

CASE REPORT

Isolated Pancreatic Tuberculosis Diagnosed by Endoscopic Ultrasound-Guided Fine Needle Aspiration: A Case Report

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ABSTRACT

Context Pancreatic tuberculosis is an extremely rare clinical entity, despite the high prevalence of tuberculosis worldwide. The pancreas is protected from direct environmental exposure; therefore most cases of pancreatic tuberculosis arise from contiguous infection from peri-pancreatic lymph nodes or rarely from hematogenous spread. Pancreatic tuberculosis can present as a cystic or solid pancreatic mass mimicking pancreatic malignancy. Diagnosing pancreatic tuberculosis is a clinical challenge and most cases are diagnosed after surgical exploration for presumed pancreatic cancer. Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is being used more frequently for imaging and sampling of pancreatic lesions. Immediate cytopathologic examination of tissue sampled by EUS increases the diagnostic yield and is standard in many institutions.

Case report Herein, we describe the case of a woman with a pancreatic mass subsequently diagnosed with pancreatic tuberculosis via EUS-FNA. Intraprocedural immediate cytologic evaluation prompted samples to be sent for appropriate microbiological culture.

Conclusion This case demonstrates the importance of real-time on-site cytopathology input during EUS-FNA procedures.

INTRODUCTION

Pancreatic tuberculosis is an extremely rare clinical entity, especially in immunocompetent individuals. In most instances, it occurs in the setting of disseminated or miliary tuberculosis. Tuberculosis of the pancreas may mimic malignancy by presenting as a solid or mixed solid/cystic lesion on imaging studies. Diagnosis usually is made on surgical exploration. Herein, we describe a case of isolated primary pancreatic tuberculosis in an otherwise healthy adult woman. Diagnosis of pancreatic tuberculosis was made using EUS-FNA.

CASE REPORT

A 71-year-old African-American woman with hypertension presented to her primary care physician with mild epigastric discomfort and back pain. Her symptoms started insidiously 3 weeks prior to presentation and were unrelated to meals or bowel movements. She denied fever, jaundice and nausea. The back pain was worse when lying supine. Ibuprofen and famotidine did not relieve her symptoms. Physical examination was unremarkable with a benign, non-tender abdomen and no localized spinal tenderness. Initial laboratory evaluation revealed a mild normocytic anemia (hematocrit: 31.4%; reference range: 34.1-43.3%). Serum electrolytes, blood urea



Figure 1. CT scan image revealing a large hypodense mass involving the head and neck of the pancreas and seemingly invading the left lobe of the liver.

nitrogen (BUN), creatinine, bilirubin, transaminases, amylase and lipase were normal. Alkaline phosphatase was minimally elevated (193 IU/L; reference range: 40-125 IU/L). Thoracic and lumbar spine X-rays were unremarkable. The patient was treated empirically with omeprazole (20 mg/day) and advised to stop ibuprofen.

She returned to her primary care physician 3 weeks later with a 8 kg weight loss, malaise, and continued epigastric and back pain. A computed tomographic (CT) scan of the abdomen and pelvis was performed revealing a large complex heterogeneous mass (6.8x8.4 cm) in the neck of the pancreas that appeared to invade the liver (Figure 1). The mass



Figure 2. Endoscopic ultrasound guided fine needle aspiration of the pancreatic mass.

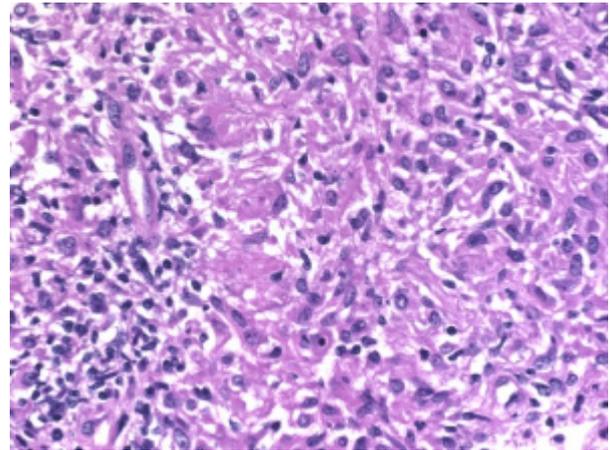


Figure 3. Cell block prepared from the pancreatic fine needle aspirate demonstrating granulomatous inflammation including histiocyte aggregates, lymphocytes and neutrophils (hematoxylin and eosin, 400x).

encased the portal vein and hepatic artery; the superior mesenteric vessels and splenic vein were patent. There was no evidence of pancreatic duct or bile duct dilatation. The patient was referred to an oncologist given concern for an unresectable pancreatic cancer. A CT-guided biopsy was performed revealing atypical cells with an inflammatory component, but no definitive evidence of malignancy.

The patient was then referred for EUS-FNA for a tissue diagnosis. EUS revealed a large, heterogeneous mass with poorly defined margins (Figure 2) that appeared to displace the left hepatic lobe rather than invade it. The lesion appeared atypical for a primary pancreatic neoplasm. EUS-FNA was performed with immediate cytologic interpretation revealing granulomatous inflammation (aggregates of epithelioid histiocytes, lymphocytes and plasma cells) (Figure 3). Given the preliminary cytologic findings, additional FNA samples were obtained and sent for mycobacterial and fungal stains and culture.

The final cytologic reading reported granulomatous inflammation without evidence of malignancy. Stains for acid fast bacilli and fungal organisms were negative. The patient refused any additional evaluation at that time. Five weeks later, acid fast bacilli were cultured from the FNA sample and



Figure 4. CT scan image showing resolution of pancreatic mass after three months of anti-tubercular treatment.

identified as *Mycobacterium tuberculosis* by deoxyribonucleic acid (DNA) probe.

The patient was referred to an infectious disease expert. Chest X-ray was normal and a CT scan of the chest did not reveal pulmonary nodules or lymphadenopathy. An abdominal CT scan did not reveal any other intra-abdominal pathology except the complex pancreatic mass as mentioned above. There was no evidence to suggest disseminated or pulmonary tuberculosis and she was diagnosed to have isolated primary pancreatic tuberculosis. She was not immunosuppressed and serological testing for human immunodeficiency virus (HIV) infection was negative. There was no history of travel to endemic areas. Interestingly, a few of the patient's classmates in grade school had died of tuberculosis. This remains the only known exposure.

Anti-tubercular treatment was initiated with four drug therapy (isoniazid, rifampin, pyrazinamide, ethambutol) pending sensitivities. The *Mycobacterium tuberculosis* isolate returned resistant to ethambutol; therefore, she continued on a three drug regimen for two months after which she received isoniazid and rifampin for total treatment duration of six months. Three months into treatment, the pancreatic mass had disappeared on repeat CT imaging (Figure 4). She tolerated the treatment well,

gained weight, and was asymptomatic 4 months after completing therapy.

DISCUSSION

Almost one third of the world's population is infected with *Mycobacterium tuberculosis*, claiming approximately 2 million lives per year. After years of decline, the number of tuberculosis cases in the United States increased 20% from 1985 to 1992, likely related to the acquired immune deficiency syndrome (AIDS) epidemic. In 2003, the tuberculosis prevalence in the United States was 5.1/100,000 population. In the United States, most cases occur in foreign-born persons as compared to US-born persons with a prevalence of 23.4/100,000 population vs. 2.7/100,000 population, respectively [1].

Abdominal tuberculosis is uncommon, in the past accounting for 12% of tuberculosis cases in the United States [2]. Abdominal tuberculosis usually affects the bowel, particularly the ileo-cecal area but can also occur in the liver, spleen and mesenteric lymph nodes [3, 4]. Pulmonary and abdominal tuberculosis co-exist in only 5-36% of patients [5].

Pancreatic tuberculosis is extremely rare even in countries with high endemism. Bhansali, in a 300 case review of surgically confirmed abdominal tuberculosis in India, found no cases of pancreatic tuberculosis; the majority involved the alimentary canal (196/300, 65.3%), whereas the remaining (104/300, 34.7%) involved lymph nodes or the peritoneum [3]. Most cases of pancreatic tuberculosis appear to occur in the setting of miliary tuberculosis, as supported by two large reviews. Auerbach did not find any cases of isolated pancreatic tuberculosis in 1,656 autopsies performed on tuberculosis-infected patients. Two-hundred ninety-seven patients (17.9%) in his series had acute generalized miliary tuberculosis, with 14 of these (4.7%) having tubercular involvement of the pancreas [6]. In another review of 526 autopsies of patients with miliary tuberculosis, pancreatic involvement was found in only 11 cases (2.1%) [7].

Fewer than 40 cases of isolated pancreatic tuberculosis have been reported. The rarity of this infection is supported by several observations. The pancreas is uniquely situated in the retroperitoneum, protected from direct environmental exposure. Purified lipases, pancreatic extracts, and DNAses appear to have antimycobacterial effects [8, 9]. Thus, the pancreas is relatively resistant to mycobacterial invasion, requiring a large intrapancreatic inoculum of *Mycobacterium tuberculosis* to cause pancreatic lesions [10]. The two postulated routes of spread are directly from involved peripancreatic lymph nodes and more rarely from hematogenous spread.

Common clinical manifestations include abdominal pain (75%) and anorexia with weight loss (69%). Approximately 50% of patients with pancreatic tuberculosis have fever and night sweats, whereas back pain and jaundice occur less commonly (31-40%) [11]. Infrequently, pancreatic tuberculosis may present as acute pancreatitis with radiographic findings of pancreatic enlargement and edema [12, 13]. Other rare manifestations include obstructive jaundice, gastrointestinal bleeding via direct invasion of a peripancreatic artery, pancreatic abscess, chronic pancreatitis, diabetes, and splenic vein thrombosis [14, 15, 16, 17, 18]. Laboratory abnormalities include anemia, lymphocytopenia, elevated erythrocyte sedimentation rate, elevated transaminases, and alkaline phosphatase seen in approximately 50% of cases [11].

Radiographically, complex cystic lesions are reported more frequently than solid masses. Findings that may suggest mycobacterial infection include the presence of rim-enhanced lymph nodes in the peripancreatic region or the mesentery, ascites, and a thickened bowel wall in the ileo-cecal region [19, 20]. As the clinical and radiographic presentation mimics pancreatic cancer, preoperative diagnosis of pancreatic tuberculosis is rare. Most reported cases have been diagnosed via laparoscopic biopsy or at laparotomy. Percutaneous (ultrasound or CT-guided) FNA has more recently diagnosed pancreatic tuberculosis, however there are

less than 10 reported cases worldwide [21, 22]. This may be due to the fact that acid fast bacilli are rarely seen on FNA specimens and culture of *Mycobacterium tuberculosis* requires prolonged incubation. Additionally, as percutaneous FNA is usually performed for the suspicion of pancreatic cancer, the FNA sample is not routinely sent for mycobacterial stain and culture.

EUS-FNA has emerged as an excellent tool to both image and sample pancreatic lesions [23]. It is the most sensitive and specific method to identify pancreatic masses, and the American Joint Commission on Cancer now recommends EUS-FNA as the preferred diagnostic modality for pancreatic masses [24]. The presence of an on-site cytologist for immediate interpretation is common practice in most high volume EUS centers [25]. On-site cytologic evaluation has been shown to increase the diagnostic yield by 10-15% [26, 27, 28] and can decrease procedure time and potential complications through avoidance of unnecessary needle passes once diagnostic tissue is obtained.

The patient presented was felt to have unresectable pancreatic cancer. Her ultimate diagnosis was isolated primary pancreatic tuberculosis based on imaging and a positive culture of an EUS-FNA sample. On-site cytology feedback was crucial to the successful outcome of this case, as immediate interpretation of the FNA sample directed the appropriate cultures, and ultimate curative therapy. To our knowledge, this is the first reported case of isolated primary pancreatic tuberculosis diagnosed by EUS-FNA.

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