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Coexistence of pancreatic tuberculosis with systemic brucellosis: a case report

Case Report

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Abstract: Isolated pancreatic tuberculosis is an extremely rare clinical entity and is difficult to diagnose particularly in immunocompetent individuals. Clinical findings and symptomatology of brucellosis are often similar to tuberculosis thus making the differentiation amongst the two entities difficult. We report a case of pancreatic tuberculosis with systemic brucellosis in a 29 year old veterinarian who presented with epigastric pain and loss of appetite. Initial investigations revealed leukocytosis with moderately elevated transaminase, gamma glutamyl transferase, amylase and lipase levels. Imaging studies revealed an anechoic multiloculated cyst in the body and tail of the pancreas. Given the patient's occupational risk coupled with the presence of a positive Brucella agglutination test (with a titer of 1:320); a diagnosis of pancreatitis secondary to brucellosis was given. In addition to standard pancreatitis therapy of bowel rest with intravenous fluid/electrolyte replacement, anti-brucellosis therapy was also administered. The patient's initial response to therapy was positive however, 6 weeks into therapy, his abdominal pain recurred and repeat CT scan revealed the development of a pseudocyst in the pancreas. After failing a second attempt at conservative supportive therapy, the patient underwent an explorative laparotomy. Histological examination of the resected pancreatic specimen showed necrosis and was positive for tuberculosis by polymerase chain reaction. Herein, we describe the first case reported in the medical literature of the coexistence of systemic brucellosis with pancreatic tuberculosis. We suggest that the possibility of the coexistence of brucellosis with tuberculosis be kept in mind when assessing pancreatitis patients in endemic regions and in individuals with occupational risk hazards.

Keywords: *Pancreatitis • Tuberculosis • Brucellosis*

1. Introduction

Extrapulmonary tuberculosis frequently poses a diagnostic challenge due to its vague clinical features and ability to mimic other diseases [1,2]. Of all the possible extra-pulmonary tuberculosis manifestations, pancreatic tuberculosis is amongst the rarest manifestation, particularly in an immunocompetent host. This particular form of the disease has a low index of suspicion amongst physicians and lack of specific clinical features [3-6].

Brucellosis is a systemic disease in which any organ system of the body can be involved. Clinical findings, symptomatology and the histopathologic signs of brucellosis are very similar to tuberculosis, thus, differentiating the two entities may be difficult.

Here, we discuss a patient who presented with pancreatic tuberculosis and concurrent systemic

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brucellosis. To our knowledge and upon extensive review of the medical literature, this is the first case report of the coexistence of systemic brucellosis with pancreatic tuberculosis.

2. Case Report

A 29 year old male veterinarian presented with epigastric pain and loss of appetite. He was from a region in Central Turkey endemic for brucellosis and tuberculosis. The patient had no history of tobacco use, alcohol abuse and had no family history of pancreatitis. In addition, the patient had no history of tuberculosis or brucellosis.

The current symptomatology had started 3 weeks prior to presentation with abdominal pain, nausea and loss of appetite. The patient described the pain as continuous, moderate in intensity, without radiation or intensification with change of posture. There had been no fever, vomiting, hematemesis or hematochezia. On admission, the patient's vital signs revealed a body temperature of 37.5˚C, heart rate of 95 bpm, respiratory rate of 18/min and arterial blood pressure of 130/80 mmHg. Physical examination revealed diffuse epigastric tenderness on palpation with mild abdominal distention. There was no evidence of rebound tenderness, guarding, hepatosplenomegaly, ascites, icterus or other signs of jaundice. The rest of the physical examination was unremarkable.

Laboratory analysis revealed a mild, normocytic anemia (hemoglobin: 11.1 g/dl; reference range (RR): 13.5-16 mg/dl, hematocrit: 32.3%; RR: 34.1-43.3%) and an increased white blood cell count of 19 600 mm^3 (RR: 4 000-10 000 mm^3) with 89% neutrophils, 7% lymphocytes, 3% monocytes, 1% eosinophils. Liver function tests revealed mild elevations in serum aspartate amino transferase (AST) of 55 (RR: 5-40) and alanine amino transferase (ALT) of 64 (RR: 5-40). Serum bilirubin was 1.3 mg/dl (RR: 0.2-1.0 mg/dl), conjugated fraction 0.77 mg/dl (RR: 0.01-0.3 mg/dl). Alkaline phosphatase was 102 U/L (RR: 35-125 U/L) and gamma glutamyl transferase was 78 U/L (RR: 10-45 U/L). Serum amylase was high at 123 U/L (RR: 17-115 U/L) and the lipase was high at 76 U/L (RR: 0-60 U/L).

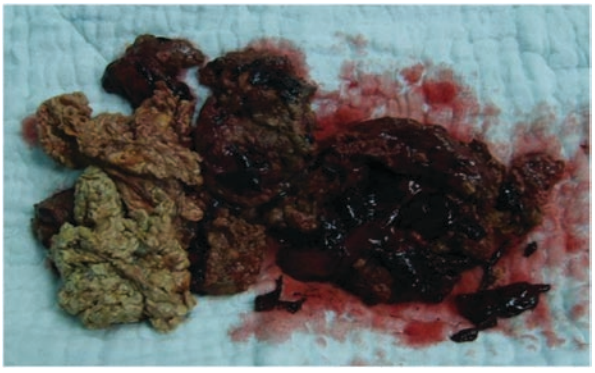
An ultrasonogram was performed and the liver, gallbladder, portal vein and biliary system were found to be normal. The pancreatic head was 48 mm in size with echogenic features consistent with acute pancreatitis. A 6×10 cm anechoic multiloculated cystic lesion was visualized in the region of the body and the tail of the pancreas consistent with a pseudocyst. A computed tomographic (CT) scan of the abdomen and pelvis revealed a 10×10.5×8 cm complex cystic mass on the anterior part of the pancreas. Based on these findings, a diagnosis of pancreatitis with pseudocyst formation was made and an antibiotic (imipenem 500 mg I.V. qid) was started along with supportive care. Serologic testing for Cytomegalovirus, Epstein-Barr virus, Rubella virus, HIV, Hepatitis B and Hepatitis C virus was performed and all were negative. The serum agglutination test for Brucella was positive at a titer of 1:320 however blood cultures failed to grow the organism. Because of the patient's occupational risk coupled with the positive Brucella agglutination test, a diagnosis of pancreatitis secondary to brucellosis was made.

As a result, the antibiotic regimen was changed to doxycycline, 100 mg orally every 12 hours, and streptomycin, 1 g I.M. daily. Two days into therapy, the patient displayed clinical improvement. He remained afebrile, abdominal pain significantly decreased and by the 7th day of hospitalization his amylase and lipase levels returned to the normal range. He was subsequently discharged after 2 weeks of hospitalization with streptomycin and doxycycline for ongoing anti-brucellosis therapy.

After 42 days of anti-brucellosis treatment, the patient returned to the hospital for an outpatient follow-up evaluation and was noted to have a 10 kg weight loss along with nausea, vomiting, moderate abdominal tenderness and the development of icterus. An ultrasonogram was repeated at this time and revealed a slightly larger pancreatic head at 50 mm with similar echogenic features of ongoing acute pancreatitis. A 15×10 cm anechoic multiloculated cystic lesion was seen in the region of the body and the tail of the pancreas. A CT scan of the abdomen and pelvis revealed a complex cystic mass on the anterior part of the pancreas consistent with an increase in size of the original pseudocyst. The CT scan also revealed the presence of splenomegaly as well as lymphadenopathy adjacent to the hepatogastric ligament. A second Brucella agglutination test was positive, however at a lower titer of 1:160.

After surgical consultation and discussion of the case in interdisciplinary rounds, it was decided that the patient undergo cystogastrostomy and cholecystectomy. Polymerase chain reaction (PCR) testing for tuberculosis was performed on intra-operative histologic samples of the cystic lesion and were found to be positive. Cystic fluid cultures remained negative for tuberculosis as well as fungal and bacterial growth. Extensive evaluation for pulmonary tuberculosis was negative on CT scans as well as bronchoalveolar lavage. Based on these results the patient was diagnosed with isolated primary pancreatic tuberculosis. A four drug anti-tubercular regimen was started with isoniazid, rifampicin, pyrazinamide and

Figure 1. The pancreas in cross section after the necrosectomy revealing caseating necrosis.



streptomycin. On post-operative day 16, the patient developed an episode of bright red hematemesis which required an emergency esophagogastroduodenoscopy (EGD). Due to unremarkable EGD findings, an exploratory laparotomy was performed revealing blood, caseating material and necrosis in the retroperitoneum. The hematoma was drained and in the right paracolic region, caseating granulomas were noted. Due to ongoing hemorrhage resulting in hemodynamic compromise, the patient expired intra-operatively despite aggressive resuscitation measures. During autopsy the pancreas was found to be necrotic (Figure 1).

3. Discussion

Tuberculosis is systemic disease with protean manifestations caused by *Mycobacterium tuberculosis*. Approximately 15% of cases involve extrapulmonary sites [1,2]. Abdominal tuberculosis is an uncommon site of extrapulmonary infection and it is seen in 12% of patients with miliary tuberculosis [1,2]. Abdominal tuberculosis usually affects the ileocecal region, abdominal lymph nodes and peritoneum [2]. Infection of the pancreas by *M. tuberculosis* is extremely unusual in immunocompetent individuals even in miliary tuberculosis. Bahansali, in a review of 300 surgically confirmed abdominal tuberculosis cases in India, found no cases of pancreatic involvement [7]. Auerbach reported pancreatic involvement in up to 4.7 of cases among 297 autopsy patients with miliary tuberculosis [8]. Up to now, the review of the medical literature has reported close to 50 cases of pancreatic tuberculosis. The rarity of this infection may be attributed to the presence of pancreatic enzymes that hinder the seeding of *M. tuberculosis* to the pancreas [3,4]. In addition, the retroperitoneal positioning of the pancreas may be a protective factor against direct environmental exposure. The pathogenesis of pancreatic tuberculosis remains speculative and may involve: 1) Pancreatic involvement during miliary disease, 2) Hematogenous dissemination from an occult site elsewhere (possibly the lungs) or 3) Direct spread from contiguous lymph nodes [4,6].

Pancreatic tuberculosis may present with a wide variety of manifestations, including fever, abdominal pain, anorexia, weight loss, obstructive jaundice, acute or chronic pancreatitis and gastrointestinal hemorrhage [3-6,9-11]. The nonspecific symptomatology and lack of clinical findings therefore, make the clinical diagnosis of pancreatic tuberculosis practically impossible. Radiographically, pancreatic enlargement, edema, abscess and complex cystic lesions are seen [4,9,12,13]. However, these radiographic findings are also nonspecific. Since the clinical and radiographic presentations are nonspecific and often mimic pancreatic cancer, preoperative diagnosis is rare [14-16]. Laboratory findings are also nonspecific for tuberculosis involving the pancreas, thus, the diagnosis of pancreatic tuberculosis is usually based on histopathologic and microbiologic testing [3-6,9]. However, it must be remembered that bacteriologic confirmation may not be possible in many patients. PCR is a highly specific assay and may give a positive result even when special staining techniques and cultures of these lesions are negative [5].

Similar to tuberculosis, brucellosis remains a major infectious disease problem in Turkey. Human brucellosis generally occurs by ingestion of unpasteurized dairy products or through the consumption of undercooked meat from cattle, sheep, goat or swine. It is an occupational disease affecting individuals with exposure to the organism through work with livestock or animal products. It is characterized by a variety of often nonspecific clinical symptoms of fever, myalgia, and general malaise [17]. It may also manifest with localized disorders of specific organs or tissues. As in tuberculosis, the pancreas is a rare target organ for brucellosis. The clinical features of brucellar pancreatitis and that of pancreatic tuberculosis are no different than pancreatitis due to other etiologies [18,19]. As was the case in our patient, the occupational risk coupled with positive Brucella agglutination titers enabled us to strongly consider the diagnosis of pancreatitis secondary to brucellosis. We attributed blood culture negativity for *Brucella spp*. to the fact that the patient had been on broad spectrum antibiotics in the recent past. Tuberculosis was not considered initially as the patient had an occupational risk along with positive serologies for Brucella. Thus, anti-brucellosis therapy was started. However, despite drops in his Brucella agglutination titer to 1:160 during the 4th week of treatment, other diagnostic possibilities were entertained as the patient's

clinical course and radiological findings worsened. Because of the patient's worsening clinical status in the setting of an unclear exact etiology of his necrotizing pancreatitis, an exploratory laparotomy was undertaken. Up to that point, the patient's preliminary diagnosis was pancreatitis attributed to brucellosis; however, upon discovery of *M. tuberculosis* by PCR from intra-operative pancreatic pseudocyst fluid, the diagnosis was changed accordingly to isolated pancreatic tuberculosis with coexisting systemic brucellosis.

In conclusion, we suggest that although uncommonly seen, the coexistence of brucellosis with tuberculosis should be kept on the differential diagnosis in endemic regions and in patients with associated risk factors for brucellosis, particularly in complicated pancreatitis cases. With such cases where pancreatitis appears to keep recurring, or with clinical worsening despite standard therapy or with the development of loculated fluid and/or pseudocyst formation, one should keep an index of suspicion, particularly if the patient fits the profile. If definitive diagnosis has not been achieved, molecular and histologic evaluation would be warranted by invasive means such as fine needle aspiration, or if necessary by exploratory laparotomy.

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