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Case report

Bacillus cereus meningoencephalitis in an immunocompetent patient

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ABSTRACT

Central nervous system (CNS) infection from *Bacillus cereus* (*B. cereus*) is rare and usually occurs in immunosuppressed patients or in a presence of invasive CNS devices. Our case reported here is a very rare case of an immunocompetent elderly patient without any CNS devices who was diagnosed with *B. cereus* meningoencephalitis and bacteremia. According to our patient, preceding gastrointestinal (GI) symptoms and trans-sphenoidal hypophysectomy could be the precipitating factors. A positive blood culture should not be concluded as a contamination but prompt repeating another set of blood culture for a better clinical judgment. Given its abrupt clinical course and high mortality rate, high index of suspicion for rapid detection and management is needed for a preferable clinical outcome. Empiric treatment with intravenous vancomycin is reasonable before a susceptibility result becomes available.

Background

Bacillus cereus (*B. cereus*) is facultatively anaerobic, spore-forming, Gram-positive, rod-shaped bacteria that present in the environment. It is one of the most common causes of food poisoning but infrequently can result in invasive extra-intestinal infections such as wound, eye, and respiratory tract infection [1–3]. It can also cause systemic infections including bacteremia and endocarditis [4,5]. Central nervous system (CNS) infection from *B. cereus* is rare and usually associated with invasive CNS devices or immunosuppressed status. Herein, we report a case of an elderly patient without any invasive CNS devices or immunosuppressive agents who was diagnosed with *B. cereus* meningoencephalitis and bacteremia.

Case presentation

An 80-year-old patient with history of irritable bowel syndrome (IBS) and secondary adrenal insufficiency resulting from trans-sphenoidal hypophysectomy of a pituitary tumor eight years ago was re-admitted to the hospital with an acute onset of altered mental status and high-grade fevers 12 hours after being recently discharged from the previous hospitalization.

The patient was previously hospitalized for four days with fatigue, abdominal pain, diarrhea, nausea, and vomiting, which were attributed to acute adrenal insufficiency resulting from poor compliance to corticosteroid treatment. During the past two years, the patient was admitted several times with the same diagnosis and clinical presentations. The patient's medications included daily 20-milligram hydrocortisone and aspirin. The patient was originally from Mexico and moved to the United States 20 years ago. The patient denied using tobacco products, ethanol, and recreational drugs. There were no recent history of travel, sick contact, animal contact, and recent consumption of deli meats or unpasteurized dairy products. The patient was afebrile, however, the emergency room provider thought that this could be early symptoms and signs of sepsis, thus blood cultures were obtained and they did not grow any organisms. All symptoms improved after correction of hyponatremia and administration of systemic corticosteroid. The patient was feeling well before being discharged.

The patient presented to the emergency department 12 hours later. On examination, the temperature was 40 °C, the pulse rate 108 per minute, the blood pressure 131/78 mmHg, the respiratory rate 13 breaths per minute, and the oxygen saturation 99% while the patient was breathing on ambient air. The patient appeared confused and would not answer questions or follow commands. Complete neurological assessment was difficult to perform due to altered mental status, however, only rigid neck was observed and the patient was able to move all extremities. The rest of the exam was otherwise unremarkable. Blood tests showed leukocytosis with white blood cell (WBC) count of 16,990 cells/μL with polymorphonuclear cells (PMN) of 87.5%. Meningoencephalitis was suspected, thus empirical antimicrobial therapy with

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vancomycin, cefepime, ampicillin, and acyclovir was initiated. The computed tomography (CT) of the head without contrast and CT angiography of the head and neck revealed no evidence of acute intracranial pathology. Unfortunately, given the presence of a pacemaker, a magnetic resonance imaging (MRI) of the brain could not be performed for further information. Lumbar puncture was performed and the cerebrospinal fluid (CSF) analysis revealed WBC of 1317 cells/μL (86% neutrophils, 10% monocytes, and 3% lymphocytes), protein of 496 mg/dL, and glucose of less than 5 mg/dL; the result was consistent with a bacterial infection. Gram stain of the CSF showed no organisms. CSF polymerase chain reaction (PCR) did not detect any of the following pathogens: Escherichia *coli* K1, *Haemophilus influenzae*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Streptococcus agalactiae*, *Streptococcus pneumoniae*, cytomegalovirus (CMV), enterovirus, herpes simplex virus (HSV) type 1 and 2, varicella zoster virus (VZV), human herpesvirus (HHV) type 6, human parechovirus, and *Cryptococcus neoformans/gatti*. The antimicrobial regimen was de-escalated to intravenous ceftriaxone 2 g every 12 h. Bacterial and mycobacterial cultures from the CSF were negative. Two sets of blood cultures were obtained on two consecutive days of hospitalization due to no clinical improvement after initiation of intravenous antibiotics. One out of two blood culture bottles drawn on admission and a day after admission grew *Bacillus cereus*. Given the fact that there were two positive blood cultures, it was considered the most likely etiology of meningoencephalitis in this patient. Transthoracic echocardiogram did not reveal any vegetations of the native valves and pace maker leads. Intravenous vancomycin 0.75 g (adjusted dose) every 12 h was added. The CSF was subsequently sent for broad-range 16s rDNA PCR for definitive diagnosis. *B. cereus* was only susceptible to vancomycin and gentamicin, thus ceftriaxone was discontinued. The patient was treated with intravenous vancomycin for a total of 14 days without any adverse reactions. The patient had complete resolution of all the symptoms and subsequently was discharged nine days after the presentation. The result of the broad-range 16s rDNA PCR of the CSF came back positive for *B. cereus* confirming the diagnosis of CNS infection.

Methods

Our literature review of *B. cereus* was based on PubMed database. English keywords were used. The first search term "*Bacillus cereus* meningoencephalitis" yielded 7 articles (6 items are available in English). The second search term "*Bacillus cereus* meningitis" yielded 22 articles (17 items are available English). The abstracts of the articles retrieved from all two searches were reviewed, and the references from pertinent articles were reviewed to identify additional case reports. A total of 31 relevant publications were identified and the full articles on 41 patients with CNS infection from *B. cereus* were available for review.

Discussion and conclusions

Bacillus cereus is a Gram-positive, facultatively anaerobic, spore-forming bacilli which is widespread in the environment especially in soil or dust. Consequently, the contamination of this organism in hospital environment is inevitable. Study from Barrie et al. [6] showed association between *B. cereus* infection in patients and contamination of the organism in hospital environment. It can usually cause self-limited toxin-mediated gastrointestinal (GI) disease but the incidence of serious extra-intestinal infections has been increasingly reported according to previous published studies [7].

CNS infection with *B. cereus* is infrequent. It can present with various manifestations including ventriculitis, meningitis, meningoencephalitis, brain abscess, hydrocephalus, intraparenchymal, subarachnoid, and subdural hemorrhage (Table 1). The condition usually occurs in patients with defect in host defense mechanisms either from underlying primary or secondary immunodeficiency disorders, or invasive CNS procedures or devices. According to our literature review of the previous published adult and pediatric cases of *B. cereus* CNS infections (Table 1), chemotherapy may be associated with development of *B. cereus* CNS infections. Preterm delivery could also be one of the predisposing factors in pediatric patients [8]. To our knowledge, our case does not have an overt immunosuppressive condition. The daily dose of glucocorticoid replacement therapy for adrenal insufficiency is 20 mg of hydrocortisone daily (equivalent to 5 mg of prednisolone or prednisone), which is considered a physiologic dose. However, we did not do extensive workups for immunodeficiency disorders in this case, and immune dysfunction occurs with age. Immunosenescence could be a risk factor for *B. cereus* bacteremia and CNS infections in our case. Provided that there is no comparable case in the literature, it is difficult to predict the potential risk factors in this case. However, Berke et al. [9] reported a case of postoperative *B. cereus* meningitis after trans-septal trans--sphenoidal excision with retained ventriculostomy tube in a 25-year-old patient. Our patient's history of trans-sphenoidal hypophysectomy was eight years ago, true correlation of the procedure with the development of meningoencephalitis in our patient is questionable. The source of the infection in our patient has not been elucidated. One of the possibilities could be from GI tract since the patient presented with diarrhea during the previous hospitalization. The diarrhea could either be from the underlying condition of IBS or from possible prior bacterial infection. A report by Gaur et al. [10] showed that in three out of four patients with *B. cereus* bacteremia, the organism was isolated in cultures of their stools or rectal swabs obtained within 72 h of presentation of the infection. However, it is still not clear if rectal colonization could be the source of the bacteremia. Contaminated intravenous fluid during the previous admission could be another possible source of bacteremia in our patient.

Given its ubiquitous presence, the isolation of *B. cereus* from sterile clinical specimens is usually considered as a contamination, especially in immunocompetent patients. The positive blood culture for *B. cereus* in our patient was initially interpreted as a contamination considering the patient's immune status, an absence of invasive CNS devices, and a report of one positive blood culture out of the two bottles on the first day. However, one positive bottle for two consecutive days had pointed the positive blood cultures towards being from a true pathogen. Subsequently, the positive broad-range 16s rDNA PCR from the CSF for *B. cereus* confirmed the diagnosis.

B. cereus CNS infection usually has an abrupt clinical course and a high mortality rate despite aggressive treatment with broad-spectrum antimicrobial therapy. High index of suspicion is needed for rapid detection and management [11]. To date, there is still no standard guideline of treatment for *B. cereus* CNS infection, thus guidance on management comes solely from previously reported cases. The production of beta-lactamases makes *B. cereus* resistant to beta-lactam antimicrobial agents including third-generation cephalosporins but the organism is known to be susceptible to aminoglycosides, clindamycin, erythromycin, vancomycin, and chloramphenicol [7]. Vancomycin is generally considered the preferred agent for empiric therapy and was used in many reported cases including in our patient [12]. On the other hand, due to the outright and inducible resistance of *B. cereus* against clindamycin, the agent should not be used before the susceptibility results become available [13]. In our case, after the susceptibility report showed susceptibility to vancomycin, the treatment with intravenous vancomycin monotherapy for 14 days resulted in complete resolution of the clinical symptoms. The patient felt lucky that the condition was diagnosed correctly and that the patient got better with the treatment received.

This presenting case adds new learning points to the body of literature on *B. cereus* CNS infection. We believe that *B. cereus* should be included in one of the differential pathogens causing CNS infections in patients who had preceding GI signs and symptoms and with a history of trans-sphenoidal hypophysectomy regardless of duration after the procedure. A positive blood culture of *B. cereus* in one out of two obtained bottles should not be concluded as a contamination but prompt repeat another set of blood cultures for a better clinical judgment. The empiric

Table 1
Summary of previously reported cases of *Bacillus cereus* CNS infection.

Year	Author [ref]	Clinical diagnosis	Age/Sex	Outcomes	Predisposing conditions	Treatments
1970	Leffert et al. [14]	Meningitis	18 weeks /M	recovered	- Dandy-Walker cyst - Ventriculo-arterial shunt revision	- Ampicillin - Gentamicin
1977	Turnbull et al. [15]	Encephalitis with extensive necrosis of brain	1 day /F	died	- Preterm delivery - Necrotizing enterocolitis - Umbilical catheter	- Ampicillin - Gentamicin
1981	Colpin et al. [16]	Meningitis	19 years /M	died	- Post chemotherapy - Granulopenia - Central line	- Penicillin - Gentamicin
1981	Berke et al. [9]	Ventriculitis and meningitis	25 years /F	recovered	- Ventriculostomy - Trans-septal trans-sphenoidal excision of pituitary adenoma	- Chloramphenicol - Vancomycin
1981	Hendrickx et al. [17]	Meningoencephalitis with complete hemorrhagic necrosis of the brain	8 days /F	died	- Preterm delivery - Ventricular puncture - Central line	- Ampicillin - Gentamicin - Erythromycin
1984	Garcia et al. [18]	Leptomeningitis	32 years /M	recovered	- Ommaya reservoir	- Penicillin - Chloramphenicol
1988	Feder et al. [19]	Meningitis	47 days /F	recovered	- Preterm delivery - Central line	- Ampicillin - Chloramphenicol
1989	Jenson et al. [20]	Cerebritis, hemorrhagic necrosis, meningitis	3 years /M	recovered	- Post chemotherapy + intrathecal methotrexate - Immunosuppression - Severe neutropenia	- Chloramphenicol - Vancomycin - Gentamicin - Rifampin
1991	Weisse et al. [21]	Meningitis Meningitis	5 days /M 24 days /M	recovered recovered	- Preterm delivery - Myelomeningocele sac rupture - None	- Ampicillin - CeftazidimeVancomycin - Gentamicin - Chloramphenicol
1992	Barrie et al. [6]	Hydrocephalus Cerebellar hematoma	55 years /F 41 years /F	died died	- Ventricular drain - Post-operative course of acoustic neuroma - Ventricular drain - Post operative course of microdissection of trigeminal nerve	- Vancomycin - Vancomycin - Chloramphenicol
1995	Marley et al. [22]	Meningoencephalitis, subarachnoid hemorrhage, liver and myocardium necrosis	26 years /M	died	- Post chemotherapy - Immunosuppression - Severe neutropenia	- Ceftazidime
1997	Akiyama et al. [23]	Leptomeningitis, subarachnoid hemorrhage, liver and stomach necrosis	64 years /M	died	- Post chemotherapy - Immunosuppression - Central line	- Piperacillin - Gentamicin - Cefoperazone - Cefotaxime - Ampicillin
1997	Berner et al. [24]	Meningitis	18 months /M	recovered	- Ventriculo-peritoneal drain	- Vancomycin - Fosfomycin
1999	Tokieda et al. [8]	Multiple brain parenchyma, subdural, epidural, subarachnoid hemorrhage Wide spread softening and hemorrhagic necrosis of the brain	4 days /F 5 days /F	died died	- Hydrop fetalis - Unknown	- Ampicillin - Gentamicin - Ampicillin - Cefotaxime
1999	Musa et al. [25]	Leptomeningeal and neural necrosis	30 years /M 43 years /M 14 years /M	died died died	- Severe neutropenia - Central line - Severe neutropenia - Post chemotherapy - Neutropenia	- Ceftazidime - Amikacin - Ceftazidime - Amikacin - Ceftazidime - Amikacin
2000	Tuladhar et al. [26]	Intraventricular hemorrhage	14 days /M	died	- Preterm delivery	- Vancomycin - Gentamicin - Imipenem - Clindamycin - Ciprofloxacin
2000	Marshman et al. [27]	Fulminant meningitis	41 years /F	recovered	- Anterior fossa repair - Spinal drainage	- Teicoplanin - Gentamicin - Ciprofloxacin - Erythromycin
2001	Gaur et al. [10]	Right basal ganglia infarction Meningoencephalitis Meningoencephalitis, hydrocephalus Multiple brain abscess concern for septic emboli	20 years /F 15 years /F 13 years /F 10 years /F	died died survived with severe sequele survived with mild sequele	- Intrathecal chemotherapy - Neutropenia - Central line	- Vancomycin
2001	Chu et al. [28]	Meningitis with liquefactive necrosis of the brain	30 days /M	died	- Preterm delivery - Bronchopulmonary dysplasia - Dexamethasone use	- Vancomycin - Amikacin
2003	de Almeida et al. [29]	Meningitis	16 years /F	died	- Post bone marrow transplant - Immunosuppression	- Ceftazidime - Imipenem

(*continued on next page*)

Table 1 (*continued*)

Year	Author [ref]	Clinical diagnosis	Age/Sex	Outcomes	Predisposing conditions	Treatments
2004	Heep et al. [30]	Ventriculitis, hemorrhagic necrotizing lesion	14 days /M	not reported	- Ventriculostomy tube	- Vancomycin - Gentamicin - Meropenem
2005	Haase et al. [31]	Meningoencephalitis, flaccid hemiparesis	19 years /M	recovered	- During chemotherapy Central line	- Ceftazidime - Teicoplanin - Ampicillin - Amikacin - Ciprofloxacin - Clindamycin
2005	Lequin et al. [32]	Meningoencephalitis Meningoencephalitis Meningoencephalitis, ventriculitis	5 days /F 5 days /F 13 days /F	died died died	- Preterm delivery - Preterm delivery - Respiratory distress syndrome - Preterm delivery - Central line	- Amoxicillin - Cefotaxime - Vancomycin - Amikacin - Vancomycin - Amikacin - Amoxicillin - Cefotaxime - Vancomycin - Clindamycin
2008	Manickam N et al. [33]	Meningoencephalitis with hemorrhagic necrosis and liquefaction of brain tissue	8 days /M	died	- Preterm delivery	- Ampicillin - Gentamicin - Vancomycin - Cefotaxime - Acyclovir
2009	Lebessi et al. [34]	Meningitis	3 days /M	recovered	- Unknown	- Ampicillin - Vancomycin - Netilmicin
2010	Drazin et al. [35]	Meningoencephalitis with brain abscess	7 days /F	recovered	- Preterm delivery	- Vancomycin - Amikacin - Gentamicin - Meropenem
2012	Horii et al. [36]	Meningitis	2 months /F	recovered	- Preterm delivery - Prior blood stream infection	- Meropenem - Clindamycin - Linezolid
2012	Stevens et al. [11]	Meningitis	73 years /F	recovered	- Ommaya reservoir - Intrathecal methotrexate and hydrocortisone	- Vancomycin - Cefepime
2013	Tatara et al. [37]	Meningoencephalitis and septicemia	60 years /M	recovered	- Myelodysplastic syndrome - Pancytopenia	- Vancomycin - Ciprofloxacin - Micafungin
2020	Koizumi Y et al. [38]	Meningitis and bacteremia	54 years /F	recovered	- During chemotherapy - Leukocytopenia	- Meropenem - Vancomycin - Linezolid - Acyclovir

[a]Treatment refers to antimicrobial therapy for the whole duration of illness.

treatment with intravenous vancomycin is reasonable before a susceptibility result becomes available.

Ethics approval

Not applicable.

Consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author's contributions

The manuscript was read and approved by all the authors. **Pichaya Tao Worapngsatitaya**: writing original draft. **Jakrapun Pupaibool**: reviewing, editing, and supervising. All authors contributed to the work in this manuscript.

CRediT authorship contribution statement

Pichaya Tao Worapngsatitaya: writing-original draft preparation, software, investigation, **Jakrapun Pupaibool**: conceptualization, methodology, software, validation, writing, reviewing, editing, supervision, All authors contributed to the work in this manuscript.

Conflicts of interests

The authors have no conflicts of interests to declare.

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