Cellulitis as a Presentation of Septicemic Melioidosis

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ABSTRACT

Cellulitis with bacteremia is a rare presentation of melioidosis. The clinical presentation can mimic other common pathogens which cause cellulitis, such as group A Streptococcus, group B Streptococcus and Staphylococcus aureus. This could lead to an inadequate empirical antimicrobial therapy, which may result in a misadventure treatment outcome. We report here a fatal case of septicemic melioidosis presented with cellulitis. (J Infect Dis Antimicrob Agents 2013;30:79-83.)

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INTRODUCTION

Melioidosis is one of the most common severe bacterial infections in Southeast Asia and North Australia.¹ A study in Songklanagarind Hospital reported a prevalence of 46/100,000 admissions.² The majority of cases presented with multifocal infections and septicemia.¹ For melioidosis, presentation with skin and soft tissue infection concomitant to bacteremia is rare. In a recent retrospective study from Songklanagarind Hospital, Thailand, among 140 patients with septicemic melioidosis, there were only 2 patients with skin and soft tissue infection (1.4%), both of which had subcutaneous abscesses.² Here we report a rapidly fatal case of septicemic melioidosis presented with cellulitis.

CASE REPORT

A 36-year-old rubber tapper woman was admitted to Songklanagarind Hospital on 24 October, 2012 due to an abrupt high-grade fever with a few small blebs over her right thigh for one day. She had a 10-year history of systemic lupus erythematosus (SLE). One month before the illness, she was diagnosed severe proliferative nephritis and treated with high-dose corticosteroid and cyclophosphamide. Two days prior to admission, she developed fever and rash with a few small blebs at her right thigh. She also experienced mild pain at her right leg but was able to walk normally. She denied any history of trauma, exposure to marine or fresh water, and seafood ingestion.

On physical examination at admission, she appeared acutely ill, with a blood pressure of 120/
70 mmHg, pulse rate of 120 beats per minute, respiratory rate of 24 breaths per minute, and temperature of 39.0°C. There were a few thin-walled small blebs, 0.5 cm in diameter, with an erythematous base at the mid distal region of the right thigh. The rest of the physical examination was normal.

The initial laboratory studies disclosed the following: a white blood cell count of 3,520 cells/mm³ (N 77%, L 7%, band 10%, M 3%, Meta 3%), hematocrit of 26.9% and a platelet count of 145,000/mm³. The blood urea nitrogen level was 65.7 mg/dL and the creatinine level was 3.33 mg/dL. Liver function test showed albumin level of 1.4 g/dL, aspartate aminotransferase (AST) level of 62 IU/L, and alanine aminotransferase (ALT) level of 45 IU/L. The bilirubin and alkaline phosphatase (ALP) levels were within normal limits. Chest radiograph revealed no pulmonary infiltration.

Ceftriaxone and clindamycin were administered intravenously for empirical treatment of bacterial cellulitis, together with acyclovir for a possible herpes zoster infection as well as a stress-dosed corticosteroids. Fifteen hours later, she became hypotensive, with a blood pressure of 90/50 mmHg, persistently febrile, and developed tachycardia and tachypnea. The initially small blebs agglomerated to 3 cm in size, with thin-wall bullae and a bloody fluid content on the background of a large, irregular bordered dark purplish patch along the right thigh (Figure 1). There was no crepitus. The muscle function was normal and there was no numbness at her right leg.

She was diagnosed septic shock with a progression of the right thigh skin lesion. After the bleb fluid was collected for further microbiological studies, imipenem-cilastatin and vancomycin were given intravenously. Emergency imaging of her right thigh was requested due to the development of necrotizing fasciitis. Despite a high dose of vasopressors and fluid replacement, the patient remained hypotensive and developed cardiac arrest. She died 34 hours after hospitalization. Two sets of hemocultures and bleb-fluid culture subsequently reported growth of *Burkholderia pseudomallei*, which were susceptible to co-trimoxazole, ceftazidime, imipenem and meropenem.

**DISCUSSION**

Cellulitis with septicemia is a rare presentation of melioidosis. Its clinical presentation can mimic other common pathogens causing cellulitis, including group A streptococcus, group B streptococcus and *Staphylococcus aureus*. This could lead to an inadequate empirical antimicrobial therapy, which may result in a misadventure outcome.

Community-acquired sepsis or septic shock in the South of Thailand is accredited to *Escherichia coli* (23.1%), *Burkholderia pseudomallei* (19.3%), and *Staphylococcus aureus* (8.2%). However, it is unusual to empirically treat melioidosis in patients without a risk factor.

Our patient presented with severe skin and soft tissue infection leading to severe sepsis. She had an underlying condition of SLE and was receiving immunosuppressive agents. Patients with SLE exhibit a number of immune system abnormalities, including inhibited delayed-type hypersensitivity, reduced numbers of T cells, and reduced levels of complement and functional asplenism. The use of corticosteroids is also associated with impairments of the immune system, including reduced chemotaxis, phagocytosis and oxidative killing activities of the phagocytes, and reduced lymphokines (IL-2, TNF-α, IL-12, INF). These impairments may contribute to an increased risk of...
melioidosis in SLE. However, in a review of melioidosis patients in Thailand, SLE was not described.4

After presentation, the skin lesion progressed rapidly from a few small blebs to hemorrhagic bullae accompanied by a deterioration of her hemodynamic status. Although there were no other signs or symptoms of necrotizing fasciitis, e.g., marked pain, tenderness or crepitus, it could not be excluded. Hence, the diagnosis of primary skin and soft tissue infection with septicemia was the most likely. The common causative pathogens of cellulitis include S. pyogenes, S. aureus, group B streptococci, Vibrio spp. and Aeromonas spp.5 Based on the common causative pathogens, third-generation cephalosporin and clindamycin were the initial empirical antimicrobial agents of choice. Owning to the fact that SLE is not a risk factor for melioidosis and B. pseudomallei is not a common causative organism of cellulitis in such patients, an inadequate empirical antimicrobial therapy was administered to this patient. Moreover, as a result of the high mortality rate of melioidosis with septic shock (80%-95%)6, our patient eventually passed away.

Melioidosis is one of the most common infections in Southeast Asia and North Australia.7 A study from Songkla Ngarind Hospital reported a prevalence of 46/100,000 admissions.8

Burkholderia pseudomallei is the causative agent of melioidosis. B. pseudomallei is a small, gram-negative, oxidase-positive, motile, aerobic bacillus with occasional polar flagella. On staining, a bipolar “safety pin” pattern is seen.7 Colonies vary from smooth to rough morphologies and often become wrinkled after a few days of incubation. The characteristics of its colonies and the typical production of an acid slant with a neutral butt in triple sugar iron agar after 24 hours of incubation, with a subsequent change to an acidic pH in the butt without gas after 72 hours of incubation are useful clues for diagnosis (Figure 2).9 The organism is present in soil and surface water in endemic regions. Humans and animals are infected by percutaneous inoculation, inhalation, or ingestion.7

Figure 1. Bullae, sized ~ 3 cm in diameter on the background of a large, irregular border, dark brown-purplish patch along the right leg.

Figure 2. Typical production of an acid slant with a neutral butt in triple sugar iron agar after 24 hours of incubation.
The virulence of *B. pseudomallei* consists of surface components (lipopolysaccharide and capsular polysaccharide), exoproteins (hemolysin, phospholipase C, metalloprotease A and collagenase), type I, II, III, and V secretion systems, adhesins, fimbriae and pili. Lipopolysaccharides are endotoxins, which have an important role in sepsis and hemolysin could explain the formation of hemorrhagic blebs.\(^\text{10}\) It is an intracellular pathogen and innate immunity is the front line defender of this pathogen, whereas adaptive cellular immunity is of limited benefit.\(^\text{6}\)

The clinical manifestations of melioidosis can be categorized into 5 groups: melioidosis with septic shock, disseminated septicemic melioidosis, septicemic melioidosis, localized melioidosis and asymptomatic melioidosis.\(^\text{6}\) The majority of cases present with multifocal infection with septicemia.\(^\text{7}\)

Cutaneous manifestation in septicemic melioidosis can be classified to primary skin infection (cellulitis, cutaneous abscess and, rarely, necrotizing fasciitis) and secondary skin infection (hematologic spreading of the infection to skin and subcutaneous tissue). A recent retrospective study from Songklanagarind Hospital, Thailand, demonstrated that among 140 patients with septicemic melioidosis, only 2 patients had skin and soft-tissue infection (0.01%), both of which had subcutaneous abscesses. There was no patient with cellulitis.\(^\text{8}\) Comparing to primary skin manifestation of melioidosis in Australia, the large majority had single lesions that were nonspecific in nature, with size varying from several millimeters to several centimeters. The most common presentation was with an ulcer. Other appearances included single pustules, boils, crusted erythematous lesions, and dry asymmetric erythematous flat lesions. Cellulitis was rare. There was only one patient in this cohort who had primary skin lesion with septicemic melioidosis. Moreover, none of the patients with primary skin manifestation of melioidosis died from melioidosis.\(^\text{9}\) For secondary skin infection in septicemic melioidosis, most of the cases presented with superficial and subcutaneous abscesses, and a few cases with orbital infection.\(^\text{11,12,13,14}\)

The standard treatment of melioidosis consists of the acute and maintenance phases. Treatment of severe melioidosis with ceftazidime alone during the acute phase showed no difference in mortality rate compared to those treated with combination of ceftazidime and cotrimoxazole.\(^\text{15}\)

Furthermore, a recent study from Songklanagarind Hospital found no statistical difference in culture-confirmed recurrences among patients received cotrimoxazole alone and those who received the combination of doxycycline and cotrimoxazole for maintenance treatment of melioidosis.\(^\text{8}\) In addition, a recent study in Northeast Thailand reported that the addition of doxycycline to cotrimoxazole during the maintenance phase of therapy did not reduce the recurrence rate of melioidosis.\(^\text{16}\) Therefore, ceftazidime is considered the first-line agent of choice in the acute phase, and cotrimoxazole is recommended in the maintenance phase of melioidosis treatment.

In conclusion, cellulitis with septicemic melioidosis is a rare presentation, especially in patients with underlying SLE. Besides, the clinical presentation of melioidosis can mimic infections by other common pathogens causing cellulitis. Thus, melioidosis should be acknowledged as being a great mimicker. Inadequate empirical antimicrobial therapy could result in a fatal outcome. Hence, the differential diagnosis of melioidosis should be considered in patients from the South of Thailand without risk factors of melioidosis.
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References


