JAMA Dermatology Clinicopathological Challenge

Vesicular Rash in a Neutropenic Infant

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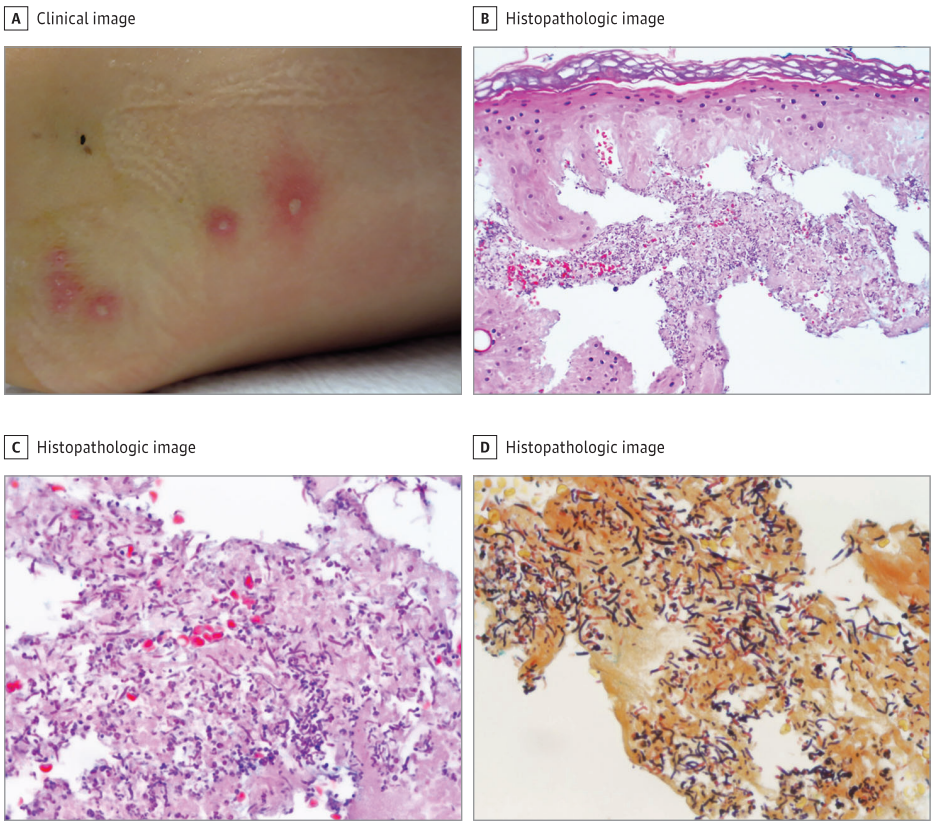

Figure. A, Scattered vesicles with an erythematous base on the lower back. B, Hematoxylin and eosin stain (original magnification ×200). C, Hematoxylin and eosin stain (original magnification ×600). D, Gram stain (original magnification ×600).

A female infant with relapsed refractory infantile acute lymphoblastic leukemia, blast crisis (>60% blasts), and central nervous system involvement was admitted for reinduction chemotherapy with cytarabine, vincristine, daunorubicin, methotrexate, and dexamethasone. Seventeen days after her last day of chemotherapy, while neutropenic, she became febrile and developed several vesicles with an erythematous base on the lower back (**Figure**, A) and left thigh. Tissue and blood cultures and a punch biopsy specimen of a vesicle on the lower back were obtained. Hematoxylin-eosin (Figures, B and C), gram (Figure, D), and periodic acid-Schiff stains were performed on the punch biopsy. Testing for herpes simplex virus and varicella zoster virus were also ordered.

WHAT IS YOUR DIAGNOSIS?

- **A.** Herpes simplex virus
- **B.** Disseminated varicella zoster virus
- **C.** Listeriosis
- **D.** Cutaneous *Bacillus cereus* infection

Diagnosis

D. Cutaneous *Bacillus cereus* infection

Microscopic Findings and Clinical Course

Microscopic evaluation of the punch biopsy specimen revealed focal epidermal and subepidermal necrosis (Figure, B) associated with numerous filamentous bacilli with septa (Figure, C). Gram stain revealed numerous gram-variable rods in the necrotic epidermis and dermis (Figure, D). The periodic acid-Schiff staining findings were negative for fungal elements. The polymerase chain reaction testing results for herpes simplex virus (HSV) and varicella zoster virus (VZV) were negative. Tissue and blood culture findings were positive for *B cereus*. Gentamicin and vancomycin were initiated for *B cereus* bacteremia. A computed tomographic scan with contrast of both thorax and brain was obtained revealing lesions consistent with disseminated *B cereus* in the liver and brain. Unfortunately, the patient died shortly after the diagnosis.

Discussion

Bacillus cereus is a gram-positive or gram-variable, spore-forming, aerobic rod found in soil, vegetables, marine environments, intestinal tracts of invertebrates, and human skin.[1] Owing to its ubiquitous nature, it is often considered a contaminant when found in cultured specimens. The ability of *B cereus* to cause food poisoning and invasive infections is well documented.[1,2] Invasive *B cereus* infections are primarily observed in immunocompromised patients, such as neonates and individuals with hematologic malignant diseases.[1,2] The rising incidence of *B cereus* infections is likely secondary to indwelling intravascular catheters and fluoroquinolone prophylaxis for prolonged neutropenia.[2] Other risk factors include direct inoculation, trauma, and contaminated hospital materials.

The clinical manifestations of *B cereus* infections in patients with indwelling catheters or medical devices are variable and include fever, bacteremia, pneumonia, endophthalmitis, necrotizing fasciitis, osteomyelitis, endocarditis, cerebral abscess, and death.[1] Primary cutaneous *B cereus* infections typically present as isolated vesicles, bulla, or pustules at the primary inoculation site or via contamination of a preexisting wound in the setting of trauma or surgery. In reported cases of primary cutaneous *B. cereus* infections in immunocompromised and immunocompetent patients, blood culture findings were negative and/or direct inoculation was documented in all cases.[3-8] Primary cutaneous infections have not been associated with systemic symptoms or bacteremia.[5]

Secondary cutaneous manifestations of *B cereus* bacteremia have not previously been described. Our patient presented with multiple, discrete vesicles on an erythematous base over the lower back and thighs in the setting of systemic symptoms and positive blood culture findings prior to the development of any rash or skin lesions. To our knowledge, this case is the first report of *B cereus* septicemia presenting as scattered vesicles. While the exact etiology in this patient is unknown, an indwelling catheter was determined to be the most likely portal of entry.

The differential diagnosis for a vesicular or pustular eruption in a neutropenic patient includes HSV, VZV, drug eruption, Sweet syndrome, leukemia cutis, allergic or irritant contact dermatitis, invasive fungal infection, and listeriosis. The gold standard for diagnosing *B cereus* infections is tissue and/or blood cultures. When the skin is involved, a biopsy specimen should be obtained and sent for routine histologic analysis, gram stain, and bacterial/fungal cultures to exclude other etiologies. Flow cytometry should also be considered in patients with a preexisting diagnosis of leukemia to rule out leukemia cutis.

Bacillus cereus is a highly resistant pathogen. The organism expresses a zinc dependent BcII metallo-β-lactamase that binds penicillins, cephalosporins, and carbapenems. Therefore, *B cereus* is resistant to all β-lactam medications (including cephalosporins), except for carbapenems. The first-line treatment is vancomycin or clindamycin; fluoroquinolones and imipenem are considered second-line therapies.[9] However, resistance to carbapenems, fluoroquinolones, and clindamycin is being reported, especially in patient populations where the incidence of *B cereus* infections are increasing (eg, individuals with malignant disease or neutropenia).[10]

Bacillus cereus should be considered in the differential diagnosis for any vesicular and pustular skin eruption in an immunocompromised patient. Cutaneous manifestations may be an early sign of *B cereus* bacteremia or sepsis, which should prompt early and aggressive antibiotic therapy, as illustrated by this case.

ARTICLE INFORMATION

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