Alerts, Notices, and Case Reports

Spontaneous Group B Streptococcal Meningitis in a Patient With Cirrhosis

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GROUP B STREPTOCOCCI (*Streptococcus agalactiae*) are the leading cause of sepsis and meningitis in neonates.[1,2] The importance of invasive group B streptococcal infections in adults has been increasingly recognized.[3,4] The most common sites of adult infection are skin or soft tissue, blood (bacteremia) with no identifiable source, urinary tract, and lungs (pneumonia).[5] Group B streptococcal meningitis in adults is relatively rare and often associated with underlying medical conditions such as diabetes mellitus, cancer, renal failure, cardiac disease, steroid use, and collagen vascular disease.[6,7] To our knowledge, there has been no previous case of group B streptococcal meningitis reported in an adult with advanced liver disease.

We present the case of a patient with cirrhosis due to chronic hepatitis C infection in whom spontaneous group B streptococcal meningitis developed. This case shows the susceptibility of cirrhotic patients to unusual infections and the ease with which bacterial meningitis might be mistaken for hepatic encephalopathy in a patient with advanced liver disease.

Report of a Case

The patient, a 52-year-old man, was brought to the emergency department after being found confused and agitated. He had a known history of biopsy-proved cirrhosis due to chronic hepatitis C infection and previous admissions for hepatic encephalopathy. The patient had been well until three days before admission, when he had right upper quadrant pain, diarrhea, and vomiting. Increasing shortness of breath and increasing lethargy subsequently developed. The morning of admission, the patient was found agitated and unresponsive.

On arrival at the emergency department, the patient was confused, agitated, and jaundiced. He was afebrile but was noted to have tachycardia, hypertension, and tachypnea. Brudzinski's and Kernig's signs were absent. His lungs were clear, and cardiac examination revealed a grade II/VI systolic murmur at the left lower sternal border. Abdominal examination revealed no distension or obvious ascites. There was no abdominal tenderness and no hepatomegaly. The spleen tip was palpable in the left upper quadrant. On mental status examination, the patient was awake, but wildly agitated and combative. He moved all extremities spontaneously and had symmetric deep tendon reflexes. Rectal examination showed Hemoccult-positive brown stool.

Laboratory values included a leukocyte count of 16.7 $\times$ 10^9 cells per liter (16,700 cells per mm^3), of which 0.73 (73%) were neutrophils and 0.20 (20%) were lymphocytes. The hematocrit was 0.32, and the platelet count was 51 $\times$ 10^9 per liter (51,000 per mm^3). A serum sodium level was 134 mmol per liter; potassium, 4.5 mmol per liter; chloride, 104 mmol per liter; bicarbonate, 16 mmol per liter; blood urea nitrogen, 18.0 mmol per liter (51 mg per dl); and creatinine, 150 μmol per liter (1.7 mg per dl). The serum bilirubin level was 128 μmol per liter (7.5 mg per dl); serum aspartate aminotransferase, 62 U per liter (normal, 10 to 29); and serum alanine aminotransferase, 40 U per liter (normal, 6 to 27). A prothrombin time was 19 seconds (normal, 11 to 13.6), and a venous ammonia level was 42 μmol per liter (71 μg per dl; normal, 0 to 35 μmol per liter). Arterial blood gas values with the patient receiving supplemental oxygen at 4 liters per minute showed a pH of 7.39, a P_{CO_2} of 29 mm of mercury, and a P_{O_2} of 94 mm of mercury.

Orogastric aspirate revealed Gastroccult-positive dark material without gross blood. The patient's altered mental state was initially ascribed to hepatic encephalopathy exacerbated by gastrointestinal bleeding, and a regimen of lactulose enemas was started. The patient was agitated out of proportion to that usually seen with hepatic encephalopathy, however, and with concomitant leukocytosis, the diagnosis of bacterial meningitis was considered. He was intubated for airway protection and given ceftriaxone sodium, 1 gram intravenously. A chest radiograph revealed bilateral upper lobe infiltrates, and a noncontrast computed tomographic scan of the head was unremarkable. A lumbar puncture was done and revealed 50 $\times$ 10^6 erythrocytes per liter (5,000 per mm^3) and 36.75 $\times$ 10^6 leukocytes per liter (3,675 per mm^3), of which 0.88 (88%) were neutrophils and 0.12 (12%) were mononuclear cells. A cerebrospinal fluid (CSF) glucose level was 0.61 μmol per liter (11 mg per dl), and the CSF protein value was 3.4 grams per liter (343 mg per dl).

Cultures of CSF and blood grew group B streptococci sensitive to penicillin. The patient's regimen was promptly switched to intravenous penicillin G, 24 million units per day, but multisystem organ failure rapidly developed, with acute renal failure, hepatic failure, and the adult respiratory distress syndrome. On the ninth hospital day, increasing pulmonary infiltrates developed, and he had worsening oxygenation and progressive hepatic dysfunction. Despite broadening of the patient's antibiotic regimen to cover nosocomial pneumonia, he died on the 15th hospital day. No further cultures grew out group B streptococci.

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Discussion

Group B streptococci are the leading cause of neonatal sepsis and meningitis, with an estimated incidence of 1.8 per 1,000 live births.[2] In adults, the incidence of invasive group B streptococcal infections appears to be increasing. Population-based studies in metropolitan Atlanta, Georgia, have shown an incidence of 4.4 cases per 100,000 nonpregnant adults in 1993, nearly double that of the same population studied retrospectively from six years earlier.[3,5] Older persons are at a substantially increased risk of invasive group B streptococcal infection, with an incidence in those 60 years of age or older of 18 cases per 100,000.[5] A recent multivariate analysis revealed that patients with cirrhosis are also at a significantly increased risk (odds ratio, 9.7) for community-acquired invasive group B streptococcal infection.[4] Other conditions that have been shown to predispose to community-acquired invasive group B streptococcal infection include diabetes mellitus, stroke, breast cancer, decubitus ulcer, and neurogenic bladder.

Of all adult cases of invasive group B streptococcal infection, meningitis accounts for only 3% to 4%.[2,4-6] In all, 52 cases of group B streptococcal meningitis in adults have been reported in the English-language literature from 1966 to the present. A recent review of these cases showed that the average age of patients affected is 54 years, although there appears to be a bimodal distribution with peaks in the third and in the eighth decades of life.[6] Comorbid conditions are associated with adult group B streptococcal meningitis in more than half the cases.[6,7] The precise immunologic mechanisms by which these conditions predispose to invasive group B streptococcal disease have not yet been elucidated. To date, no case of group B streptococcal meningitis has been reported in an adult patient with advanced liver disease.

Patients with chronic liver disease are more susceptible to bacterial infections because of reduced activity of the mononuclear phagocyte system,[8] as well as depressed opsonic activity of serum and ascites.[9] Dysfunction of macrophage Fcγ receptors has been demonstrated in patients with alcoholic cirrhosis and may predispose to bacterial infection.[10] Although complement levels may be normal in chronic liver disease, there are deficiencies in complement activation, opsonization, and neutrophil chemotaxis.[11] Alterations in intestinal flora, gastrointestinal hemorrhage, and frequent invasive diagnostic testing may also play a role in susceptibility to bacterial infections. In a recent prospective study of 170 patients with cirrhosis requiring admission to a hospital, bacterial infections developed in 47%, although no cases of meningitis were found.[12]

The current case illustrates the fact that in a patient with cirrhosis, bacterial meningitis may be easily mistaken for hepatic encephalopathy. This patient was initially thought to have hepatic encephalopathy on the basis of mental status changes associated with known cirrhosis, evidence of gastrointestinal bleeding, and an elevated serum ammonia level. Given his agitation out of proportion to that usually seen with hepatic encephalopathy, however, alternative diagnoses such as bacterial meningitis were considered, and a lumbar puncture was done. The precise source of this patient's bacteremia is unknown. Pneumonia accounts for 12% of cases of group B streptococcal infection,[4] but this organism was not isolated from the patient's sputum. Group B streptococcal peritonitis has been described, but was not suggested by this patient's clinical presentation. In all cases of invasive group B streptococcal infections in adults, the most common finding is bacteremia without an evident source.[4,5]

Despite prompt empiric treatment with antibiotics and appropriate narrowing of the therapeutic regimen to penicillin G when CSF and blood cultures grew out *S agalactiae*, multisystem organ failure developed, and this patient died. This clinical course is consistent with mortality data from the 52 previously reported cases of adult group B streptococcal meningitis. In those cases, the overall mortality was 27%. In patients with associated comorbidity, however, mortality was 45% compared with 0% in patients without associated illness.[5]

Vaccines for group B streptococci are currently being developed.[13] Although much attention has been focused on the application of these vaccines to perinatal care, the increasing incidence of invasive group B streptococcal disease in adults necessitates attention. Further study into the host mechanisms that predispose to group B streptococcal infection may point to subgroups of adults, such as those with cirrhosis, who might benefit from immunoprophylaxis.

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