CASE REPORT

Acute Pancreatitis Associated with Brucellosis

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ABSTRACT

Context Acute pancreatitis can be caused by a variety of infectious agents but it is regarded as an extremely rare complication of brucellosis.

Case report We briefly describe a 56-year-old man who presented with acute pancreatitis, fever, myalgia, and other clinical symptoms. *Brucella melitensis* was cultured from his blood. All clinical manifestations gradually resolved with the institution of intramuscular streptomycin and oral doxycycline therapy.

Conclusion Acute pancreatitis may rarely be a complication of infection with *B. melitensis*. In areas where brucellosis is endemic, it should be kept in mind that acute pancreatitis may result from infection with brucella organisms.

INTRODUCTION

Brucellosis is a disease of domestic and wild animals that is transmittable to humans (zoonosis). It is a systemic infection in which any organ or system of the body can be involved [1]. Acute pancreatitis associated with *Brucella* infection is extremely rare and only four cases have been reported in the literature until now [2, 3, 4, 5]. We wish to briefly describe the occurrence of acute pancreatitis in a patient with documented brucellosis along with a review of the literature on this rare complication of brucellar systemic infection.

CASE REPORT

A previously healthy 56-year-old man presented with a week-long history of fever, generalized myalgia and arthralgia, low back pain, anorexia and sweating. A few hours before admission he experienced a sudden onset of abdominal pain accompanied by nausea and vomiting. He had no history of previous similar attacks, alcohol abuse, cholelithiasis, parotitis or skin rashes, abdominal trauma or surgery, or ingestion of raw milk or medications. The patient was a stock-breeder and lived in an area of Northwestern Greece where brucellosis is endemic. On admission, his vital signs were as follows: arterial blood pressure 125/80 mmHg, heart rate 95 min^{-1}, respiration rate 18 min^{-1}, and body temperature 38.6°C. Physical examination revealed diffuse epigastric tenderness and mild abdominal distension, but no rigidity, organomegaly or ascites. Bowel sounds were diminished and digital rectal examination was normal. Other physical findings were unremarkable. Hematological tests revealed a normal hematocrit and platelet count, and an increased white blood cell count of 12,800 mm^{-3} (reference range:

4,000-10,000 mm^{-3}) with 82% polymorphs, 16% lymphocytes, 1% eosinophils and 1% monocytes. Renal function tests and a lipid profile were normal. Liver biochemistry revealed slightly increased aminotransferases (alanine aminotransferase 85 U/L (ALT: reference range: 0-35 U/L) and aspartate aminotransferase 68 U/L (AST: reference range: 0-35 U/L). Serum amylase levels were markedly increased (880 U/L; reference range: 25-115 U/L) and urine amylase levels were 2,400 U/L (reference range: 0-400 U/L). A urine sediment test was normal. A chest X-ray and an electrocardiogram were also normal. Abdominal ultrasonography showed a normal gallbladder, liver, and common bile duct. The pancreas was poorly imaged due to the presence of intra-abdominal gases. A subsequent computed tomography (CT) scan revealed the presence of mild swelling of the pancreas without any additional abnormality. Repeated viral antibody screening (including cytomegalovirus, mumps, Epstein-Barr virus, herpes simplex viruses I and II, HIV I and II, hepatitis A, B and C viruses and echoviruses) was all negative as were serological tests for mycoplasma, *Leptospira*, *Legionella*, and toxoplasmosis. A purified protein derivative (PPD; Mantoux) skin test was negative. *Brucella* agglutinins were present in a titer of more than 1/1,280. Blood and urine cultures for common organisms were negative, but a blood culture grew *B. melitensis* after 8 days of incubation.

The patient was initially placed on intravenous fluids and parenteral cefamandol and metronidazole. On the second hospital day, at which time the result of serum agglutination for brucellosis became available, the antibiotic regimen was changed to doxycycline, 100 mg orally every 12 hours, and streptomycin, 1 g i.m. daily. Three days later, the patient felt much better. He had a normal temperature on the sixth hospital day and the abdominal pain gradually lessened. He resumed oral feeding following a low fat diet. Serum amylase levels returned to the normal range on the seventh hospital day. After completing a two-week course of streptomycin therapy, the patient was discharged on doxycycline 100 mg twice daily for a further 4 weeks. A follow-up 2 months after discharge indicated no evidence of active brucellosis. The patient was symptom-free, his serum amylase was normal and serum agglutination for brucellosis was 1/80. The patient completed doxycycline therapy without experiencing any adverse effects.

DISCUSSION

Acute pancreatitis may have diverse etiologies, most commonly, biliary stones and alcoholism. Pancreatitis may be secondary to viral and bacterial infection or parasitic infestation [6, 7]. Common viruses associated with acute pancreatitis include mumps, hepatotropic viruses, coxsackieviruses and echoviruses [7, 8]. Bacterial agents include *Mycoplasma pneumoniae*, *Salmonella* , *Shigella* , *Campylobacter* , hemorrhagic *Escherichia coli*, *Legionella* and *Leptospira* [6, 9]. Pancreatitis associated with these infections is most likely secondary to released toxins [6]. Usually, acute pancreatitis is not the primary manifestation of these infections. Direct involvement of the pancreas or ampulla with parasites, including *Ascaris lubricoides*, *Clonorchis sinensis*, *Cryptosporidium* and *Toxoplasma*, is a common cause of pancreatitis in some populations [3, 6, 7].

Gastrointestinal symptoms are noted in 40% of patients with brucellosis with anorexia, weight loss, constipation and abdominal pain being the most common [2]. Abnormal gastrointestinal findings are present in 12% of patients, where hepato-splenomegaly is the most common [2]. Abdominal pain is usually mild and vague. Occasionally, severe brucellar gastrointestinal localizations such as brucellar hepatitis with abscess formation, splenic abscess, spontaneous rupture of the spleen, cholecystitis, peritonitis, intestinal obstruction or perforation, erosive colitis and pancreatitis, may present with localized and intense abdominal pain [2, 10].

In the 1930s and 1940s, brucellar localization in the pancreas was an autopsy finding and

was rarely reported in patients in whom active brucellosis was present [2]. In recent years, the disease has been described in four single case reports of *B. melitensis*-induced pancreatitis. Madkour and Karawi were the first to report a case of acute brucellar pancreatitis [2]. Al-Awadhi *et al*. reported the second case [3], followed by Aleman *et al*. and Odeh and Oliven [4, 5]. In Madkour's series of 500 patients with active brucellosis, acute pancreatitis occurred in only one patient (0.2%) [2]. No cases of acute pancreatitis were reported among the 100 patients who were diagnosed with brucellosis at the University Hospital of Ioannina in Northwestern Greece and whose cases were followed for at least one year [1]. Also, in a prospective study of 530 patients with brucellosis in Spain, there were no cases of brucellar pancreatic involvement [11]. These data highlight the rarity of this complication in the course of brucellar infection.

Clinical features of brucellar pancreatitis are similar to those of pancreatitis due to other causes [2, 3]. Systemic features of active brucellosis and other brucellar localizations may precede the development of pancreatitis [2, 3, 4, 5]. The abdomen is tender with decreased bowel sounds and variable degrees of rigidity. The serum amylase level is significantly elevated and there may be a slight increase in serum aminotransferase levels possibly due to coexistent hepatic involvement. Abdominal imaging studies may reveal a diffusely enlarged pancreas. In all four cases reported, blood cultures for *Brucella* organisms were positive for *B. melitensis,* and *Brucella* agglutinins were significantly raised. This was also true in our case. It is hypothesized that pancreatitis associated with brucellosis results from hematogenous infection or reflux of infected bile into the pancreatic duct [3].

The clinical diagnosis of brucellosis can be difficult because of varying presentations, and a high index of suspicion is needed in order to reach the correct diagnosis. It is important to obtain a detailed history which includes occupation, avocations, travel to or living in enzootic areas, and ingestion of high-risk foods, such as unpasteurized dairy products. In most cases of active infection, the standard agglutination tests are positive at titers of 1/160 or higher [12, 13]. The brucella enzyme-linked immunoabsorbent assay (ELISA) is the most sensitive and specific serologic assay, and it may be positive when other tests are negative [13, 14]. The diagnosis is made with certainty when *Brucellae* are recovered from the blood, bone marrow or other tissues [13]. The rate of isolation ranges from 15% to more than 90% depending on the method used [15]. Incubation of blood cultures for 3 or more days may be required. Most laboratories now use continuous monitoring automated blood culture systems (e.g. BACTEC or BacT/Alert) which have improved the time to isolation [13]. Recently, a test using a polymerase chain reaction (PCR) has been developed. This test is promising for the detection and rapid diagnosis of the *Brucella* species in human blood cultures [16]. A PCR test for samples other than blood has also been described [17]. A combination of PCR-ELISA testing appears to be a highly sensitive and specific method for diagnosis [18]. The wide application of these tests will aid in diagnosing brucellar infection and its local complications rapidly and efficiently.

Management of the patient with acute brucellar pancreatitis includes supportive therapy with infusion of intravenous fluids, nasogastric tube suctions, analgesia and antibiotic treatment of active brucellosis using a two-drug regimen (e.g. streptomycin or netilmicin for 15-30 days and doxycycline or rifampicin for 8-12 weeks) [2]. The response to treatment was favorable in all four cases reported in the literature. Our patient recovered completely with a regimen consisting of streptomycin for 2 weeks and doxycycline for 6 weeks.

CONCLUSION

In conclusion, acute pancreatitis is a rare manifestation of active brucellosis. It is prudent to evaluate all patients presenting with symptoms and signs suggestive of acute

pancreatitis for brucellosis, especially in areas where the disease is endemic.

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