Training and Research in Tuberculosis and the Centre of Excellence for Extrapulmonary Tuberculosis at the All-India Institute of Medical Sciences (AIIMS) in New Delhi published an evidence-based duration guideline for treating abdominal tuberculosis.[30]

For abdominal TB, a six-month ATT standard first-line treatment is a strong recommendation. The evidence is based on a study of three randomized controlled studies with 328 participants, two from India and one from South Korea. One trial included both gastrointestinal and peritoneal TB patients, whereas the other two exclusively included gastrointestinal TB patients. Children of HIV-positive people were not included in any of the studies. The studies weakness are we don't know whether relapse rates differ between patients treated for six months and those treated for nine months. (RD 0.01 95% CI: 0.01-0.04%, 328 participants, 3 studies, very low-quality evidence). Patients are more likely to complete shorter regimens and are exposed to less adverse effects of ATT when treated for six months; nevertheless, the disadvantages of six months treatment is that recurrence is higher with shorter regimens, though present research does not support this. Some patients may require an ATT extension, which should be determined by the treating doctor, considering the patient's total ATT dose. The group's gastroenterologist pointed out that some individuals have long-term effects, which might induce symptoms that resemble relapsed abdominal TB or treatment failure. It's critical to distinguish this patient, who has peritoneal adhesion or luminal strictures, from those who have active tuberculosis. ATT should not be continued in these patients since it may be harmful.[30]

It's important to remember that TB requires long-term therapy, and the right medication can lead to drug-induced liver injury (DILI) and acute liver failure.[22] The existence of obstructive jaundice as a clinical manifestation of pancreatic TB, on the other hand, does not change the medications or dosages, but it is important to constantly monitor these individuals for drug-induced liver injury. A full assessment of

clinical symptoms, weight, a live function test, and repeat imaging to confirm resolution or improvement in radiological findings should all be included in the follow-up.

With cases of poor or no response, drug resistance testing should be done before starting therapy, and MRD-TB antibiotic regimens should be considered. When considering a drug, it's vital to remember that resistance to one treatment might lead to resistance to a whole family of drugs. It is critical to ensure that patients follow treatment regimens to reduce the impacts of drug resistance.[11,29]

Role of Endoscopy as Treatment Option in Pancreatic Tuberculosis

Most patients of pancreatic tuberculosis respond well to anti-tuberculosis drugs. However, if the tuberculous mass is enlarged or causes symptoms even after anti-tuberculosis drugs have been consumed for certain period of time, minimally invasive procedures should be considered such as endoscopic internal drainage, percutaneous catheter drainage, or biliary stenting. [2,16,29] EUS-guided fine-needle aspiration allows us not only to obtain tissue samples for PCR diagnosis but also to perform therapeutic aspiration of the abscess as it is shown in one case of pancreatic tuberculosis abscess reported by Maulahela et al.[13]

Patients with no pancreatic duct strictures or pancreatic duct-pseudocyst communications, as well as those with immature or infected pseudocysts, or those who are at high surgical risk, or who are malnourished, preferably to have percutaneous catheter drainage.[1,16]

Role of Surgery in Pancreatic Tuberculosis Treatment

There is limited role of surgical intervention in pancreatic tuberculosis. Surgical intervention is often required in pancreatic tuberculosis where a diagnosis is not established with percutaneous or EUS guided approaches. Surgery procedure may include diagnostic laparotomy with laparoscopic biopsy or may include Whipple's resection for presumed malignancy.[2,29] 80 % of pancreatic cancer case is unexpectedly diagnosed through explorative laparotomy.[31]

CONCLUSION

Pancreatic tuberculosis is a very rare condition with a various range of non-specific clinical presentation and image features overlapping with those seen in pancreatic neoplasia. A combination of diagnostic modalities should be done to establish a diagnosis of pancreatic tuberculosis. Currently, direct histopathological examination is the best way of diagnosing tuberculosis. US/CT/EUS-guided biopsy is the recommended diagnostic technique. A EUS-guided biopsy is better than the US or CT-guided biopsy. In addition, PCR can also aid the diagnosis of pancreatic tuberculosis in cases where there is strong suspicion for pancreatic tuberculosis but definitive diagnosis is not possible or fails with image-guided biopsy. It is important to review imaging studies properly before planning any form of surgical treatment to prevent costly and risky procedures. Most patients with pancreatic tuberculosis respond well to anti-tuberculosis drugs. However, if the tuberculous mass is enlarged or causes symptoms even after anti-tuberculosis drugs have been consumed for certain period of time, minimally invasive procedures can be done such as endoscopic internal drainage. Surgery intervention is often required in pancreatic tuberculosis where a diagnosis is not established with percutaneous or EUS guided approaches.

Authors' contributions

Yusuf SA, Raraswati A, Koesnadi MI wrote the review article. Maulahela H conducted the review and editing the contents of the article.

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