CASE REPORT

Meningitis due to *Bacillus cereus*: A case report and review of the literature

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Bacillus cereus is infrequently associated with invasive central nervous system (CNS) disease. Infection is associated with conditions that lead to reduced host immunity and provide direct access to the CNS, such as spinal anesthesia and ventricular tubes and shunts. A case of ventriculitis secondary to *B cereus* in a patient receiving intrathecal chemotherapy is reported, along with a review of the current literature. *B cereus* can colonize medical devices, thus posing a risk for invasive disease. Despite aggressive treatment with broad-spectrum anti-infectives, the mortality of CNS invasive *B cereus* is high. Clinicians should not dismiss Gram-positive rods resembling *Bacillus* species from normally sterile sites as contaminants in critically ill patients. Appropriate antibiotic therapy should be promptly initiated to limit morbidity and mortality.

Key Words: Bacillus cereus *meningitis*

La méningite attribuable au *Bacillus cereus* : un rapport de cas et une analyse bibliographique

Le *Bacillus cereus* s'associe rarement à une maladie invasive du système nerveux central (SNC). L'infection est liée à des pathologies qui réduisent l'immunité de l'hôte et procurent un accès direct au SNC, telles qu'une rachianesthésie et des tubes et dérivations ventriculaires. Les auteurs rendent compte d'un cas de ventriculite secondaire à un *B cereus* chez un patient sous chimiothérapie intratéchale et présentent une analyse des publications à jour. Le *B cereus* peut coloniser les dispositifs médicaux, posant ainsi un risque de maladie invasive. Malgré un traitement énergique au moyen d'anti-infectieux à large spectre, la mortalité attribuable au *B cereus* invasif du SNC est élevée. Les cliniciens ne devraient pas rejeter la possibilité que des bacilles Gram positif évocateurs d'espèces de *Bacillus* dans les foyers normalement stériles soient des contaminants chez les patients gravement malades. Il faudrait amorcer rapidement une antibiothérapie pertinente pour limiter la morbidité et la mortalité.

Bacillus cereus is a spore-forming, Gram-positive, or Gram-variable, rod bacterium that is ubiquitous in the environment. It is a well-known cause of gastrointestinal illness, but has been associated with extraintestinal disease, as well (1). Central nervous system (CNS) involvement with *B cereus* is rare, but has been described in association with both immunosuppression and CNS invasive devices. *B cereus* is intrinsically resistant to beta-lactam antibiotics (1), and CNS infections with this organism are associated with high mortality. A case involving a 73-year-old woman with chronic myelogenous leukemia and an Ommaya reservoir who developed ventriculitis with *B cereus* is reported, along with a review of the literature on invasive CNS infections with *B cereus*.

CASE PRESENTATION

A 73-year-old Afghani woman with a history of chronic myelogenous leukemia, complicated by leukemic meningitis, on therapy with bosutinib (an experimental tyrosine kinase inhibitor) and monthly intrathecal methotrexate and hydrocortisone administered via an Ommaya reservoir, presented to her oncology clinic for a scheduled intrathecal methotrexate/hydrocortisone infusion. On presentation, the patient was clinically well and her cerebrospinal fluid (CSF) revealed no white blood cells. One day later, she developed headache, generalized weakness and confusion and presented to the emergency department. She was tachycardic, febrile (38.7°C), lethargic, had nuchal rigidity and a systolic murmur (grade 3/6) at the left sternal border. She had leukocytosis with a leukocyte count of 19.2×10^9 cells/L with 96% neutrophils, and CSF analysis revealed 4.02×10^9/L white blood cells with 99% neutrophils, a protein level of 1.21 g/L, and a glucose level of 4.88 mmol/L. A gram-stain of teh CSF revealed Gram-variable rod bacteria (Figure 1). Blood and CSF cultures were sent for analysis and empirical therapy with vancomycin and cefepime was initiated. By hospital day 2, both the headache and her mental status had improved. Blood and CSF cultures grew *B cereus*, which was susceptible to vancomycin. The Ommaya reservoir was removed on hospital day 3. Repeat blood cultures were negative and she underwent transesophageal echocardiography that revealed no vegetations. The patient completed five weeks of therapy with intravenous vancomycin with subsequent microbiological cure and clinical recovery.

METHODS

A literature review of *B cereus* meningitis was performed using the MEDLINE/PubMed database. All searches were limited to English-language articles published since 1950. The first search term "*Bacillus cereus* meningitis" yielded 32 articles. A second search using the search term "*Bacillus cereus* central nervous system infections" yielded 32 articles. A third search was performed using the terms "*Bacillus cereus* meningoencephalitis", which yielded eight articles. The abstracts of the articles retrieved from all three searches were reviewed, and the references from pertinent articles were examined to identify additional reports. A total of 21 relevant publications were identified and details on 32 patients with CNS infection with *B cereus* were available for review.

DISCUSSION

Members of the *Bacillus* genus are Gram-positive or Gram-variable, spore-forming rod bacteria, which are ubiquitous in the environment. Clinical infections caused by *B cereus* fall into six broad groups: local infections of wounds, burns, or the eye; bacteremia; CNS infections; respiratory infections; endocarditis; and food poisoning.

We report a case of *B cereus* CNS infection associated with the use of an Ommaya reservoir and intrathecal chemotherapy. Since 1950 there have been 22 (including the present case) published case reports of CNS infections with *B cereus* (Table 1). Reported manifestations of CNS *B cereus* infection include ventriculitis, meningitis, leptomeningitis, hydrocephalus, intraparenchymal, subarachnoid subdural hemorrhage and brain abscess (2-24).

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TABLE 1
Central nervous system manifestations of *Bacillus cereus*

Authors (reference), year	Age*/sex	Clinical picture	Treatment	Outcome	Risk factors
Present case 2008	73/F	Leukemic meningitis	Vancomycin	Recovered	Ommaya reservoir
Garcia et al (5), 1984	32/M	Leptomeningitis	Penicillin, chloramphenicol	Recovered	Ommaya reservoir
Hendrickx et al (6), 1981	8d/F	Complete hemorrhagic necrosis of the brain	Ampicillin, gentamicin	Died	Ventricular puncture
Barrie et al (4), 1992	55/F 41/F	Hydrocephalus Hematoma	Vancomycin Chloramphenicol	Died	Ventricular drain
Berke et al (7), 1981	25/F	Bilateral papilledema, bilateral hemianopsia	Chloramphenicol, vancomycin	Recovered	Ventriculostomy
Heep et al (8), 2004	14d/M	Ventriculitis, hemorrhagic necrotizing lesions	Vancomycin, gentamicin, meropenem	Not reported	Ventriculostomy tube
Leffert et al (9), 1970	126d/M	Meningitis	Gentamicin, ampicillin	Recovered	Ventriculoarterial shunting
Haase et al (10), 2005	19/M	Meningoencephalitis, flaccid hemiparesis	Cyclosporine, methotrexate then ceftazidime then teicoplanin, ampicillin, amikacin, ciprofloxacin, clindamycin	Recovered	Broviac catheter
Tokieda et al (11), 1999 (2 cases)	4d/F 5d/F	Multiple brain parenchyma, subdural, epidural, and subarachnoid hemorrhage; and widespread softening and hemorrhagic necrosis of the brain	Ampicillin, gentamicin, cefotaxime	Died	Peripheral venous catheter; nasal feeding tube
Feder et al (12), 1988 (2 cases)	51/M 47d/F	Sequelae included Brain damage, hydrocephalus, hypotenia and hyper-reflexia	Chloramphenicol	Recovered	Gun shot wound; contaminated intravenous catheter
Manickam et al (13), 2008	8d/M	Hemorrhagic necrosis and liquefaction of brain tissue	Ampicillin, gentamicin	Died	Not identified
Akiyama et al (14), 1997	64/M	Leptomeningitis, subarachnoid hemorrhage, bacterial infiltration; liver and stomach necrosis	Piperacillin, gentamicin, cefoperazone, cefotaxime, ampicillin	Died	Immunosuppression post chemotherapy
Marely et al (15), 1995	26/M	Meningoencephalitis, subarachnoid hemorrhage, bacterial infiltration; liver and myocardium necrosis	Ceftazidime	Died	Immunosuppression post chemotherapy
Lequin et al (16), 2005 (3 cases)	5d/F 5d/F 13d/F	Meningoencephalitis, ventriculitis	Amoxicillin/clafuran, vancomycin, amikacin, clindamicin	Died	Preterm delivery, central line catheter
Jenson et al (17), 1989	3/M	Cerebritis, hemorrhagic necrosis, meningitis	Chloramphenicol, vancomycin, gentamicin, rifampin	Recovered	Immunosuppression postchemotherapy
Musa et al (18), 1999 (3 cases)	30/M 43/M 14/M	Leptomeningeal and neural necrosis	Ceftazidime, amikacin, vancomycin, gentamicin, ampicillin, tazobactam	Died	Immunosuppression postchemotherapy
de Almeida et al (19), 2003	16/F	Meningitis	Ceftazidime, imipenem	Died	Immunosuppression post marrow transplant
Tuladhar et al (20), 2000	14d/M	Intraventricular hemorrhage	Vancomycin, gentamicin, imipenem, clindamycin, ciprofloxacillin, immunoglobulin therapy	Died	Not identified
Gaur et al (21), 2001 (4 cases)	20/F 10/F 13/F 15/F	Meningitis, leptomeningitis, brain abscess, meningoencephalitis, hydrocephalus	Vancomycin	Died	Intrathecal chemotherapy
Marshman et al (22), 2000	41/F	Meningitis	Teicoplanin	Recovered	Cerebrospinal fluid fistula repair
Weisse et al (23), 1991 (2 cases)	5d/M 21d/M	Meningitis	Vancomycin, gentamicin, chloramphenicol	Recovered	Myelomeningocele; none
Chu et al (24), 2001	28d/M	Meningitis	Vancomycin, amikacin	Died	Bronchopulmonary dysplasia, dexamethasone used

** Age is presented as years, unless otherwise indicated with d, which denotes days. F Female; M Male*

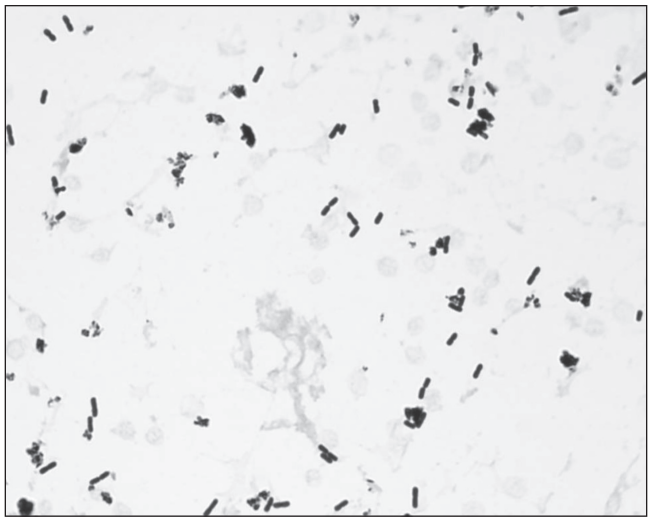

Figure 1) *Gram stain of cerebrospinal fluid showing Gram-variable rod bacteria*

The ubiquitous presence of *B cereus* makes environmental contamination of hospitals and clinics inevitable (2). Van der Zwet et al (3) reported an outbreak of *B cereus* infections in a neonatal intensive care unit associated with contaminated manual ventilation balloons, and Barrie et al (4) reported contamination of hospital linen by *B cereus*. Although rare, CNS infections with *B cereus* occur when host defense mechanisms are compromised, either by invasive CNS/vascular devices and/or by underlying immunodeficiency. We suspect that, becasue our patient was undergoing intrathecal chemotherapy, the frequent manipulation of the Ommaya reservoir led to bacterial contamination with *B cereus* and subsequent invasive disease. Previous cases of *B cereus* CNS disease have reported ventriculostomy tubes, ventricular punctures, central venous catheters, nasal feeding tubes and immunosuppression as risk factors (4,5,6-12,14-19). Only Garcia et al (5) reported the presence of an Ommaya reservoir as a risk factor. *B cereus* produces several toxins, including hemolysins and phospholipases, both believed to be important virulence determinants (1).

Despite aggressive treatment with broad-spectrum anti-infectives, the crude mortality is high (66%, including the present case, and excluding a case without a documented outcome). The high mortality is likely a reflection of underlying disease severity and comorbid illnesses. *B cereus* produces beta-lactamases and is resistant to beta-lactam antibiotics, including third-generation cephalosporins. *B cereus* is typically susceptible to aminoglycosides, clindamycin, vancomycin, chloramphenicol and erythromycin (1). Guidance on management of CNS *B cereus* infections is from case reports because no prospective trials or treatment guidelines exist.

The present case adds to the body of literature on CNS infections with *B cereus*, and is the second case to describe an Ommaya reservoir as a potential risk factor. We underscore the potential risk that a foreign body may pose for invasive disease with *B cereus*. Intraocular foreign bodies have been significantly associated with severe *B cereus* endophthalmitis (25,26). CNS invasive devices, such as Ommaya reservoirs, may pose a similar risk. These devices should be placed and accessed with strict attention to aseptic technique to minimize bacterial contamination and invasion. Additionally, when Gram stain or culture reveals Gram-positive rods resembling *Bacillus* species from normally sterile sites, such as blood or CSF, in critically ill immunosuppressed patients with invasive devices, these should not be dismissed as contaminants. Clinicians should be aware of the potential for *B cereus* CNS infection, and initiate prompt and appropriate antimicrobial therapy in an attempt to limit both morbidity and mortality.

SUMMARY

CNS disease with *B cereus* is an infrequent occurrence. Reports of invasive CNS disease exist in both pediatric and adult populations. Risk factors for CNS invasive disease include immunosuppression and invasive devices. Because *B cereus* is a ubiquitous environmental organism, CNS invasive devices, such as Ommaya reservoirs, should be placed and accessed with strict attention to aseptic technique to minimize bacterial contamination and invasion. The crude mortality rate is high, underscoring the clinical significance of CNS invasive disease with *B cereus*. For critically ill patients with invasive devices and immunosuppression, the presence of *Bacillus* species from normally sterile sites should not be dismissed as contaminants. To limit morbidity and mortality, clinicians should have a high index of suspicion for *B cereus* CNS infection, and initiate prompt and appropriate antimicrobial therapy.

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