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CASE REPORT

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Nosocomial meningitis: A case of Bacillus cereus central nervous system infection

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Abstract

We present a case of nosocomial Bacillus cereus meningitis, a rare cause of central nervous system infection with significant morbidity and mortality. While often contaminants, gram positive bacilli in the bloodstream of immunocompromised hosts requires a high index of suspicion to deliver timely antibiotic therapy.

Keywords: *Bacillus; immunocompromised; transplant; leukemia; meningitis*

Case presentation

History

A 35-year-old female from the suburban Midwest with an unremarkable past medical history presented with fatigue, fevers, night sweats, and weight loss over the course of several weeks. Initial laboratory work-up revealed pancytopenia. She was admitted, and a bone marrow biopsy was performed that revealed Philadelphia chromosome-positive B-cell acute lymphoblastic leukemia (B-ALL). She was started on Rituximab, Hyperfractionated Cyclophosphamide, Vincristine, Adriamycin, and Dexamethasone (R-HyperCVAD) in addition to the tyrosine kinase inhibitor, Dasatinib. Prophylaxis included pentamidine inhaled solution and acyclovir.

Her initial fever, presumed malignancy-related, resolved with initiation of chemotherapy. She tolerated the initial several days of chemotherapy well apart from occasional mild transfusion reactions consisting of an urticarial rash. However, on day 3 of therapy, she complained of fever and headache.

Physical exam

On exam, the patient appeared to be in moderate distress and discomfort. Temperature was 101.8°F (38.8°C), blood pressure 78/36 mmHg, pulse 114 beats per minute. She was disoriented and minimally cooperative with exam. She had an anterior tongue ulceration that had been present since admission, as well as mucositis. Her examination was otherwise unremarkable. She had no focal neurologic deficits, signs of meningismus, abdominal tenderness, skin rashes, or new adventitious breath sounds. Her peripherally-inserted central catheter was in place and without signs of infection.

Laboratories

Laboratory studies revealed a white blood cell count of 0.4 K/uL (reference range 4-10 K/uL). A differential was not performed at our institution given leukopenia to less than 0.5 K/uL. Hemoglobin of 7.9 g/dL (reference range 12-16 g/dL). Platelet count of 36 K/uL (reference range 150-400 K/uL). Hepatic function tests significant for aspartate aminotransferase of 53 IU/L (reference range 8-30 IU/L) and alanine aminotransferase of 125 (reference range <= 35 IU/L). Fibrinogen was 136 mg/dL (reference range 150-450 mg/dL). Other routine laboratory tests were normal. A urinalysis was without leukocyte esterase or nitrite. Blood and urine cultures were collected. A chest roentgenogram was obtained without evidence of new cardiopulmonary disease. Preliminary gram stain of the peripheral blood cultures revealed gram-positive bacilli. Rapid DNA sequencing of the peripheral blood was negative for Listeria species. Blood cultures from each of one central and one peripheral site rapidly speciated to Bacillus cereus.

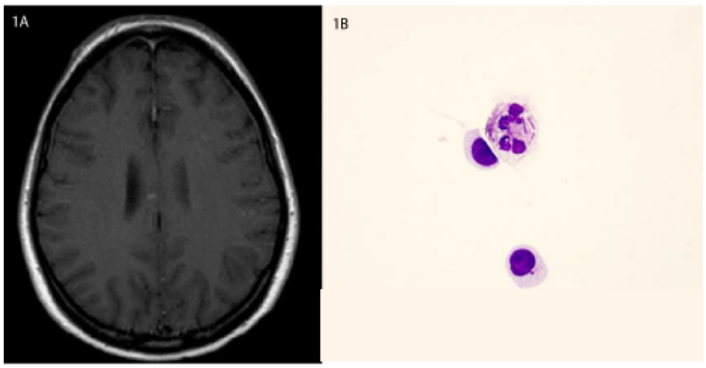

Figure 1. A. MR Brain, leptomeningeal enhancement. B. CSF gram stain, neutrophil containing gram-positive bacilli.

Other studies

Patient obtained magnetic resonance imaging of the brain which revealed: "multiple foci of enhancement and diffusion abnormality likely related to leptomeningeal disease, infectious including unusual bacterial or fungal infection, versus neoplastic in nature" (Figure 1A).

A lumbar puncture was performed. The opening pressure was 27.5 cm H2O (reference range 7-18 cm H_2O). Cerebrospinal fluid (CSF) chemistry analysis revealed protein of 117 mg/dL (reference range 15-45 mg/dL) and glucose of 43 mg/dL (reference range 50-70 mg/dL). Cell count revealed 116 red blood cells and 31 leukocytes. Of the leukocytes, 17% were neutrophils, 81% were lymphocytes, and 2% were histiocytes.

HSV polymerase chain reaction (PCR) of the CSF was negative. Gram stain ultimately revealed few gram-positive bacilli. Pathology review showed no signs of atypical lymphocytes, but revealed neutrophils containing gram-positive bacilli [figure 1B]. Culture yielded no growth. Universal PCR analysis of the cerebrospinal fluid later confirmed the presence of *Bacillus cereus.*

Treatment and course

After her index fever, the patient was given 4 liters of intravenous fluids and started on intravenous cefepime and vancomycin with improvement of her blood pressure and heart rate. After blood cultures revealed gram-positive bacilli negative for Listeria species, the patient was given one dose of intravenous tobramycin. She had an anaphylactic reaction that was successfully treated with intramuscular epinephrine. When blood cultures revealed B. cereus, cefepime was discontinued and intravenous meropenem was added to her antibiotic regimen.

In the following several days, the patient continued to intermittently fever as high as 103.5˚F (39.7˚C). The patient's headache continued to worsen and she became progressively lethargic and more frequently disoriented. An ophthalmologic exam was performed which ruled out retinal involvement of her central nervous system infection. A transthoracic echocardiogram was obtained to rule out endocarditis.

Over the coming week, the patient started to clinically improve. The patient received a total of 6 days of carbapenem therapy, which was discontinued after clinical improvement and susceptibilities returned demonstrating susceptibility to vancomycin. She was continued on vancomycin IV to a goal trough of 15-20 ug/mL for a total of 21 days. With continued antibiotic treatment, she regained her baseline mentation without any neurologic sequelae.

Discussion and conclusion

Bacillus cereus is an aerobic-to-facultative, catalase-positive, spore-forming, gram-positive or gram-variable bacillus. It is a bacterium that has inherent resistance to most beta-lactam antibiotics, including penicillins and cephalosporins. It is often sensitive to vancomycin, aminoglycosides, carbapenems, clindamycin, and chloramphenicol.

It is most commonly associated with an acute gastroenteritis mediated by its toxins. However, in can also cause endocarditis, ocular infections, skin and soft tissue infections, and CNS infection [1]. These systemic infections are more commonly seen in intravenous drug users and immunosuppressed patients. Risk factors for a poor prognosis in a B. cereus blood stream infection include neutropenia, CNS symptoms at onset of fever, and central venous catheter insertion [2].

While rare, CNS infection by B. cereus can be devastating. The mortality is approximately two-thirds [3]. In addition, it can be complicated by intracranial hemorrhage or abscess formation [4-6]. At present, there is insufficient evidence regarding the optimal antibiotic regimen for treatment of B. cereus CNS infection. No prospective trials have been performed and no treatment guidelines exist. However, many studies suggest treatment with vancomycin. Some studies suggest adding a carbapenem or an aminoglycoside to vancomycin to ensure adequate bactericidal activity in the CNS [2,4,6].

The source of the patient's B. cereus infection remains unclear, but several possibilities were proposed. It may have come from the fruits available to her in the hospital, namely bananas, which she ate frequently. In an epidemiologic review of 5 cases of B. cereus CNC infection at Brigham and Women's Hospital, it was thought that the common source may have been fresh fruits [7]. We also considered her mucositis as a point of entry. Finally, her PICC may have represented a source. This was removed to give a line holiday of at least 48 hours. However, catheter tip cultures were negative.

One notable feature of this patient's B. cereus CNS infection was her good outcome. One protective factor may have been the patient's age. Younger patients with B. cereus meningitis tended to have better outcomes [2]. Another protective factor was likely prompt administration of appropriate antibiotic therapy [2-6]. She received vancomycin within several hours after her index fever. While the B. cereus in the patient's blood culture was initially thought to be a contaminant, the intracellular gram positive bacilli appreciated on CSF gram stain significantly heightened our concern. There should be a low threshold to start and continue vancomycin for gram positive bacilli on peripheral blood gram stain in an acutely sick immunocompromised patient. Finally, there exists the possibility that administration of multiple antibiotics with activity against B. cereus may have improved bactericidal activity in the CNS. This is supported by IDSA guidelines that recommend against using Vancomycin as a single agent for community-acquired streptococcal meningitis, despite its activity against the causative organism, as studies have suggested that there is poor entry of vancomycin into the CSF in the setting of steroid use and decreased CNS inflammation [8,9]. However, additional studies should be done to determine the efficacy of administration of multiple antibiotics for the treatment of B. cereus meningitis.

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