Invasive *Bacillus cereus* infection in a renal transplant patient: A case report and review

Susan John MD FRCPC¹, John Neary MD¹, Christine H Lee MD FRCPC^{1,2,3}

S John, J Neary, CH Lee. Invasive *Bacillus cereus* infection in a renal transplant patient: A case report and review. Can J Infect Dis Med Microbiol 2012;23(4):e109-e110.

Bacillus cereus is a common cause of gastrointestinal diseases. The majority of individuals with *B cereus*-related food poisoning recover without any specific treatment. It can, however, rarely cause invasive disease in immunocompromised patients.

Key Words: *Bacillus cereus*; Food poisoning; Septicemia, Rhabdomyolysis

Bacillus cereus is a spore-forming Gram-positive *Bacillus* species and is a relatively common cause of food-borne gastrointestinal illness. Symptoms are mediated by an enterotoxin and an emetic toxin, and usually resolve with supportive management. The emetic toxin, which is cytotoxic, can cause rhabdomyolysis and has been associated with fulminant liver failure. Immunosuppression is one of the risk factors for developing invasive disease due to *B cereus* (1-4).

There are two reported cases of rhabdomyolysis associated with *B cereus* food poisoning in immunocompromised patients, both of which resulted in a fatal outcome (5,6). A case involving an immunocompromised patient who developed sepsis with extensive rash and rhabdomyolysis following ingestion of food contaminated with *B cereus*, is described.

CASE PRESENTATION

A 65-year-old man presented to the acute tertiary care centre of St Joseph's Healthcare (Hamilton, Ontario) with vomiting and fever. His medical history consisted of microscopic polyangiitis, a perinuclear antineutrophil cytoplasmic antibody vasculitis and related chronic renal failure, which was managed with azathioprine and prednisone. His baseline creatinine levels ranged between 160 µmol/L and 170 µmol/L. He was previously treated with cyclophosphamide and was switched to azathioprine two months before presentation. He also had a history of coronary artery bypass, hypertension and dyslipidemia. One day before his presentation, he had ingested a salami and bologna sandwich he had purchased from a local grocery store. Two hours later, he developed vomiting and generalized weakness. The next day, he was admitted with a diagnosis of food poisoning when he presented with fever and persistent vomiting. Twenty-four hours following his admission, he developed diffuse nonpruritic, erythematous papular and vesiculopustular rash and continued to experience fever. He was noted to have elevated creatinine and creatine kinase (CK) levels, consistent with rhabdomyolysis and was transferred to the coronary care unit. He was initiated on piperacillin-tazobactam.

His temperature was 39.8°C, blood pressure was 109/75 mmHg, heart rate was 87 beats/min, respiratory rate was 20 breaths/min and his oxygen saturation was 90% on 2 L of oxygen via nasal prong. Other than the presence of diffuse rash, the physical examination was normal. Dermatological examination revealed diffuse, discrete

Une infection à *Bacillus cereus* envahissante chez un patient greffé du rein : rapport de cas et analyse

Le *Bacillus cereus* est une cause courante de maladie gastro-intestinale. La majorité des individus présentant un empoisonnement alimentaire lié au *B cereus* se rétablissent sans traitement spécifique. Cependant, dans de rares cas, cet organisme peut causer une maladie envahissante chez les patients immunodéprimés.

Figure 1) Rash before initiation of meropenem and vancomycin

erythematous papular and vesiculopustular lesions involving the face, anterior and posterior trunk and bilateral arms, hands and legs as shown in Figure 1. There was no conjunctival, mucosal, palm or sole involvement. The lesions were nontender.

Laboratory investigations revealed a white blood cell count of $3.5 \times 10^9/L$, a hemoglobin level of 93 g/L and a platelet count of $77 \times 10^9/L$, suggestive of relative pancytopenia. Blood film demonstrated toxic granulation. His creatinine and urea levels were elevated (271 µmol/L and 15.3 mmol/L, respectively). His CK level on admission was 806 U/L, which increased to 32,924 U/L within 48 h. Urinalysis showed blood and protein. A test to detect myoglobin in his urine was not performed. He had metabolic acidosis with a venous pH of 7.26, PCO_2 of 33 mmHg and a bicarbonate level of 14 mmol/L. His lactate, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were 3.8 mmol/L, 473 U/L and 86 U/L, respectively. His blood calcium, phosphate and urate concentrations were 1.53 mmol/L, 1.47 mmol/L and 545 µmol/L, respectively, with a lactate dehydrogenase level of 1562 U/L. Three sets of blood cultures and a urine culture were negative. A chest x-ray showed bilateral interstitial markings.

He received intravenous normal saline and bicarbonate for the management of rhabdomyolysis. Antibiotics were switched from

¹Department of Medicine, ²Hamilton Regional Laboratory Medicine Program, St Joseph's Healthcare; ³Department of Pathology and Molecular Medicine, McMaster University, Hamilton, Ontario

Correspondence: Dr Christine H Lee, Department of Pathology and Molecular Medicine, McMaster University, Hamilton Regional Laboratory Medicine, St Joseph's Healthcare 50 Charlton Avenue East, 424 Luke Wing, Hamilton, Ontario L8N 4A6. Fax 905-521-6083, e-mail cleec@mcmaster.ca

piperacillin-tazobactam to vancomycin at a dose of 1 g every 48 h and meropenem 500 mg every 12 h for possible disseminated *B cereus* infection.

The patient's family brought in the components of the sandwich ingested by the patient. Within 24 h of incubation, the meat grew *B cereus*. A portion of the meat was also sent to the public health laboratory for the detection of *B cereus* toxin. The toxin testing was not performed because less than 100 count/g of *B cereus* was isolated from the food. The patient improved significantly within 72 h of initiating intravenous vancomycin and meropenem, with resolution of the fever and skin lesions. The CK and the serum creatinine levels improved to 489 µmol/L and 219 µmol/L, respectively. He completed a two-week course of vancomycin and meropenem. At six months' follow-up, the patient was doing well and his serum creatinine level had returned to baseline.

DISCUSSION

We report a case of sepsis with both rhabdomyolysis and papular, vesicular skin rash due to *B cereus* infection. The combination of these two features occurring in a single patient has not been described previously.

B cereus is a ubiquitous organism found in soil, vegetation, dairy products and rice, and causes either an emetic or diarrheic syndrome. The emetic syndrome, which resembles *Staphylococcal aureus* enterotoxin foodborne illness, develops after a short incubation period (0.5 h to 6 h) due to the emetic toxin, cereulide (7,8). The toxin is resistant to heat, cold, pH variations and proteolysis and, as a result, is often seen in food poisoning outbreaks (7,8). The diarrheic syndrome is caused by heat labile enterotoxins produced in the gut following the consumption of contaminated food. The incubation period of diarrheic syndrome is longer, ranging from 6 h to 24 h (1,2).

B cereus can cause local skin and wound infections, and invasive diseases such as bacteremia, central intravascular catheter-associated infection, endocarditis, osteomyelitis and meningoencephalitis. *B cereus* endophthalmitis can occur following a penetrating ocular trauma or injection drug use (1,2).

Rhabdomyolysis is a syndrome characterized by elevated serum concentrations of creatine phosphokinase and myoglobinuria leading

to renal dysfunction. Rhabdomyolysis can be precipitated by trauma, ischemia, metabolic and electrolyte abnormalities, drugs and a variety of infectious diseases. The proposed mechanism of muscle damage includes toxin generation and direct bacterial invasion (9).

B cereus bacteremia associated with rhabdomyolysis has been reported in two patients (3,4). Both patients were immunocompromised and experienced a fatal outcome directly due to *B cereus* infection. In the first case, postmortem examination revealed diffuse muscle necrosis with infiltration of Gram-positive bacilli in the quadriceps. Infiltration of Gram-positive bacilli was also found in the lung, spleen and liver with acute tubular necrosis of the kidney.

There have also been two reported cases of fulminant liver failure associated with elevated CK levels in immunocompetent patients infected with *B cereus* following the ingestion of contaminated food (10,11). The emetic toxin cereulide was implicated in both cases, potentially as a mitochondrial toxin. The patient described in the first case died, whereas the second patient had a good outcome, with normalization of liver function following appropriate therapy.

We believe our patient's skin lesions were likely due to *B cereus* infection. According to a review of 10 pediatric cases of primary cutaneous *B cereus* infection in neutropenic patients treated for cancer or aplastic anemia, vesicles or pustules were seen only on the limbs (12). Culture of the vesicle fluid or wound drainage grew *B cereus*, but blood cultures did not grow the bacteria. In each case, the vesicles responded promptly to appropriate antibiotics including vancomycin, as was the case with our patient.

The majority of cases of *B cereus*-related food poisoning require supportive management only. Individuals with invasive disease require antimicrobial therapy. *Bacillus* species produce beta-lactamases and are usually resistant to penicillins and cephalosporins. Vancomycin, aminoglycosides, carbapenem, clindamycin and ciprofloxacin are usually active in vitro (1,2).

B cereus should be considered as a serious pathogen in both immunocompromised and immunocompetent patients because it can cause sepsis, rash, rhabdomyolysis and acute fulminant liver failure. Prompt recognition and treatment with an appropriate antibiotic are essential, especially in immunocompromised patients, to prevent significant morbidity and mortality.

REFERENCES

1. *Bacillus cereus* infections. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. Red Book: 2009 Report of the Committee on Infectious Diseases, 28th edn. Elk Grove Village: American Academy of Pediatrics; 2009:227-8.
2. Fekete T. *Bacillus* Species and Related Genera Other than *Bacillus anthracis*. In: Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. Philadelphia: Churchill Livingstone, 2010:2727-31.
3. Schafer D, Sorrell M. Power failure, liver failure. N Engl J Med 1997;336:1173-4.
4. Arnaout MK, Tamburro RF, Bodner SM, et al. *Bacillus cereus* causing fulminant sepsis and hemolysis in two patients with acute leukemia. J Pediatr Hematol Oncol 1999;21:431-5.
5. Tomiyama J, Hasegawa Y, Nagasama T, et al. *Bacillus cereus* septicemia associated with rhabdomyolysis and myoglobinuric renal failure. Jpn J Med 1989;28:247-50.
6. Sanfructuoso C, Caballero MD, Vazquez I, et al. Rhabdomyolysis associated with septicemia after autologous bone marrow transplantation. Bone Marrow Transplant 1997;19:95. (Lett)
7. Carlin F, Fricker M, Pielaat A, et al. Emetic toxin-producing strains of *Bacillus cereus* show distinct characteristics within the *Bacillus cereus* group. Int J Food Microbiol 2006;109:132-8.
8. Granum PE, Lund T. *Bacillus cereus* and its food poisoning toxins. FEMS Microbiol Lett 1997;157:223-8.
9. Singh U, Scheld M. Infectious etiologies of rhabdomyolysis: Three case reports and review. Clin Infect Dis 1996;22:642-9.
10. Mahler H, Pasi A, Kramer JM et al. Fulminant liver failure in association with the emetic toxin of *Bacillus cereus*. N Engl J Med 1997;336: 1142-1148
11. Posfay-Barbe KM, Schrenzel J, Frey J, et al. Food poisoning as a cause of acute liver failure. Pediatr Infect Dis J 2008;27:846-7.
12. Henrickson K, Shenep J, Flynn P, et al. Primary cutaneous *Bacillus cereus* infection in neutropenic children. Lancet 1989;18:601-3.