

Hemorrhagic Bullous Lesions Due to *Bacillus cereus* in a Cirrhotic Patient

To the Editor:

A 42-year-old man with hypertension, hypothyroidism, and alcohol-related cirrhosis was admitted for evaluation of rapidly deteriorating mental status. He was referred from a rehabilitation facility where he had been admitted 4 days earlier after a hospitalization for hepatorenal syndrome and pneumonia. He was alert and ambulating until the day of the current admission. On arrival he was hypotensive (54/42 mm Hg); hypothermic (35°C, rectally); and unresponsive, except to painful stimuli. Jaundice, hepatosplenomegaly, ascites, and bilateral lower extremity edema were noted. There were multiple tense and flaccid bullous lesions containing serosanguineous fluid over both tibias and calves, without crepitus (Figure 1).

Laboratory test results revealed leukocytosis (total leukocytes, 10,900/mm³ [reference range, 4500–10,800/mm³]), hypoglycemia (glucose, <20 mg/dL [reference range, 74–106 mg/dL]), renal insufficiency (serum creatinine, 2.5 mg/dL [reference range, 0.66–1.25 mg/dL]), metabolic acidosis (pH, 7.1 [reference range, 7.35–7.45]; bicarbonate, 13 mmol/L [reference range, 22–30 mmol/L]; lactic acid, 11.9 mmol/L [reference range, 0.7–2.1 mmol/L]), liver dysfunction (aspartate aminotransferase, 576 IU/L [reference range, 15–46 IU/L]), and coagulopathy with evidence of diffuse intravascular

coagulation (total platelets, 75,000/mm³ [reference range, 150,000–450,000/mm³]; international normalized ratio, 9.5 [reference range, 0.8–1.2]; partial



Figure 1. Left tibia with multiple hemorrhagic bullae and surrounding erythema and edema. The characteristic serosanguineous drainage was seen at the lower edge of the distal bulla.

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The authors report no conflict of interest.

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thromboplastin time, 108 seconds [reference range 23.0–35.0 seconds]; fibrinogen, 145 mg/dL [reference range, 228–501 mg/dL]; D-dimer, >20 $\mu\text{g/mL}$ [reference range, 0.01–0.58 $\mu\text{g/mL}$]). Computed tomography of the pelvis and legs showed ascites, extensive subcutaneous edema, and cutaneous blisterlike lesions superior to the level of the ankles bilaterally. No gas, foreign bodies, collections, asymmetric facial thickening, or evidence of infection across tissue planes was present (Figures 2 and 3).

Specimens of blood and aspirates from the bullae at multiple lower leg sites were sent for microbiologic evaluation. The blood specimens were inoculated at bedside into aerobic and anaerobic blood culture bottles and incubated in an automated blood culture system. The aspirate samples were inoculated to trypticase soy agar with 5% sheep blood,

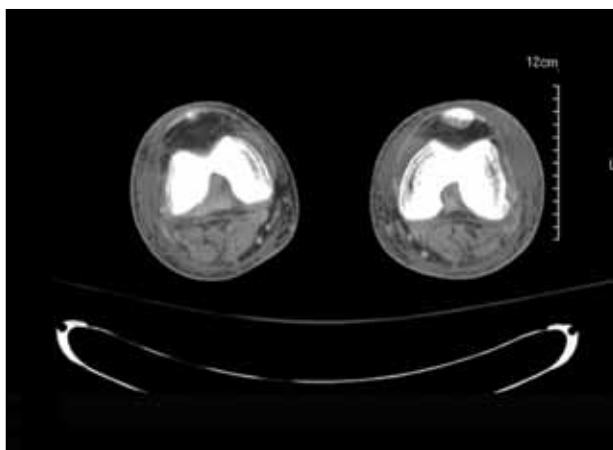


Figure 2. Computed tomography of the legs with extensive subcutaneous edema and fluid collections around the knees.

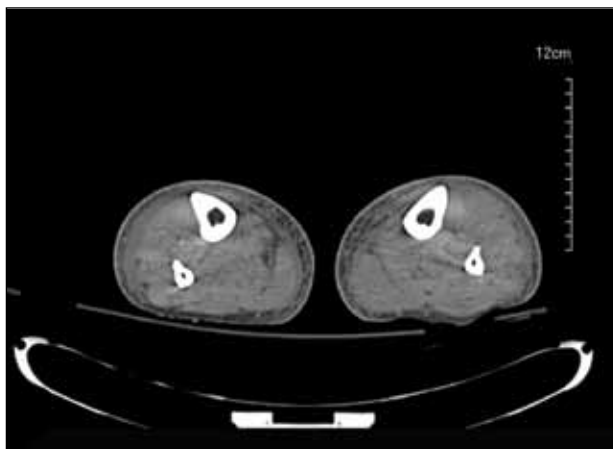


Figure 3. Computed tomography of the legs with edematous changes of the anterior compartment muscles.

Columbia-nalidixic acid agar, chocolate agar, MacConkey agar, and thioglycollate broth, which were incubated at 37°C in air supplemented with 5% CO₂, and to CDC anaerobic blood agar, which was incubated under anaerobic conditions. Gram-stained smears of the aspirates from the bullae demonstrated few granulocytes and numerous large gram-positive bacilli (Figure 4). By the next day, growth of large gram-positive bacilli was detected in both aerobic and anaerobic blood culture bottles and in pure culture from all the bullae samples. The bacterial colonies on sheep blood agar were opaque and white-gray in color, with a rough surface, undulate margins, and surrounding β hemolysis. The isolate was a motile, catalase-positive, arginine-positive, salicin-positive, lecithinase-positive, and penicillin-resistant organism that was identified as *Bacillus cereus*.

Antimicrobial susceptibility testing for *B cereus* has not been standardized, but evaluation by broth microdilution suggested decreased susceptibility to penicillin (minimum inhibitory concentration [MIC], 2 $\mu\text{g/mL}$) and clindamycin (MIC, 2 $\mu\text{g/mL}$), but retained susceptibility to ciprofloxacin (MIC, ≤ 0.25 $\mu\text{g/mL}$), tetracycline (MIC, ≤ 1 $\mu\text{g/mL}$), rifampin (MIC, ≤ 1 $\mu\text{g/mL}$), and vancomycin (MIC, ≤ 2 $\mu\text{g/mL}$).

The patient was admitted to the intensive care unit and was treated initially with fluid resuscitation; transfusions; ventilatory support; and intravenous vancomycin, clindamycin, and imipenem. This regimen was changed to vancomycin and ciprofloxacin when culture and susceptibility results became available to complete a 14-day course. Signs of sepsis resolved and the mental status and skin

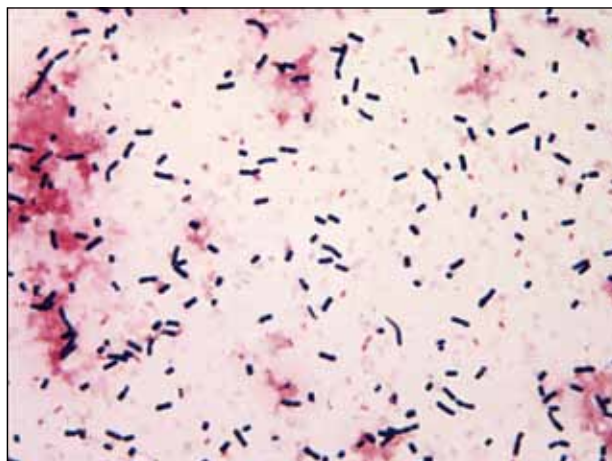


Figure 4. Gram-stained smears of bulla aspirate revealed large gram-positive bacilli and debris in material aspirated from a left lower leg bulla (original magnification $\times 100$ [oil immersion]).

lesions improved. Ultimately, the patient died due to complications of hepatic failure.

Bacillus cereus is a rod-shaped, gram-positive, facultative, aerobic organism that is widely distributed in the environment.¹ Spore formation makes *B cereus* resistant to most physical and chemical disinfection methods; as a consequence, it is a frequent contaminant in materials (eg, plants, dust, soil, sediment), foodstuffs, and clinical specimens.¹

Traditionally considered in the context of foodborne illness, *B cereus* is recognized increasingly as a cause of systemic and local infections in both immunosuppressed and immunocompetent patients. Nongastrointestinal infections reported include fulminant bacteremia, pneumonia, meningitis, brain abscesses, endophthalmitis, necrotizing fasciitis, and central line catheter-related and cutaneous infections.^{1,2}

Cutaneous lesions may have a variety of forms and appearance at initial presentation, including small papules or vesicles that progress into a rapidly spreading cellulitis^{1,2} with a characteristic serosanguineous draining fluid,² single necrotic bullae,³ and gas-gangrenelike infections with extensive soft tissue involvement resembling clostridial myonecrosis.^{1,4} Single or multiple papulovesicular lesions can even mimic cutaneous anthrax.^{1,4} Necrotic or hemorrhagic bullous lesions,³ such as those observed in our patient, are rare.

Exposed areas such as extremities and digits are most often affected, presumably due to entrance of spores from soil, water, decaying organic material, or fomites through skin microabrasions or trauma-induced wounds.¹ Once in the tissue, the crystalline surface protein layer (S-layer) of the bacilli promotes adhesion to human epithelial cells and neutrophils,⁵ followed by release of virulence factors including proteases, collagenases, lecithinase-like enzymes, necrotizing exotoxinlike hemolysins, phospholipases, and most importantly a dermonecrotic vascular permeability factor.^{1,5} Toxins produced by *B cereus* are similar to those closely related to *Bacillus anthracis*, the agent of anthrax.^{1,2}

When large gram-positive bacilli are observed in tissue or wound specimens, initial therapy should address both aerobic (*Bacillus* species) and anaerobic (*Clostridium* species) organisms.^{1,4,6} Once *B cereus* is recovered, treatment should rely on susceptibility testing of the isolate. *Bacillus cereus* produces β -lactamase, thus penicillin and cephalosporin should be avoided.¹ Vancomycin, clindamycin, aminoglycosides, and fluoroquinolones are the drugs of choice.^{1,3,4,6} Daptomycin and linezolid also are active in vitro,¹ but clinical experience with these agents is limited.

Necrotic infection or deep tissue involvement requires surgical intervention.

Numerous other organisms can cause cellulitis and soft tissue infections with hemorrhagic bullae.^{1,3,6} Streptococci, particularly *Streptococcus pyogenes*, and occasionally staphylococci are the primary consideration in normal hosts without trauma.^{3,6} In immunocompromised patients, including those with cirrhosis, diabetes mellitus, and malignancy, *Clostridium perfringens* and gram-negative organisms such as *Escherichia coli*, other enteric bacteria including *Pseudomonas aeruginosa*, *Aeromonas*, and halophilic *Vibrio* species are more frequent.^{3,6}

We describe a patient with underlying cirrhosis who developed bilateral lower extremity hemorrhagic bullous lesions and sepsis due to infection with *B cereus*, an emerging cause of serious infections in patients with underlying immunocompromising conditions such as cirrhosis, diabetes mellitus, and malignancy. Hemorrhagic bullae in immunocompromised patients are associated with sepsis and rapidly progressive illness, and rapid treatment is essential. *Bacillus cereus* should be included as a consideration in the differential diagnosis and management of patients presenting with bullous cellulitis and sepsis.

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