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Klebsiella pneumoniae Septic Arthritis in a Cirrhotic Patient with Hepatocellular Carcinoma

Despite septic arthritis is increasingly being reported in elderly patients with diabetes or alcoholism, reported cases of spontaneous bacterial arthritis in cirrhotic patients are extremely rare. We present the first reported case of *K. pneumoniae* septic arthritis and spontaneous bacterial peritonitis in a cirrhotic patient with hepatocellular carcinoma. *K. pneumoniae*, one of the most common causative organisms of spontaneous bacterial peritonitis in cirrhotic patients, was isolated from both the blood and the joint fluid, which suggests that the route of infection was hematogenous. After the treatment with cefotaxime and closed tube drainage, the condition of the patient was improved, and subsequently, the joint fluid became sterile and the blood cultures were proved negative. Therefore, this case provides further evidence for the mode of infection being bacteremia in cirrhotic patients and suggests that the enteric bacteremia in cirrhotics may cause infection in different organ systems.

Key Words : *Arthritis, Infectious; Liver Cirrhosis; Carcinoma, Hepatocellular; Klebsiella pneumoniae*

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INTRODUCTION

Septic arthritis is usually of hematogenous origin and is increasingly reported in elderly patients who often have underlying medical conditions such as diabetes, malignancy, chronic renal failure, rheumatoid arthritis, alcoholism, stem cell transplant recipients, and AIDS (1, 2). Although spontaneous bacterial peritonitis is a frequent and serious complication in cirrhotic patients with ascites, spontaneous bacterial arthritis is a rare complication of bacteremia in cirrhotic patients (3, 4). We describe the first reported case of a 65-yr-old patient with liver cirrhosis and hepatocellular carcinoma who developed *Klebsiella pneumoniae* septic arthritis and peritonitis.

CASE REPORT

A 65-yr-old woman presented to the emergency room with right knee arthralgia. The patient had suffered from pain in the right knee for 4 hr. The patient had been well until about 4 yr earlier, when liver cirrhosis developed. Two years ago, the patient received a diagnosis of hepatocellular carcinoma, which was managed with 4 times of percutaneous ethanol injection therapy. The admitting temperature was 38.8℃, pulse rate 84/min, respiration rate 20/min, and blood pressure 100/60 mmHg. On physical examination, the patient appeared icteric. There were no abnormal findings in the chest. The abdomen was distended; a fluid wave and a mild splenomegaly were noted, but the liver was not palpable. The right knee joint was swollen, and the tenderness was noted in palpation. Laboratory investigations revealed a hemoglobin of 10.6 g/dL, a white cell count of 9,100/μL with 75.5% polymorphoneuclear leukocytes (PMNs), and a platelet count of 78,000/μL. The erythrocyte sedimentation rate (ESR) was 98 mm/hr. The prothrombin time was 24.2 sec (3.2 in international normalized ratio), and the partial thromboplastin time was 56.9 sec (vs. a control of 35 sec). The blood chemistry were AST 91 IU/L, ALT 75 IU/L, alkaline phosphatase 181 IU/L, total bilirubin 7.24 mg/dL, direct bilirubin 3.39 mg/dL, albumin 2.8 g/dL, BUN 17.5 mg/dL, creatinine 0.9 mg/dL, sodium 126 mEq/L, and potassium 4.5 mEq/L. The hepatitis B surface antigen was positive. Antihepatitis C viral antibody was negative. Alpha-fetoprotein was 189.1 ng/mL.

Aspiration of the ascites revealed a xanthochromic fluid with total WBC count 620/μL (PMN 490/μL), red blood cell 250/μL, and albumin 0.7 g/dL. Serum ascites albumin gradient was 2.1 and ascites culture was negative. Aspiration of the right knee joint revealed a turbid fluid with a white cell count of 22,900/μL (95% PMNs) and Gram stain showed Gram-negative bacilli. The patient received treatment with cefotaxime 4 g/day intravenously. In addition, the patient received arthroscopic irrigation with closed tube drainage. *Klebsiella pneumoniae* grew subsequently from the joint fluid and the blood. Susceptibility of the isolate was determined with the disk diffusion method and it was susceptible to cephalothin, gentamicin, amikacin, ampicillin-sulbactam, ticarcillin-clavulata, piperacillin-tazobactam, cefozitin, ciprofloxacin, imipenem, trimethoprim-sulfamethosazole, aztreonam,

and ceftazidime, as well as to cefotaxime, the antibiotics that the patient was on. The patient responded to the antibiotic therapy and closed tube drainage. The condition of the patient slowly improved, and subsequently, joint-fluid cultures were sterile.

Abdominal computerized tomography showed multi-nodular hepatocellular carcinoma (a 2.8 cm enhanced nodule in the anterior superior segment of right lobe, and a 2.8 cm enhanced nodule in the medial segment of left lobe) with the intact portal vein.

Despite resolution of the infection, the patient's liver function was deteriorated. The patient developed progressive jaundice, azotemia, and hepatic coma and died on the thirty-first day after the admission. Autopsy was refused.

DISCUSSION

We present a case of spontaneous bacterial arthritis and spontaneous bacterial peritonitis in a cirrhotic patient with hepatocellular carcinoma. *K. pneumoniae* was isolated from both the blood and the joint fluid, suggesting that the route of infection was hematogenous. Despite the use of sensitive methods, ascites culture is negative among approximately 40% of the patients with clinical manifestations suggestive of spontaneous bacterial peritonitis (SBP) and increased ascites PMNs (5-8). The condition of the increased PMN count in ascites and negative culture has been known as a variant of SBP, since the short- and long-term course of patients with either condition is the same (6, 7, 9). The low proportion of positive ascites cultures is probably due to the relatively low concentration of bacteria in ascites, compared to infections in other body fluids (3).

SBP develops in about 8% of the cirrhotic patients with ascites. It is particularly frequent, if the cirrhosis is severely decompensated. The risk of developing SBP is greater in those with a coexisting gastrointestinal bleeding, a previous episode of SBP or low ascitic protein levels (3, 10). SBP is blood-borne and in 90% monomicrobial. The causative organisms are mainly of intestinal origin with representatives of the normal aerobic flora. Gram-negative aerobic bacteria from the family of Enterobacteriaceae and non-enterococcal *Streptococcus* spp. are the most common organisms isolated from ascites. The three most common isolates are *Escherichia coli*, *Klebsiella pneumoniae* and the pneumococci. It is proposed that these enteric organisms cross the intestinal mucosal barrier to the mesenteric lymph nodes (a process known as bacterial translocation) and enter the systemic bloodstream via the thoracic duct. Animal models have confirmed that bacterial translocation is involved in the pathogenesis of SBP (10).

Another manifestation of the bacteremia resulting from the bacterial translocation is spontaneous bacterial empyema (SBEM). Xiol et al. reported that most episodes of SBEM in cirrhotics was not associated with SBP (11), suggesting that infected ascites diffusing across the diaphragm is not the mechanism involved and supporting the possibility of bacterial translocation. The bacteremia seen in cirrhotics may also be responsible for the increased incidence of bacterial endocarditis (12). There has also been a report of bacterial meningitis in cirrhosis (13). Taken together, these cases suggest that the enteric bacteremia that is seen in cirrhotics may cause infection in several different organ systems.

The incidence of septic arthritis in the elderly has doubled in the last 40 yr, although the incidence is still low (0.005-0.006%) (1, 14). Goldenberg et al. emphasized the role of local as well as systemic factors in predisposing to Gram-negative bacterial joint infections (15). It is known that joint trauma and arthritic conditions increase the risk of septic arthritis (1). Underlying medical conditions such as diabetes, malignancy, chronic renal failure, alcoholism, rheumatoid arthritis, stem cell transplant recipients, and AIDS have been associated with an increased incidence of septic arthritis (1, 2). This is believed to be related to an underlying immunocompromised state.

Spontaneous bacterial arthritis is a rare complication of bacteremia in cirrhotic patients (4). The knee joint is the most commonly affected, while the shoulder, sternoclavicular joint, and ankle may also be involved. The most commonly implicated bacteria are *E. coli* and *Streptococcus agalactiae*. There have been cases of *Staphylococcus aureus* and *Plesiomonas shigelloides* (4, 16-22). In our case, *K. pneumoniae* was isolated from the joint fluid, which is one of the most common isolates from ascites in patients with SBP. According to a review of the English literature, *K. pneumoniae* septic arthritis in the elderly is uncommon (1, 23). Therefore, we postulate that the patient's knee effusion became seeded during primary *K. pneumoniae* bacteremia of enteric origin related to liver cirrhosis.

In conclusion, the fluid-filled peritoneum of the cirrhotic provides an impaired local immune response resulting in bacterial peritonitis, and, in a similar manner, the fluid-filled knee joint in our patient provided an impaired local immune response, resulting in a Gram-negative bacillary arthritis. The case we present is the first description of *K. pneumoniae* septic arthritis and spontaneous bacterial peritonitis developing in the course of a primary enteric bacteremia in a cirrhotic patient with hepatocellular carcinoma.

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