Sepsis and Meningoencephalitis Caused by *Bacillus cereus* in a Patient with Myelodysplastic Syndrome

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**Abstract**

We herein report the findings of a case of myelodysplastic syndrome that was complicated by septicemia and meningoencephalitis, both of which were caused by *Bacillus cereus*. In contrast to all of the previous cases of *B. cereus* that have been seen at our institution, this patient did not have any invasive devices, such as a central venous catheter, that could have acted as a conduit for a *B. cereus* infection. Although *B. cereus*-induced meningoencephalitis is often lethal, the immediate treatment with a regimen of antibiotics including vancomycin was effective in eradicating the infection and, therefore, in reversing both the septicemia and the meningoencephalitis.

**Key words:** *Bacillus cereus*, myelodysplastic syndrome, meningoencephalitis, septicemia


**Introduction**

*Bacillus cereus* (*B. cereus*) is a gram-positive, spore-forming, rod-shaped bacterium that is widely distributed in the environment. The *Bacillus* species, with the exception of *Bacillus anthracis*, has often been regarded as contamination when the bacterium is isolated from clinical specimens. However, *B. cereus* is now recognized as a potential pathogen, causing food poisoning and localized wound infections as well as serious infections such as pneumonia, meningitis and septicemia (1). The bacterium produces a variety of extracellular toxins including phospholipase, proteases, hemolysins and enterotoxins (1, 2). Indeed, many cases of *B. cereus*-induced non-gastrointestinal infections have been reported, particularly in immunocompromised patients, intravenous drug users, neonates and patients with intravascular shunts (1, 3, 4). We herein report the findings of a case of hypoplastic myelodysplastic syndrome (MDS) and obsessive-compulsive disorder (OCD), comorbid with severe *B. cereus* septicemia and meningoencephalitis. The infection was eradicated following treatment with a regimen of antibiotics, including vancomycin.

**Case Report**

A 60-year-old man visited our hospital in May of 2011 due to a three-month history of palpitation, dyspnea and general fatigue. A hematological examination revealed pancytopenia: a white blood cell (WBC) count of 0.9×10^9/L, a neutrophil concentration of 0.4×10^9/L, a hemoglobin (Hb) concentration of 4.9 g/dL and a platelet (Plt) count of 30×10^9/L. Bone marrow aspiration revealed the presence of severe hypocellular bone marrow with dysplasia in all lineages, and an increase in the percentage of myeloblasts (13.2%). A chromosomal analysis demonstrated the presence of no abnormal karyotypes. Therefore, we diagnosed this case as hypoplastic myelodysplastic syndrome (refractory anemia with excess blasts-2). The patient also had a history of OCD; therefore, we started him on a daily administration of fluvoxamine maleate (225 mg/day).

Due to his severe anemia and thrombocytopenia, the patient was repeatedly treated with transfusions of both red blood cells and platelets. Although he had suffered from an intermittent headache since the beginning of October 2011, computed tomography (CT) of the brain did not reveal any

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Brain disorders. In late October 2011, however, the patient developed an aggravated headache accompanied by a high fever (approximately 39°C). Therefore, he was taken to our emergency room and immediately hospitalized. His consciousness was clear, and no abnormal neurological signs were found. By that time, however, his neutropenia had significantly progressed (0.01×10^9/L) and his blood showed a positive reaction for procalcitonin (0.71 ng/mL) with a high level of C-reactive protein (CRP) (4.65 mg/dL). These results suggested that he had febrile neutropenia; therefore, he was given cefepime (3 g/day) and micafungin (200 mg/day) as an empirical therapy. However, he rapidly became delirious and his consciousness continued to decline. His temperature rose to 40°C and the level of CRP also markedly increased to 29.0 mg/dL (Figure). We examined the cerebrospinal fluid (CSF) and found that the number of polymorphonucleocytes (239/mm^2) and the protein concentration (116 mg/dL) had increased, but the glucose concentration was depressed (100 mg/dL, serum-glucose: 230 mg/dL). Furthermore, gram-positive rod-shaped bacteria were isolated from his blood culture. Based on these findings, we diagnosed the patient as having bacterial meningitis accompanied by septicemia. Since the bacteria showed Bacillus-like morphological characteristics, we replaced the cefepime treatment with a combination of vancomycin (3 g/day) and ciprofloxacin (600 mg/day). The next day, B. cereus was isolated from each of two sets of blood cultures as the causal bacteria for the septicemia. Although an examination of the CSF clearly revealed that the patient also had bacterial meningitis, we could not isolate B. cereus from the CSF culture. However, magnetic resonance imaging (MRI) of the brain demonstrated a wide edematous lesion that spread over the white matter area of the right hemisphere on both the T2 and the fluid-attenuated inversion recovery images (Figure). The diffusion-weighted imaging showed a reduction of water diffusion, suggesting that the lesion had abscess (data not shown). In addition, the susceptibility-weighted imaging revealed hypo-intense areas along the brain surface vessels that indicated the deposition of hemosiderin (data not shown). These MRI observations were consistent with a diagnosis of meningioencephalitis due to B. cereus (5). Furthermore, there were no other bacteria isolated from the CSF culture. Based on these findings, we concluded that his meningitis was also caused by B. cereus.

The patient’s blood culture became negative for B. cereus following 6 days of treatment with the new course of antibiotics. Furthermore, the levels of polymorphonucleocytes in the CSF became non-detectable at ten days. Since the patient had also been diagnosed with neuroleptic malignant syndrome, his CRP level remained high and he continued to exhibit a consciousness disturbance and a high grade fever; however, following treatment with dantrolene sodium hydrate for his neuroleptic malignant syndrome, all of these clinical symptoms rapidly improved. The edematous lesion
was reduced by the antibiotic treatment (Figure). He was discharged from our hospital on the hospital day 67.

**Discussion**

Between 2009 and 2012, there have been 25 patients in our hospital who have tested positive for *B. cereus* based on their blood cultures. Among these 25 cases, we dismissed 14 patients as having false-positives due to contamination, as these patients demonstrated no clinical symptoms and only showed positivity for the bacterium in one of the two sets of blood cultures. Therefore, 11 patients were finally diagnosed with a *B. cereus* infection (Table). It is important to note that all 11 of these patients were set with central or peripheral venous catheters. These patients were most likely infected through such catheters. In contrast, the causal bacterium for severe septicemia and cause meningitis and encephalitis in immunocompromised patients (3, 4, 7). In fact, *B. cereus* infection has been found in patients with various hematological disorders including acute leukemia, malignant lymphoma and also in patients treated with immunosuppressive therapies (7-9). Although it is less common, MDS could also be considered a background hematological disease, thus serving as a mechanism through which *B. cereus* septicemia could be developed with meningitis and encephalitis complications. Since the present patient had not been treated with any immunosuppressive therapies such as cyclosporine A, MDS was his only risk factor for severe *B. cereus* infection.

In the 11 patients found with *B. cereus* infection in our hospital, none had encephalitis (Table). However, there have been several case reports detailing *B. cereus*-induced encephalitis. These reports demonstrated that the patients with encephalitis sometimes developed a cerebral hemorrhage, and that the condition of such patients rapidly deteriorated (4, 5, 7, 8). Therefore, an early treatment with effective antibiotics is crucial to prevent the death of these pa-

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**Table. Clinical Characteristics and Treatment Outcome of Patients with *B. cereus* Infection**

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Background Disease</th>
<th>Symptom</th>
<th>Catheters</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>79</td>
<td>M</td>
<td>Cerebral Infarction</td>
<td>Septicemia</td>
<td>Peripheral Vein</td>
<td>MEPM</td>
<td>Alive</td>
</tr>
<tr>
<td>63</td>
<td>F</td>
<td>Polymyositis Dermatosclerosis</td>
<td>Septicemia Cellulitis</td>
<td>Peripheral Vein</td>
<td>VCM + MEPM</td>
<td>Alive</td>
</tr>
<tr>
<td>66</td>
<td>M</td>
<td>MDS</td>
<td>Pneumonia</td>
<td>Peripheral Vein</td>
<td>VCM + DRPM</td>
<td>Alive</td>
</tr>
<tr>
<td>40</td>
<td>M</td>
<td>Crohn's Disease</td>
<td>Bacteremia</td>
<td>Peripheral Vein</td>
<td>Removed</td>
<td>Alive</td>
</tr>
<tr>
<td>45</td>
<td>M</td>
<td>Gastric Cancer</td>
<td>Septicemia</td>
<td>Central Vein</td>
<td>PIPC/TAZ</td>
<td>Death</td>
</tr>
<tr>
<td>90</td>
<td>M</td>
<td>Urinary Tract Infection Chronic Renal Failure</td>
<td>Septicemia</td>
<td>Central Vein</td>
<td>VCM + MINO</td>
<td>Alive</td>
</tr>
<tr>
<td>38</td>
<td>M</td>
<td>ALL</td>
<td>Septicemia Shock</td>
<td>Central Vein</td>
<td>None</td>
<td>Death</td>
</tr>
<tr>
<td>54</td>
<td>F</td>
<td>Cerebral Hemorrhage</td>
<td>Septicemia</td>
<td>Peripheral Vein</td>
<td>VCM</td>
<td>Alive</td>
</tr>
<tr>
<td>44</td>
<td>F</td>
<td>Myoma Uteri (post operation)</td>
<td>Septicemia</td>
<td>Central Vein</td>
<td>VCM</td>
<td>Alive</td>
</tr>
<tr>
<td>61</td>
<td>F</td>
<td>Injury &amp; Obstruction of Lacteal Duct</td>
<td>Septicemia</td>
<td>CV port</td>
<td>PIPC/TAZ</td>
<td>Death</td>
</tr>
<tr>
<td>88</td>
<td>M</td>
<td>Starvation</td>
<td>Septicemia</td>
<td>Central Vein</td>
<td>VCM</td>
<td>Alive</td>
</tr>
</tbody>
</table>

Patients. It is important to note that \textit{B. cereus} is resistant to some \(\beta\)-lactam antibiotics including penicillin as well as to some cepham antibiotics (1). However, some carbapenem antibiotics as well as some glycopeptide antibiotics such as teicoplanin and vancomycin are effective. Vancomycin, in particular, is known to be one of the most potent drugs for \textit{B. cereus} infection. Of the 11 patients determined to have a \textit{B. cereus} infection in our hospital, all 6 of the patients who were treated with vancomycin survived, but only 1 of the 2 patients who were treated with meropenem survived. In the present case, cefepime had no effect, but the combination of vancomycin and ciprofloxacin was effective in eradicating the infection.

In conclusion, a severe \textit{B. cereus} infection is lethal. Therefore, the immediate administration of appropriate antibiotic therapy is vital when gram-positive rod bacteria are found in the blood or CSF cultures of a patient with a disturbed consciousness.

The authors state that they have no Conflict of Interest (COI).

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References


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