A fatal rhabdomyolysis with the presence of *Bacillus cereus* on blood culture: description of a clinical case

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Summary

Bacillus cereus is a Gram-positive bacterium that is ubiquitously present. It is often involved in gastrointestinal infections and food poisoning, but it can rarely cause serious non-gastrointestinal tract infections, particularly in immunocompromised individuals. The pathogenicity of *B. cereus* is predominantly derived from the production of tissue-destructive exoenzymes, including hemolysins, phospholipases, and proteases. Here, we present a case of bacteremia due to *B. cereus* in an elderly patient, admitted to the emergency room for respiratory failure and rhabdomyolysis after a fall.

The microorganism was detected through blood culture and identified using the MALDI-TOF technique. Despite the rapid start of antibiotic therapy, laboratory data have highlighted how this bacterium, through its virulence factors, can be lethal in the case of rhabdomyolysis, worsening the inflammatory response and subverting the host-microorganism relationship in its favor.

Introduction

Bacillus cereus (*B. cereus*) is a rod-shaped, Gram-positive, spore-forming aerobic or facultative anaerobic, motile bacterium found ubiquitous in various natural and human-made environments [2].

B. cereus is sometimes found in small quantities in raw, dried, and processed foods, such as pasta or rice, but is rarely fatal in immunocompetent individuals [4]. Gastrointestinal and non-gastrointestinal pathogenicity of *B. cereus* is associated with the secretion of various toxins: if ingested, it can cause emetic syndrome or diarrhoeal syndrome. The emetic syndrome is due to the production of an emetic toxin, cereulide, responsible for the dysfunction of the mitochondrial beta-oxidative process. The diarrhoeic syndrome is caused by heat-labile enterotoxins produced in the gut following the consumption of contaminated food [1]. Non-gastrointestinal infections are rare, but *B. cereus* can also cause meningitis, endocarditis, endophthalmitis, pneumonia, soft tissue infections, and bacteremia [6].

Here, we describe a case of *B. cereus* infection at the Rivoli Hospital (Turin, Italy) in an elderly patient hospitalized with the diagnosis of rhabdomyolysis following a fall, whose blood cultures were positive for this opportunistic pathogen.

Case Report

An 82-year-old smoker man presented to the Emergency Room in Rivoli Hospital, sent by his general practitioner, for a suspected

stroke. In the morning, his wife found him asleep on the floor beside the bed. Upon awakening, he reported that he had fallen but did not remember the dynamics of the accident. During the general practitioner's visit, the patient was slow, and his speech was sluggish.

Upon admission, he appeared confused and, even if cooperative, cachectic but apyretic, presenting ecchymosis and bilateral edema of the limbs. Signs of substance abuse and gastrointestinal and urinary tract infections were excluded.

The man was hypertensive, with benign prostatic hyperplasia and renal insufficiency (Estimated Glomerular Filtration Rate, eGFR, 22 mL/min/1.73 m^2), and was being treated for his underlying pathologies with therapies based on calcium antagonists, diuretics (furosemide), allopurinol and supplements to aid urination.

Upon physical examination, there was ecchymosis on the right hip from the prolonged stay on the ground, but no fractures.

The patient remained in the Emergency Room for two days, during which his serum parameters were investigated, and then he was admitted to a medical ward. The analysis demonstrated a significant increase in inflammation markers: C-reactive protein level of 7.90 mg/dL increased to 11.50 mg/dL, 13.70 mg/dL and 17.10 one day after the recovery in the medical ward; on the other hand, CK level of 5.074 U/L decreased to 4.120 U/L, 1.910 U/L and 489 U/L one day after the ward recovery, supporting the diagnostic hypothesis of rhabdomyolysis (incoming myoglobin equal to 1.090 ng/mL).

On the third day, the man was admitted to the medical facility; he had a febrile episode (37.8°C) with a slight increase in serum procalcitonin up to 0.73 ng/mL: two blood cultures were immediately performed, and empiric antibiotic therapy was started (piperacillin/tazobactam 2.25 g three times a day; linezolid 600 mg twice daily).

The aerobic blood culture was detected as positive on the BD BACTEC™ FX Blood (Becton Dickinson, Milan, Italy) after 10 hours of incubation, with positivity for a Gram-positive bacillus on microscopic examination (Gram stain performed with automatic stainer Vanica Aerospray, Genoa, Italy). The blood sample was sown on CHROMID® CPS® Elite Agar, CHROMID® Candida Agar, and Chocolate Agar PolyViteX (in CO_2 enriched atmosphere). After 1 hour and 1h30, respectively, anaerobic blood cultures were also detected as positive. An anaerobic bottle was sown on Chocolate agar PolyViteX, Schaedler agar + 5% sheep blood Schaedler Neo. Vanco. Agar + 5% sheep blood in aerobic and anaerobic conditions.

For identification, we applied the MicroScan WalkAway (Beckman Coulter, Cassina de' Pecchi, Italy) with a P49 panel, but the Gram-positive rod bacteria were not identified.

The isolated microorganism was sent to the Piedmont Reference Center for identification with MALDI-TOF mass spectrometry that revealed the presence of *B. cereus*.

Table 1. Antibacterial susceptibility testing results from blood culture according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints (version 13.0, released 2023.01.01).

Drug	Susceptibility test Diameter	Interpretation
Ciprofloxacin	≥50 mm	S
Clindamycin	≥17 mm	S
Erythromycin	≥24 mm	R
Imipenem	≥30 mm	S
Linezolid	≥22 mm	S
Vancomycin	≥10 mm	S
Meropenem	≥25 mm	S

S, susceptible; R, resistant.

The isolate was plated onto Mueller Hinton Agar for Kirby-Bauer disk diffusion antibiotic susceptibility testing according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints (Table 1).

Despite empirical therapy and the proven sensitivity of the strain to the antibiotics used, the patient unfortunately died on the fourth day.

Discussion

B. cereus is a toxin-producing, facultatively anaerobic, Gram-positive rod-shaped bacterium [1]. It is commonly found in the environment and soil and can contaminate food [2].

Clinical manifestations of *B. cereus* infection include gastrointestinal disease syndromes or extra-gastrointestinal infections. Gastrointestinal syndromes are divided into two types of illnesses, according to the production of two different toxins: one thermolabile, responsible for diarrhea, and the other thermostable, responsible for vomiting [7].

Extra-gastrointestinal syndromes caused by *B. cereus* can occur in patients who use intravenous drugs, who have central venous access catheters, or with mucosal injuries/compromise in neutropenic patients [8]. The immunocompromised, particularly those with underlying hematologic malignancies, are at high risk for this type of infection with bacillus species [8].

The pathogenicity of *B. cereus*, whether intestinal or non-intestinal, is associated with the production of hemolysins, phospholipases, and proteases [3].

The source of the infection in this patient remains unknown: he presented to the emergency room with a fever and was subjected to uroculture and blood culture before starting antibiotics, but he had not experienced gastrointestinal symptoms such as vomiting or diarrhea, nor did he belong to the categories of patients at risk described above, except for being an elderly person.

At the same time, we had no specific information on whether this strain of *B. cereus* produced toxins or not. In this regard, the toxin-inflammasome axis is described as a critical determinant of inflammation, cell death and disease outcome in response to infection [3]. This, therefore, could be an additional virulence factor new to *B. cereus,* which, by activating the inflammasome pathway, could subvert the host-parasite relationship to its advantage [3].

According to a retrospective analysis in 2015, where data from 57 patients hospitalized and diagnosed with a *B. cereus* infection were analyzed, only 17% of cases were positive only in blood culture, and, out of these cases, 37.5% died as a result of infection [10].

Tomiyama *et al.* (1989) report a case of rhabdomyolysis caused by *B. cereus*, underlining how this opportunistic pathogen can prove lethal. Therefore, the virulence factors of any microorganism cannot be overlooked [9].

Conclusions

In conclusion, this case report demonstrates how, in the face of an increase in the complexity of patients with multiple pathologies, unconventional pathogens must also be addressed [5] and help the clinician in rapid and adequate treatment [9].

References

1. Celandroni F, Salvetti S, Gueye SA, et al. Identification and pathogenic potential of clinical bacillus and paenibacillus isolates. PLoS One 2016;11:e0152831.

2. Chang T, Rosch JW, Gu Z, et al. Whole-genome characterization of *Bacillus cereus* associated with specific disease manifestations. Infect Immun 2018;86:e00574-17.
3. Enosi Tuipulotu D, Mathur A, Ngo C, et al. *Bacillus cereus*: epidemiology, virulence factors, and host-pathogen interactions. Trends Microbiol 2021;29:458-71.
4. Guinebretière MH, Thompson FL, Sorokin A, et al. Ecological diversification in the *Bacillus cereus* group. Environ Microbiol 2008;10:851-65.
5. Kubota N, Kobayashi J, Kasai A, et al. Detection of *Bacillus cereus* as a causative agent of emetic food poisoning by an unconventional culture procedure. J Infect Chemother 2022; 28:1575-7.
6. Ikeda M, Yagihara Y, Tatsuno K, et al. Clinical characteristics and antimicrobial susceptibility of *Bacillus cereus* bloodstream infections. Ann Clin Microbiol Antimicrob 2015;14:43.
7. Senesi S, Ghelardi E. Production, secretion and biological activity of *Bacillus cereus* enterotoxins. Toxins 2010;2:1690-703.
8. Shimada T, Ishikawa K, Kawai F, et al. Risk factors associated with infection-related mortality of *Bacillus cereus* bacteremia in hematologic disorders. Int J Hematol 2023;118:726-30.
9. Tomiyama J, Hasegawa Y, Nagasawa T, et al. *Bacillus cereus* septicaemia associated with rhabdomyolysis and myoglobinuric renal failure. Jpn J Med 1989;28:247-50.
10. Veysseyre F, Fourcade C, Lavigne J-P, et al. *Bacillus cereus* infection: 57 case patients and a literature review. Médecine et Maladies Infectieuses 2015;45:436-40.