Case Report

Fatal spontaneous bacterial peritonitis and necrotizing fasciitis with bacteraemia caused by *Bacillus cereus* in a patient with cirrhosis

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We report a case of spontaneous bacterial peritonitis and necrotizing fasciitis caused by *Bacillus cereus* in a cirrhotic patient without preceding disruption of skin or symptoms of gastroenteritis. This rapidly fatal infection due to *B. cereus* adds to the long list of aetiologies of infectious complications among patients with cirrhosis of the liver.

Introduction

Bacillus cereus is a ubiquitous Gram-positive or Gram-variable rod-like bacterium, and the widespread distribution of *Bacillus* species in nature explains its frequent isolation in the laboratory (Thomas, 2005; Vilas-Bôas *et al.*, 2007). The clinical isolate of *B. cereus* is usually regarded as a contaminant, but it can sometimes cause gastroenteritis, bacteraemia, pneumonia and, more rarely, necrotizing fasciitis, meningitis, endocarditis, endophthalmitis and peritoneal dialysis-related peritonitis (Miller *et al.*, 1997; Gaur *et al.*, 2001; Ruiz *et al.*, 2006). Severe cases of *B. cereus* infections mainly occur in immunocompromised patients with leukaemia or other haematological malignancies, infants or intravenous drug users (Gaur *et al.*, 2001; Hernaiz *et al.*, 2003) and these infections are usually preceded by food intoxication, catheter insertion such as a ventriculoperitoneal shunt, trauma or surgical procedures (Tuazon *et al.*, 1979; Hernaiz *et al.*, 2003; Vilas-Bôas *et al.*, 2007; Shimoni *et al.*, 2008). Spontaneous bacterial peritonitis (SBP) and necrotizing fasciitis due to *B. cereus* are rare, however. We report herein a case of SBP and necrotizing fasciitis in a patient with cirrhosis of the liver.

Case report

A 47-year-old man was admitted to the hospital with presentations of progressive abdominal distension, leg oedema and jaundice that evolved together for more than 1 week. The patient had had a history of cirrhosis of the liver related to chronic hepatitis B virus infection for 3 years, which was complicated with oesophageal varices. He

had led an otherwise uneventful life without episodes of variceal bleeding, SBP or hepatic encephalopathy over the past 3 years of follow-up at an outside hospital. He reported no diarrhoea, constipation, fever or altered consciousness, and could manage daily activities rather well during the first 4 days of hospitalization. His temperature and blood pressure were normal. Physical examination was remarkable for jaundice and icteric sclera; distended abdomen with shifting dullness; and no abdominal tenderness or rebound tenderness was found while pitting oedema was noted up to the mid-tibial region without skin lesions. The results of the blood tests on admission are shown in Table 1. Ultrasonography of the abdomen showed cirrhosis of the liver with splenomegaly, massive ascites and gall bladder wall thickening, but the common bile duct and intrahepatic duct were normal. Based on the findings of physical and laboratory examinations, his stage of cirrhosis was classified as Child–Pugh class C on admission. Paracentesis was not performed initially. The patient was prescribed diuretics and intravenous albumin, and the ascites and oedema remitted gradually. In the early morning of the 5th hospital day, he experienced progressive disturbance of consciousness and fell over, causing ecchymosis on the right thigh, followed by hypotension, metabolic acidosis and acute renal failure, and the patient was admitted to the intensive care unit. Paracentesis was performed and analysis of the ascites specimen revealed a white-cell count of 8500 cells mm⁻³ with 95 % neutrophils and a red blood cell count of 4500 cells mm⁻³; the protein level was 1.8 g dl⁻¹ and the glucose level was 18 mg dl⁻¹ (serum glucose at the time of paracentesis, 172 mg dl⁻¹). The three sets of blood and ascites specimens were cultured in aerobic and anaerobic

Abbreviation: SBP, spontaneous bacterial peritonitis.

Table 1. Results of the laboratory tests performed on the 1st and 5th hospitalization days

	Reference range, adults*	1st day	5th day
White blood cell (count μl^{-1})	3500–9100	8710	2820
Haemoglobin (g dl^{-1})	12.0–15.0	11.6	13.9
Platelet ($\times 10^3 \mu\text{l}^{-1}$)	157–377	116	98
Blood urea nitrogen (mg dl^{-1})	9–23	12	25
Creatinine (mg dl^{-1})	0.6–1.5	0.8	2.7
Aspartic transaminase (U l^{-1})	11–39	126	178
Alanine transaminase (U l^{-1})	4–38	77	73
Bilirubin, total/direct (mg dl^{-1})	0.3–1.3/0.1–0.5	7.1/3.01	5.5/4.4
International normalized ratio		2.10	2.65
Albumin (g dl^{-1})	3.5–5.5	2.2	2.7
Ammonia ($\mu\text{mol l}^{-1}$)	27.2–102		135
C-reactive protein (mg dl^{-1})	<0.5		0.9

*Reference values are affected by many variables, including the patient population and the laboratory methods used.

blood culture bottles. The patient was started on intravenous ceftriaxone 2 g daily based on a presumptive diagnosis of SBP, pending the culture results. Progressive haemorrhagic bullae developed that extended from both thighs to the lower legs on the 6th hospital day. The bullae fluid was aspirated in a sterile syringe, which was transferred to the microbiology laboratory for aerobic and anaerobic cultures immediately. Gram staining of the aspirated bullae fluid revealed a few Gram-positive rods with endospores and no variability in staining. Ceftriaxone was switched to meropenem and metronidazole. Debridement was not performed because of the extremely unstable condition of the patient. Despite use of antibiotic therapy, inotropic agents and fluid resuscitation, he expired in the night of the 6th day of hospitalization due to SBP and necrotizing fasciitis with septic shock. In tests using a BacT/Alert system (bioMérieux) for culturing the blood and ascites fluid, all four aerobic and anaerobic blood culture bottles obtained during the hospital stay were positive for Gram-positive bacilli after 2 days of incubation at 35 °C. The subcultures of blood culture and the culture of aspirate fluid were directly inoculated on trypticase soy agar with 5 % sheep blood (BD) and incubated at 35 °C with 5 % CO₂ for aerobic culture, and on CDC ANA blood agar (BD) and incubated in an anaerobic GasPak jar (BD) at 35 °C for anaerobic culture. Both cultures were all positive for Gram-positive bacilli. The facultatively aerobic organism produced large, spreading greenish colonies that were β -haemolytic on trypticase soy agar with 5 % sheep blood, was catalase-positive, and motile on semi-solid motility agar. The microscopic features were a Gram-positive spore former whose cells are large rods, $1 \times 3\text{--}4 \mu\text{m}$, and whose endospores do not swell the bacterial cell. Using a BBL Crystal Gram-Positive ID kit (BD Diagnostic Systems) and the Phoenix Automated Microbiology System (BD Diagnostic Systems), all of the bacteria were identified as *B. cereus*. Identification was confirmed by PCR performed in a reference bacteriology laboratory at the National Taiwan

University Hospital and National Taiwan University College of Medicine (Taipei, Taiwan). PCR amplification of the nearly complete 16S rRNA gene (1475 bp) with two primers (primers 8FPL and 1492) was performed as described previously (Chiang *et al.*, 2004). The amplification products were purified and sequenced. The sequences were compared with published sequences in the GenBank database using the BLASTN algorithm. The 16S rRNA gene of our isolate shared 99 % sequence similarity with *B. cereus* in the GenBank database (GenBank accession no. GQ406846.1) and *B. cereus* was the closest match.

Antibiotic susceptibility was determined using the disc diffusion and MIC method (Phoenix Automated Microbiology System). The isolate was found to be susceptible to vancomycin, gentamicin, ciprofloxacin and tetracycline, intermediately susceptible to erythromycin and clindamycin, but resistant to penicillin, ampicillin and trimethoprim-sulfamethoxazole using the Clinical and Laboratory Standards Institute interpretive guidelines M100-S19 for staphylococci.

Discussion

SBP is one of the most common infectious complications among patients with cirrhosis of the liver and the risk for SBP is related to the stage of cirrhosis (Chung & Podolsky, 2001). While the most common aetiologies for SBP among those patients are *Enterobacteriaceae* and streptococcal species (Such & Runyon, 1998), SBP due to *B. cereus* without preceding abdominal intervention has not been reported before to our knowledge. All previous reports of *B. cereus*-related peritonitis were related to peritoneal dialysis or surgery (Ruiz *et al.*, 2006; Shimoni *et al.*, 2008). In this case, our patient had no symptoms suggestive of enteritis, including diarrhoea, abdominal pain or vomiting, throughout the course of infection. Since *Bacillus* species may cause colonization of the gastrointestinal tract (Thomas, 2005), we postulate that, in this patient with an advanced stage of cirrhosis of the liver and hypoalbu-

minaemia, *B. cereus* entered the body through ingestion, followed by translocation through the intestinal mucosa, resulting in bacteraemia and peritonitis due to impaired phagocytosis resulting from the cirrhosis that failed to contain and eradicate the infection. The scenario is similar to that observed in two other much more common invasive infections due to *Aeromonas* species and *Vibrio* species in Taiwan. Both species have the propensity to cause SBP, bacteraemia and necrotizing fasciitis in patients with cirrhosis of the liver (Ko *et al.*, 1998; Lee *et al.*, 2008).

Previous reports have suggested that *B. cereus* also has the potential to cause fulminant soft tissue infections that are indistinguishable from those due to clostridia, the majority of which have occurred in immunocompromised patients with neoplasms without antecedent trauma (Meredith *et al.*, 1997; Mori *et al.*, 2002). In one case of necrotizing fasciitis and brain abscess caused by *B. cereus* in a patient with myelodysplastic syndrome, *B. cereus* was isolated only from blood culture (Mori *et al.*, 2002). The necrotizing fasciitis progressed within 1 week, without bullae formation; the brain abscess and necrotizing fasciitis were cured by a prolonged combination of antibiotics without surgery. In our patient, despite normal white-cell counts, the necrotizing fasciitis progressed to a lethal stage within 2 days. The fulminant presentation was similar to that of clostridial soft tissue infection.

Because invasive infections due to *B. cereus* are rare and guidelines are not available for the antibiotic susceptibility testing of *Bacillus* species by routine disc susceptibility tests, appropriate antibiotic therapy for such infections remains to be studied, though use of carbapenems or gentamicin plus clindamycin has been suggested (Hernaiz *et al.*, 2003). *B. cereus* is often resistant to all β -lactams (except carbapenems) and imipenem seems to be active against almost all *Bacillus* species (Thomas, 2005). In this case, the patient received ceftriaxone as an empiric therapy, which is active against most of the intestinal pathogens causing SBP but is not active against *B. cereus*. The fatal outcome for this patient is likely due to the delay in timely initiation of effective antibiotic therapy and the advanced stage of cirrhosis of the liver.

In conclusion, *B. cereus* should be included in the list of aetiologies of SBP and necrotizing fasciitis in patients with cirrhosis of the liver when Gram-positive rods are identified in the clinical specimens.

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References

- Chiang, W. C., Tsai, J. C., Chen, S. Y., Hsu, C. Y., Wu, C. T., Teng, L. J. & Hsueh, P. R. (2004). Mycotic aneurysm caused by *Streptococcus constellatus* subsp. *constellatus*. *J Clin Microbiol* **42**, 1826–1828.
- Chung, R. T. & Podolsky, D. K. (2001). Cirrhosis and its complications. In *Harrison's Principles of Internal Medicine*, 15th edn, pp. 1754–1767. Edited by E. Braunwald and others. New York & London: McGraw-Hill.
- Gaur, A. H., Patrick, C. C., McCullers, J. A., Flynn, P. M., Pearson, T. A., Razzouk, B. I., Thompson, S. J. & Shenep, J. L. (2001). *Bacillus cereus* bacteremia and meningitis in immunocompromised children. *Clin Infect Dis* **32**, 1456–1462.
- Hernaiz, C., Picardo, A., Alos, J. I. & Gomez-Garcés, J. L. (2003). Nosocomial bacteremia and catheter infection by *Bacillus cereus* in an immunocompetent patient. *Clin Microbiol Infect* **9**, 973–975.
- Ko, W. C., Chuang, Y. C., Huang, G. C. & Hsu, S. Y. (1998). Infections due to non-O1 *Vibrio cholerae* in southern Taiwan: predominance in cirrhotic patients. *Clin Infect Dis* **27**, 774–780.
- Lee, C. C., Chi, C. H., Lee, N. Y., Lee, H. C., Chen, C. L., Chen, P. L., Chang, C. M., Wu, C. J., Ko, N. Y. & other authors (2008). Necrotizing fasciitis in patients with liver cirrhosis: predominance of mono-microbial Gram-negative bacillary infections. *Diagn Microbiol Infect Dis* **62**, 219–225.
- Meredith, F. T., Fowler, V. G., Gautier, M., Corey, G. R. & Reller, L. B. (1997). *Bacillus cereus* necrotizing cellulitis mimicking clostridial myonecrosis: case report and review of the literature. *Scand J Infect Dis* **29**, 528–529.
- Miller, J. M., Hair, J. G., Hebert, M., Hebert, L., Roberts, F. J., Jr & Weyant, R. S. (1997). Fulminating bacteremia and pneumonia due to *Bacillus cereus*. *J Clin Microbiol* **35**, 504–507.
- Mori, T., Tokuhira, M., Takae, Y., Mori, S., Suzuki, H., Abe, T. & Takeuchi, T. (2002). Successful non-surgical treatment of brain abscess and necrotizing fasciitis caused by *Bacillus cereus*. *Intern Med* **41**, 671–673.
- Ruiz, S. R., Reyes, G. M., Campos, C. T., Jimenez, V. L., Rojas, R. T., de la Fuente, C. G. & Esteve, A. A. (2006). Relapsing *Bacillus cereus* peritonitis during automated peritoneal dialysis. *Perit Dial Int* **26**, 612–613.
- Shimoni, Z., Mamet, Y., Niven, M., Mandelbaum, S., Valinsky, L. & Froom, P. (2008). *Bacillus cereus* peritonitis after Cesarean section. *Surg Infect (Larchmt)* **9**, 105–106.
- Such, J. & Runyon, B. A. (1998). Spontaneous bacterial peritonitis. *Clin Infect Dis* **27**, 669–674.
- Thomas, F. (2005). *Bacillus* species and related genera other than *Bacillus anthracis*. In *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*, 6th edn, pp. 2493–2496. Edited by G. L. Mandell, J. E. Bennett and R. Dolin. Philadelphia: Elsevier/Churchill Livingstone.
- Tuazon, C. U., Murray, H. W., Levy, C., Solny, M. N., Curtin, J. A. & Sheagren, J. N. (1979). Serious infections from *Bacillus* sp. *JAMA* **241**, 1137–1140.
- Vilas-Bôas, G. T., Peruca, A. P. & Arantes, O. M. (2007). Biology and taxonomy of *Bacillus cereus*, *Bacillus anthracis*, and *Bacillus thuringiensis*. *Can J Microbiol* **53**, 673–687.