Community-Acquired Methicillin-Resistant *Staphylococcus Aureus* As a Cause of Fournier's Gangrene

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ABSTRACT: Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) has become an important pathogen in aggressive skin and soft-tissue infections in patients without risk factors for nosocomial infections. We describe a case of a previously healthy adult who developed fulminant sepsis from Fournier's gangrene caused by a strain of CA-MRSA containing the Panton-Valentine leukocidin genes.
KEY INDEXING TERMS: Community-acquired *Staphylococcus aureus*; Methicillin resistant; Fournier's gangrene. **[Am J Med Sci 2008;335(4):327–328.]**

Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) has emerged as a genetic and pathologic entity distinct from hospital-acquired methicillin-resistant *Staphylococcus aureus* (HA-MRSA). Unlike HA-MRSA, CA-MRSA is isolated from patients without recent exposure to health care settings and exhibits susceptibility to multiple classes of nonbeta-actam antibiotics.[1] Although most frequently associated with skin and soft-tissue infections, CA-MRSA can also cause severe sepsis, necrotizing pneumonia, and necrotizing fasciitis.[2,3] The increasing global prevalence of this pathogen has modified empiric therapy for furunculosis and other infections for which beta-lactam antibiotics were previously routinely prescribed.[4] The vast majority of disease-causing CA-MRSA strains contain the Panton-Valentine leukocidin (PVL) genes which encode toxins associated with aggressive *S. aureus* infections.[5] Fournier's gangrene is a rapidly progressive infection of the skin and deep soft tissues of the perineum and genitalia in men. A mixed flora of enteric Gram-negative organisms and anaerobes from the GI tract commonly causes this infection. In this report, we describe a patient with Fournier's gangrene and sepsis syndrome caused by CA-MRSA.

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Submitted May 1, 2007; accepted in revised form June 15, 2007.

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Case Reports

A 57-year-old man with no significant medical history, and no recent family or personal exposure to health care facilities, presented to the Emergency Department of the Veterans Administration Medical Center with complaints of lower abdominal pain, nausea, and vomiting for 2 days. He denied tobacco or alcohol use, and any previous injection drug use. Vital signs at presentation were temperature – 100.4°F (oral), pulse – 94 beats/minute, blood pressure – 188/90 mm Hg, and oxygen saturation (oximetry) on room air – 97%. Abdominal examination revealed tenderness to palpation in the lower quadrants without peritoneal signs. No abnormalities were noted on genitourinary examination. Stool was negative for occult blood. Chest and abdominal radiographs were unremarkable. Complete blood count revealed white blood cell count of 19,000/mm^3 with 20% band forms, hemoglobin of 13.8 g/dL, and a normal platelet count. Renal and hepatic function panels were all within normal limits except for a glucose of 291 mg/dL. The patient had no previous history of diabetes. Despite the recommendations of the evaluating physician, the patient refused hospital admission and was discharged with a 10 day prescription of ciprofloxacin and metronidazole for presumed diverticulitis.

The patient returned 24 hours later with the interval development of scrotal swelling, coffee ground emesis, and paroxysmal nocturnal dyspnea. His temperature had increased to 101.1°F, pulse was 130 beats/minute and blood pressure was 116/67 mm Hg. His respiratory rate was now 50/minute. A genitourinary examination revealed severe scrotal and penile edema with 2 bullous lesions on the penile shaft. His white blood cell count had decreased to 9000/mL with 20% band forms and hemoglobin had decreased to 12.1 g/dL. The renal panel revealed a glucose of 463 mg/dL, a creatinine of 2.3 mg/dL and a prothrombin time of 21.2 seconds. The patient was directly admitted to the medical intensive care unit and placed on mechanical ventilation. His hypotension rapidly worsened and he required vasopressors. Broad-spectrum antibiotic coverage was initiated with vancomycin, piperacillin-tazobactam, and gatifloxacin. The Urology service was consulted the day of admission and a diagnosis of Fournier's gangrene was made. The patient underwent extensive debridement of his penis and perineum, as well as a complete scrotectomy the day after admission. Culture obtained during surgery grew only MRSA susceptible to clindamycin, rifampin, tetracycline, trimethoprim-sulfamethoxazole, and vancomycin.

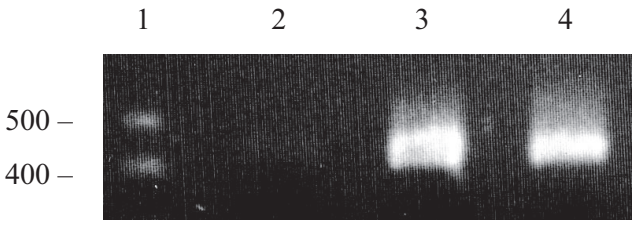

Figure 1. Detection of PVL gene locus by PCR in patient's MRSA isolate. Conditions and primers for the PCR reaction have been previously described.[6] Lane 1 – molecular weight markers, in base pairs; lane 2 – polymerase with buffer only (negative control); lane 3 – ATCC 49775 (positive control); lane 4 – patient strain from this report.

The isolate had intermediate susceptibility to levofloxacin and did not exhibit inducible resistance to clindamycin by D-test. The strain was positive for the PVL locus by PCR (Figure 1). Surgical cultures for anaerobes and admission blood cultures remained sterile. The patient had no serological evidence of HIV, hepatitis B, or hepatitis C infection. Infectious diseases was consulted and recommended clindamycin, rifampin and daptomycin with discontinuation of all other antibiotics.

The patient required multiple additional surgeries, including subsequent debridement of his perineum on 2 occasions. He gradually became normotensive and required less ventilatory support. Stool output was interfering with wound care, and consequently the patient underwent an ileostomy. After the ileostomy, he developed high fevers and hypotension and on hospital day 16 *Candida albicans* was isolated from his blood. He was placed on caspofungin but developed acute renal failure and hypotension. The patient's hypotension and renal failure progressed despite aggressive supportive care and he expired on the 24th hospital day.

Discussion

S. aureus commonly colonizes perineal skin but is an uncommon cause of Fournier's gangrene, which is typically a polymicrobial infection with enteric organisms, including anaerobes.[7] MRSA is rarely associated with perineal infections, with only 1 case report in the literature.[8] This case was a mixed infection of MRSA and anaerobes in a spinal cord injury patient with a chronic condom catheter and extensive antibiotic exposure. It was presumed to be a health care related infection and the susceptibility pattern of the MRSA is consistent with this supposition.[8] This is the first reported case of Fournier's gangrene caused by CA-MRSA, which appeared to be the sole pathogen.

The case definition of CA-MRSA infection is generally recognized as infection in the absence of recent hospitalization.[2] Moreover, CA-MRSA strains are genetically and phenotypically distinct from HA-MRSA.[5] Methicillin resistance in *S. aureus* is encoded by the *mecA* gene. This gene resides on the staphylococcal chromosomal cassette mec (SCCmec) which integrates into a consistent location in the *S. aureus* chromosome.[5] CA-MRSA strains carry smaller chromosomal cassettes than HA-MRSA strains, typically the type IV SCCmec element. The smaller cassettes carry fewer resistance genes than larger cassettes, generally resulting in susceptiblility to nonbeta-lactam antibiotics.[5] CA-MRSA strains isolated from severe infection nearly always carry the PVL locus, but the role of PVL toxins in CA-MRSA pathogenesis is not fully understood.[3,5]

Our patient exhibited features typical of CA-MRSA necrotizing infections: he had no significant exposure to health care facilities; his clinical condition rapidly deteriorated to sepsis with respiratory failure; the staphylococcal strain isolated from his infection exhibited antibiotic susceptibilities typical of CA-MRSA strains and carried a chromosomal locus containing the PVL genes.[4]

In summary, we present a patient with sepsis because of Fournier's gangrene caused by CA-MRSA. His infection met criteria for CA-MRSA including lack of exposure to health care facilities, the antibiotic susceptibility pattern of his isolate, and the presence of PVL genes. Fournier's gangrene is typically a polymicrobial infection and we cannot completely exclude other pathogens as contributing to this patient's infection. However, deep-tissue cultures at time of surgery with rapid transport of anaerobic specimens failed to show other bacterial pathogens, so we believe that *S. aureus* was the predominant organism in the infected tissue. This is the first reported case of CA-MRSA as an etiology of this infection. In addition to prompt surgical intervention, clinicians should consider the addition of coverage for CA-MRSA, based on local susceptibility patterns, when starting empiric antimicrobial therapy for Fournier's gangrene and other necrotizing soft-tissue infections.

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