

SPONTANEOUS BACTERIAL PERITONITIS AND CHYLOTHORAX RELATED TO BRUCELLA INFECTION IN A CIRRHOTIC PATIENT

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Brucellosis can affect almost all organ systems in humans. Digestive symptoms have been reported in several series. Brucella infection is a chronic systemic disease, particularly in which there is reticuloendotelial system involvement. It can cause rarely hepatitis, cholecystitis or pancreatitis in the gastrointestinal tractus. Brucella infection can rarely cause spontaneous bacterial peritonitis. Although a variety of clinical presentations and complications involving various organ systems has been reported, peritoneal involvement is a very rare presentation. There has been no reported case of massive chylothorax in a cirrhotic patient due to brucellosis in the literature. This report presents a case of spontaneous bacterial peritonitis and chylothorax caused by *Brucella melitensis*.

Key words: *Brucella melitensis*, chylothorax, spontaneous bacterial peritonitis

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INTRODUCTION

Brucellosis, a common widespread zoonosis, especially in countries of the Mediterranean region, is a multisystemic infectious disease with a wide range of clinical symptoms. It is known that *Brucella* infection is a systemic disease, but rarely, it may also cause local infections in the gastrointestinal system (i.e. hepatitis, cholecystitis, pancreatitis or colitis) (1-2). *Brucella* infections present in two clinical forms: acute and chronic brucellosis, which may resemble a number of diseases. The most prominent symptoms of acute brucellosis are fever, chills, headache, backache and myalgia or arthralgia. Splenomegaly is usually present and the liver may be palpable. A variety of clinical presentations and complications of brucellosis involving various parts of the body have been reported.

Spontaneous bacterial peritonitis (SBP) is a serious complication of cirrhosis which is seen in 15-20% of advanced cases. The most common pathogenic organisms of SBP are *Escherichia coli* and *Klebsiella pneumoniae*. *Brucella* is an extremely rare cause of peritonitis. Herein, we report an interesting case of cirrhosis complicated with chylothorax and ascites, from both of which *Brucella melitensis* were isolated.

CASE

A 60 year-old women was admitted to our hospital with complaints of abdominal pain, weakness, dyspnea, diffuse body pain and abdominal distention. She had a history of cirrhosis for five years. Although there was no history of animal keeping, eating fresh cheese and milk products were identified. On physical examination, her body temperature was 38.7°C, pulse 96/minute, and blood pressure 120/80 mmHg. Pulmonary examination revealed dullness with decreased breath sounds and fremitus over the right lung base. There was 2/6 systolic murmur. Diffuse dullness suggesting ascites was identified in the abdomen. On X-ray of chest we noticed pleural effusion in the medial and basal zones of the right lung and the shift of mediastinum to left. Diagnostic thoracentesis and paracentesis were performed. Bedside inoculation of blood culture bottles were performed.

Laboratory analyses were as follows: hemoglobin 9.3 g/dL, white blood cell count 9600/mm³ and platelet count 81000/mm³. Abnormal biochemical findings were blood urea nitrogen: 49 mg/dL, creatinine: 1.45 mg/dL, albumin: 2.7 g/dL, total bilirubin: 2.8 mg/dL, direct bilirubin: 2.1 mg/dL, alkaline phosphatase: 173 IU/L, gama-glutamyl transpeptidase: 123 IU/L. The prothrombin time was 18 seconds (INR: 1.5). Aspartate aminotransferases, Alanine aminotransferase, lactic dehydrogenase, serum total cholesterol,

triglyceride and urinary analysis were normal. Creatinine clearance was 24 mL/minute. Uremia was investigated by the nephrologists and attributed to prerenal azotemia. Erythrocyte sedimentation rate was 90 mm/hour and C-reactive protein was 46 mg/L (normal: 0-6 mg/L).

Ascitic fluid findings were as follows: gross appearance was transparent yellow, leukocytes 380 /mm³ (with 65% lymphocytes), LDH: 13 IU/L, triglyceride: 45 mg/dL, total protein: 0.33 gr/dL, albumin 0.22 gr/dL. Serum ascites albumin gradient (SAAG) was 2.48 gr/dL. The gross appearance of pleural fluid was milky and the characteristics were as transuda. The leukocyte number was 6000/ml and there was neutrophil dominancy in the pleural fluid. The Acid-fast bacillus (AFB) was negative. The level of triglyceride was 161 mg/dl. In the cytologic investigation of pleural fluid many polymorphonuclear leukocytes, erythrocytes and small amounts of lymphocytes and mesothelial cells were identified. Because of massive and symptomatic pleural effusion, the fluid was drained by thorax tube. In the sputum analysis AFB was negative and no culture was positive (including tuberculosis). Computed tomography of thorax did not demonstrate any pulmonary parenchymal pathology. The HCV antibody was positive and the patient has been followed as cirrhosis for about five years. The hepatitis B virus serology, autoimmune markers and other etiologies of cirrhosis were negative. Esophageal varices and severe portal hypertensive gastropathy were observed during upper GI endoscopy and abdominal ultrasonography revealed an atrophic nodular liver, splenomegaly and tense ascites with the portal vein thrombosis and cavernous transformation.

Because of the diffuse body pain and fever Brucella agglutination test was performed. Brucella serology showed a positive slide test, micro-agglutination titer of 1/1280. On the fourth day of admission, gram-negative coccobacilli were noted in blood culture bottles inoculated from both ascites and pleural effusion and on the sixth day, they were identified as *Brucella melitensis*. The 20 mCi ^{99m}Tc-MDP radionuclide scans of whole body bone were normal.

Ciprofloxacin (500 mg bid) and rifampin (300 mg a daily) was prescribed for six weeks for the treatment of Brucellosis. A week later, the patient's condition had improved and she became afebrile.

DISCUSSION

Defects in the host defense mechanism play a major role in the pathogenesis of SBP. There are frequent infections in cirrhotic patients, as their defenses against infectious agents are altered, and bactericidal and opsonic activities in the ascites of cirrhotic patients are reduced. Although *E. coli* and *K. pneumonia* are the most common etiological organisms, a few unusual organisms such as *Yersinia enterocolitica*, *Listeria monocytogenes* and *Brucella melitensis* may cause SBP (3-4). Most cases were associated with chronic liver disease or other underlying conditions such as continuous ambulatory peritoneal dialysis (5). Brucellosis is a zoonosis and almost all infections derive directly or indirectly from animal exposure. Human brucellosis is diagnosed on the basis of epidemiological and clinical findings and bacteriological and serological tests. Symptoms of the disease may mimic many of the diseases and show varied manifestations of acute and chronic infection. Complications of brucellosis sometimes may lead to misdiagnosis. Brucellosis exists worldwide especially in the Mediterranean basin, the Arabian Peninsula, the Indian subcontinent, in parts of Mexico and Central and South America (6). Brucellosis is endemic in some parts of our country, especially in the central Anatolian region. It is a multisystem infection that may present with a broad spectrum of clinical presentations. The most frequent symptoms are fever, chills or rigors, malaise, generalized ache, headache and fatigue. *Brucella* is usually caused by ingestion of unpasteurised dairy products or infected raw liver. Once *Brucella coccobacilli* are ingested, they enter the lymphatic system via the gastrointestinal system. A hematogenous dissemination ensues and is then followed by colonization of *Brucella* in reticuloendothelial cells of liver, spleen, lymph nodes, bone marrow and kidney. *Brucella* rarely causes infections in the gastrointestinal system such as hepatitis, cholecystitis, colitis and pancreatitis (7-8). SBP due to *Brucella* is extremely rare (9-10). Ten cases of brucella peritonitis are reported, 3 of which were culture negative. To our knowledge, this is the 11th reported case of culture-proven SBP caused by *Brucella melitensis* in a cirrhotic patient. Our patient had not only cirrhosis and SBP caused by *Brucella melitensis*, but also had massive chylothorax (possibly hepatic hydrothorax) with positive culture for brucella. There has been no reported case of massive chylothorax

in a cirrhotic patient due to brucellosis in the literature.

Pleural effusion (>500mL) in a cirrhotic patient without primary cardiac or pulmonary disease is defined as hepatic hydrothorax (HH) (11). Precipitating factors for HH are decreased colloid osmotic pressure due to hypoalbuminemia, increased azygous vein pressure due to the collaterals between portal and azygous system, fluid leakage from thoracic duct by lymphatic flow, fluid oozing from abdominal cavity to pleural cavity by channels and diaphragm, and direct leakage of pleural fluid from diaphragm (12-13). In our case diaphragmatic defect seemed to be responsible from pleural effusion since ascites and pleural cultures revealed *B. melitensis*. We suggested that this microorganism infected peritoneal fluid initially and then reached pleural space through a diaphragmatic defect. HH is seen in %1-10 of cirrhotic patients. It is reported as %67-85 in right pleura, %13-17 in left pleura and % 2-17 bilaterally (14-15). Dumont, et al has detected increased lymphatic flow in thoracic duct in cirrhotic patients with ascites (16). Peritoneal fluid may leak into pleural space from thoracic duct, diaphragmatic lymphatic channels and diaphragmatic defects.

Chylothorax, the presence of chyle in the pleural space, is commonly associated with nontraumatic etiologies. Diagnosis of chylothorax is established via direct analysis of the pleural fluid. Although the classic milky or opalescent appearance of the pleural fluid is highly suggestive, Staats et al. showed that less than 50% of chylothoraces have this characteristic feature (17). Measurement of triglycerides has become the standard, with a level above 110 mg/dl nearly diagnostic (17). A pleural fluid triglyceride level of > 110 mg/dL or the presence of chylomicrons in the pleural fluid defined the presence of chylothorax (18). In our case pleural fluid was milky, pleural fluid triglyceride concentration was higher than serum triglyceride and was 161 mg/dL. With these findings chylothorax is diagnosed.

Although there is no such consensus about the duration of treatment for *Brucella* peritonitis, we treated our patient with ciprofloxacin and rifampin for 6 weeks. Doxycycline and streptomycin was not given because of impairment of renal and hepatic functions.

In conclusion, *Brucella* may cause SBP and spontaneous bacterial pleuritis in cirrhotic patients with ascites and pleural effusion.

Brucella peritonitis is a rare clinical form of brucellosis. It should be considered especially in endemic regions, and appropriate serological and microbiological tests should be performed to confirm the diagnosis.

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