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Vascular invasion does not discriminate between pancreatic tuberculosis and pancreatic malignancy: a case series

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Abstract

Background Pancreatic tuberculosis is very rare and most commonly involves the head and uncinate process of the pancreas. It closely mimics pancreatic malignancy and is often diagnosed after pancreatico-duodenectomy. Vascular invasion is believed to be a hallmark of malignant lesions and described as a point of differentiating benign lesions from malignant lesions. We herein retrospectively evaluated the patients with pancreatic tuberculosis seen at our unit over the last 4 years for features of vascular invasion.

Methods We retrospectively analyzed the collected database of all patients diagnosed with pancreatic tuberculosis at our unit over the last four years and identified patients who had evidence of local vascular invasion and their clinical and imaging findings were retrieved.

Results Over the last four years, 16 patients (12 males) with pancreatic tuberculosis were seen and five of these 16 patients had imaging features of vascular invasion by the pancreatic head mass. Of these five patients, four were males and the mean age was 32.0±5.47 years. Of these five patients, three had involvement of portal vein and superior mesenteric vein and two had involvement of hepatic artery.

Conclusion Presence of vascular invasion does not distinguish pancreatic tuberculosis and malignancy, and, therefore, cytopathological confirmation is mandatory to differentiate between the two.

Keywords Endoscopic ultrasound, tuberculosis, pancreas

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Introduction

Pancreatic tuberculosis is very rare and most commonly involves the head and uncinate process of the pancreas [1]. The clinical and imaging features of pancreatic tuberculosis closely mimic a resectable pancreatic cancer and therefore many cases of pancreatic tuberculosis have been diagnosed after histopathological examination of the resected specimens obtained after Whipple's surgery for presumed pancreatic head malignancy [1,2]. Endoscopic ultrasound (EUS) is an excellent imaging modality for evaluation of pancreatic lesions because of high resolution images obtained by a closely placed transducer. However, we have previously shown that none of the EUS features of a mass lesion caused by pancreatic tuberculosis are distinctive and therefore cytological examination is mandatory to differentiate it from resectable pancreatic head malignancy [1].

Local vascular invasion is often considered to be an imaging feature of malignant lesions and may indicate unresectability. Vascular invasion is not usually seen in benign lesions and is considered a feature of malignancy. Vascular invasion has also not been usually reported in patients with pancreatic tuberculosis. One study on 19 patients with pancreatic tuberculosis did not find vascular invasion in any of these patients and therefore suggested that absence of vascular invasion in pancreatic head mass lesion could suggest a diagnosis of pancreatic tuberculosis [3]. However, we have previously reported two cases of pancreatic tuberculosis with local vascular invasion [4,5]. We retrospectively evaluated the patients with pancreatic tuberculosis seen at our unit over the last 4 years for features of vascular invasion and present a

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Conflict of Interest: None

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series of 5 cases of pancreatic tuberculosis with local vascular invasion.

Patients and methods

We retrospectively analyzed the collected database of all patients diagnosed with pancreatic tuberculosis at our unit over the last four years. The diagnosis of pancreatic tuberculosis was established on a basis of clinical features, radiologic findings, cytological findings and improvement in symptoms with anti-tubercular therapy (ATT). All patients had undergone contrast-enhanced computed tomography (CT) of the chest and abdomen. We identified patients who had evidence of local vascular invasion on CT and their clinical and imaging findings were retrieved. Since these pancreatic head lesions closely mimicked pancreatic malignancy, all the patients had also undergone positron emission tomography CT (PET-CT) for the purpose of staging.

EUS was performed after informed consent using the linear scanning echoendoscope (EG-3870 UTK linear echoendoscope Pentax Inc, Tokyo, Japan or GF-UCT 180; Olympus, Tokyo, Japan). The examination sought details about the size, location, appearance of the lesion with any lymphadenopathy, vascular invasion and calcifications. The diameter of the common bile duct and pancreatic duct were also noted. EUS-guided fine needle aspiration (EUS-FNA) was performed from the lesion and material obtained was immediately sent for cytopathological examination. The extrapancreatic lesions, if present were also sampled: celiac or mediastinal lymph nodes under EUS guidance and hepatic lesions under transabdominal ultrasound guidance.

The patients were treated with weight-based four drug anti-tubercular therapy (isoniazid 5 mg/kg/day, rifampicin 10 mg/kg/day, pyrazinamide 25 mg/kg/day, and ethambutol 15 mg/kg/day) and were followed-up for disappearance of symptoms and radiological improvement. As we had previously shown that pancreatic tuberculosis patients with cholestatic symptoms had resolution of their symptoms with ATT alone and had no need for biliary stenting, all these patients were also treated with ATT alone [1]. It was decided to place a biliary stent only if there was intractable pruritus, cholangitis, or worsening of cholestatic symptoms after starting ATT.

Results

Over the last four years, 16 patients (12 males) with pancreatic tuberculosis were treated at our unit and 5 of these 16 patients had imaging features of vascular invasion by the pancreatic head mass. Of these 5 patients, 4 were males and the mean age was 32.0±5.47 years (Table 1). The presentation in all patients was abdominal pain of varying duration without any associated fever or night sweats. Of these 5 patients, 4 had cholestatic jaundice but none had cholangitis. All patients had associated loss of appetite and 4 patients had loss of weight. All patients were negative for human immunodeficiency virus and none of the patients had any clinical or radiologic findings of extrapancreatic tuberculosis. Also, blood sugar was normal in all these 5 patients.

On evaluation peripancreatic lymphadenopathy was present in 3 patients. Other lymph nodes involved were celiac, precaval, supraclavicular, portal, paraaortic, internal mammary and mediastinal lymph nodes (Fig. 1 and 2). Two patients had isolated pancreatic lesions without associated lymphadenopathy and the pancreatic duct was dilated in 2 patients. In one patient (case 4) the presence of hepatic lesions further caused diagnostic confusion with metastatic pancreatic malignancy. However, ultrasound guided FNA from the hepatic lesions also revealed granulomatous inflammation confirming the diagnosis of tuberculosis. The cytological analysis of the aspirated material revealed granulomatous inflammation in all the patients whereas caseous necrosis was seen in 3/5 (60%) patients. None of the patients had acid-fast bacilli seen on Ziehl-Neelsen staining. No complications of EUS-FNA were noted.

On PET-CT, the pancreatic mass lesions, liver lesions as well as the lymph nodes were intensely fluorodeoxyglucose (FDG) avid with SUV Max value ranging from 6 to 22 (Fig. 3). Interestingly all these patients had evidence of invasion of vascular structures also causing diagnostic confusion with locally advanced or metastatic pancreatic malignancy. Of these 5 patients, 3 had involvement of portal vein and superior mesenteric vein, and 2 had involvement of hepatic artery (Table 1). The diagnosis of vascular invasion was confirmed both on CT and EUS (Fig. 4). Intraabdominal collaterals because of splenoportomesenteric vessel involvement were seen in two patients but none of the patients had esophagogastric varices.

All the patients were treated with standard 4 drug anti-tubercular therapy and showed response with disappearance of pain and jaundice within 2 weeks and liver function tests

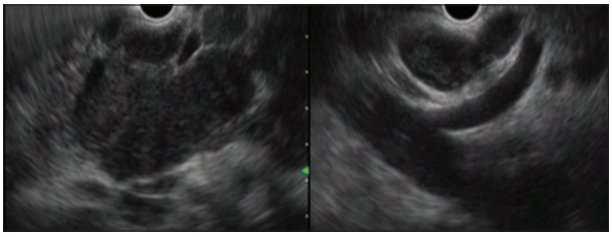

Figure 1 Endoscopic ultrasound: Mass if the head of pancreas (Left). Celiac axis lymph nodes (Right)

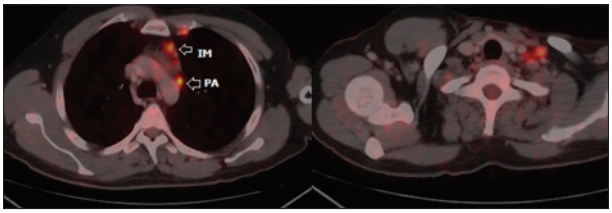

Figure 2 Positron emission tomography computed tomography: Left paraaortic (PA) and internal mammary (IM) lymph nodes (Left image). Left supraclavicular lymph node (Right image)

Table 1 Five cases with vascular invasion due to pancreatic tuberculosis

Case	1	2	3	4	5
Age	40	28	32	34	26
Gender	F	M	M	M	M
Pain	Y	Y	Y	Y	Y
Fever	N	N	N	N	N
Bilirubin (mg/dL)	16.2	0.8	4.2	8.2	4.8
Location	Head	Head and body	Head and uncinate	Head and body	Head
Vessel involved	Portal vein	Superior mesenteric vein, hepatic artery	Superior mesenteric Vein	Portal vein, superior mesenteric vein and artery, hepatic artery	Portal vein
Lymph nodes	No	Peripancreatic and precaval	Peripancreatic, portal, precaval, celiac, mediastinal, left internal mammary and left supraclavicular	Peripancreatic	No
PD dilatation	Y	N	N	Y	N
Cytology	Granulomatous inflammation, stain for AFB negative	Granulomatous inflammation, stain for AFB negative	Granulomatous inflammation, stain for AFB negative	Granulomatous inflammation, stain for AFB negative	Granulomatous inflammation, stain for AFB negative

F, Female; M, Male; Y, Yes; N, No; AFB, Acid fast bacilli; EUS, Endoscopic ultrasound; PD, Pancreatic duct

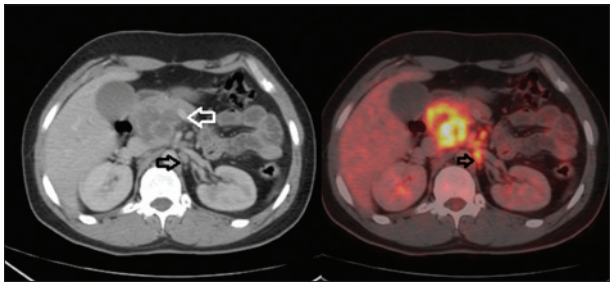

Figure 3 Left Image: Mass with hypodense necrotic areas in head of pancreas. It is seen closely abutting the superior mesenteric vein (white arrow). Small paraaortic lymph node is also seen (black arrow). Right image: corresponding positron emission tomography image showing intense fluorodeoxyglucose uptake

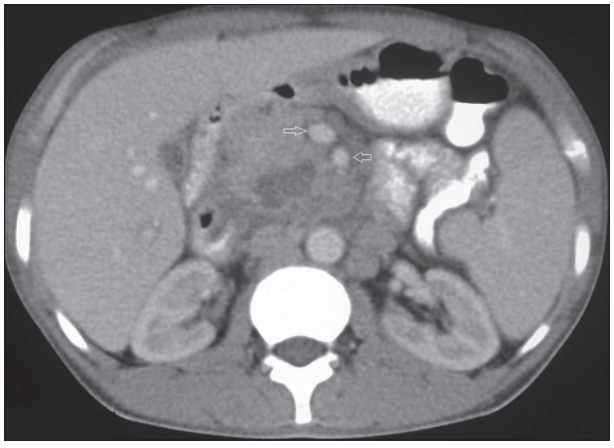

Figure 4 A large mass in the head of pancreas encasing superior mesenteric artery and vein (arrows)

normalized within 2-16 weeks. These patients underwent abdominal ultrasound at 16-20 weeks of starting ATT and complete resolution of the mass was seen in all 5 patients. Moreover, the vessels that were seen on initial imaging to be infiltrated by the mass were found to be normal on follow-up ultrasound. However, intraabdominal collaterals seen initially could also be seen on follow-up imaging. The hyperbilirubinemia improved with anti-tubercular therapy alone and no biliary interventions were needed. No toxicity of ATT was observed in any patient.

Discussion

Pancreatic tuberculosis is an uncommon condition usually seen in developing countries but has also been reported with increased frequency from western world [6]. It usually afflicts the region of the head of the pancreas and is often misdiagnosed as pancreatic malignancy and may result in unwarranted pancreatic resections [1,2]. Even on EUS, pancreatic tuberculosis is not distinguishable from pancreatic malignancy and presents as hypoechoic lesions as in malignancy [1]. Even on FDG-PET, tuberculosis closely mimics pancreatic malignancy and the standardized uptake values can be as high as those for malignant lesions [1,7]. Vascular invasion of the abdominal vessels is often regarded as a feature of locally advanced malignancy. One of the studies has reported this as a point of distinction between pancreatic tuberculosis and pancreatic malignancy [3].

Previously, only a few case reports have recognized vascular involvement in patients with pancreatic tuberculosis [4,5,8]. In the present series, both arterial as well as venous involvement was observed in patients and 2 of 5 patients with splenoportomesenteric vessel involvement had intraabdominal collaterals, thereby suggesting significant vessel involvement leading on to impairment of venous circulation. Also, all

patients had excellent response with resolution of pain and jaundice with standard weight-based anti-tubercular therapy. Moreover, the involved vessels appeared normal on follow-up imaging.

As there are no distinctive clinical, laboratory or radiological features including vascular invasion for distinguishing pancreatic tuberculosis from pancreatic cancer, histopathological or cytological confirmation is necessary for establishing the diagnosis of pancreatic tuberculosis. Percutaneous imaging or EUS-FNA sampling for staining, cytology, bacteriology, culture and polymerase chain reaction assay is essential for establishing the diagnosis of pancreatic tuberculosis [1,9,10]. The microscopic features of tuberculosis observed on cytology are caseation necrosis, granuloma and presence of acid fast bacilli. In our earlier study we found that the majority of patients with pancreatic tuberculosis (83.3%) had granulomas with acid fast bacilli being seen in only 1 of 6 (16.7%) and culture for *Mycobacterium tuberculosis* being positive in 1 of 2 patients (50.0%) tested [1].

Another important and controversial issue is the question of identifying patients with pancreatic head mass who should undergo EUS-FNA. It is widely accepted that patients with unresectable mass or patients who are poor surgical candidates should undergo FNA before deciding upon radiotherapy or chemotherapy [11]. However, the issue of doing FNA in patients with resectable pancreatic head mass is more controversial. The proponents of not doing FNA argue that tissue diagnosis is not going to alter the management and therefore is not necessary and will also put the patients at risk of complications. Their argument is further supported by the fact that the sensitivity of EUS-FNA ranges from 85-90% and thus having up to 15% false negative results [11]. The supporters of doing FNA argue that histological diagnosis before surgery may alter management as certain disorders like lymphoma, small cell metastasis, and tuberculosis do not need surgery. They also suggest that EUS-FNA offers the opportunity to visualize the pancreatic mass, judge its relation with surrounding vessels, and also obtain a tissue diagnosis without the risk of tumor seeding along the needle tract as well as with very low complication rates [12]. Moreover, some surgeons and patients would like to have a definitive diagnosis of malignancy before undergoing major surgical resections. We feel that the practice of doing EUS FNA in resectable pancreatic head masses should be based upon local experience and FNA may be avoided in patients having a clinical setting of pancreatic adenocarcinoma. But, the centers with high frequency of pancreatic tuberculosis especially the ones in tropical countries like ours should adopt the practice of doing FNA in all cases as there are no distinctive clinical, laboratory or radiological features for distinguishing pancreatic tuberculosis from pancreatic cancer and a correct pre-operative histological diagnosis can avoid unnecessary surgery.

In conclusion, pancreatic tuberculosis is a potential mimic of invasive pancreatic malignancy and the presence of vascular invasion does not distinguish one condition from the other.

Summary Box

What is already known:

- Pancreatic tuberculosis is very rare condition that commonly involves head and uncinate process of the pancreas
- The clinical and imaging features of pancreatic tuberculosis closely mimics that of resectable pancreatic cancer
- Local vascular invasion is often considered to be an imaging feature of malignant lesions

What the new findings are:

- Both arterial as well as venous involvement can be seen in patients with pancreatic tuberculosis
- Vascular invasion cannot exclude possibility of benign pancreatic diseases like tuberculosis

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