Severe Necrotizing Fasciitis in a Human Immunodeficiency Virus-Positive Patient Caused by Methicillin-Resistant Staphylococcus aureus

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Methicillin-resistant Staphylococcus aureus (MRSA) is a rarely reported cause of necrotizing fasciitis. We report an unusually severe case of MRSA necrotizing fasciitis in a previously undiagnosed AIDS patient. Molecular analysis revealed that the strain had the USA300/spa1 genotype, now an abundant cause of community-acquired MRSA infection.

CASE REPORT

A 36-year-old Hispanic male with no previously recognized significant medical conditions presented to the emergency department (ED) of an outlying community hospital with a chief complaint of exquisite right arm pain, lethargy, fever, and shortness of breath. He had been treated 2 weeks previously with clindamycin for right axillary hidradenitis following a self-reported spider bite. The patient had no recent traumatic injury or known contact with methicillin-resistant Staphylococcus aureus (MRSA). Although the skin infection failed to resolve, he had been otherwise asymptomatic and did not seek further medical attention until awakening that morning with acute distress. Physical examination in the ED revealed a tensely edematous and markedly erythematous right upper arm and shoulder. The right hand and fingers were cool, but they retained complete range of motion. The results shown by a chest X-ray were unremarkable despite coarse breath sounds and the deep soft tissue infection. All analytes measured in the initial chemistry and coagulation panels were within normal limits. He was diagnosed with severe cellulitis, septic shock (blood pressure, 58/32; pulse, 130; temperature, 99.4°F; white blood cell count, 1,600/μl), and possible necrotizing fasciitis. Empirical antimicrobial treatment was initiated immediately with vancomycin, imipenem/cilastatin, rifampin, and voriconazole. Histologic analysis of the surgically excised tissue revealed features typical of necrotizing fasciitis (Fig. 1). Despite initial improvement following surgical intervention and antimicrobial therapy, the septic shock persisted (maximum temperature, 103.4°F; average blood pressure, 100/60) and the necrotizing fasciitis continued to spread to the bilateral chest walls, right abdomen, and right back. He was transferred to a tertiary-care hospital for continued evaluation and management of the severe MRSA infection. Nine additional debridement procedures were performed. Tissues collected during these surgical interventions grew rare MRSA strains with identical susceptibility patterns (Table 1). The hospital course was also complicated by adrenal insufficiency, mild coagulopathy, and iatrogenic anemia. The patient gradually improved, and he was discharged to a rehabilitation center.

Of note, screening and confirmatory studies performed during the diagnostic evaluation at the outside hospital were positive for human immunodeficiency virus (HIV) infection. Further evaluation of this new diagnosis was not pursued until the life-threatening MRSA infection completely resolved. At discharge, his CD4+ cell count and HIV viral load were <20 cells/mm³ and 358,000 copies/ml, respectively. These initial laboratory values (CD4+ < 200 cells/mm³ and viral load > 100,000 copies/ml) fulfill criteria for progression to AIDS and initiation of highly active antiretroviral therapy. A multidrug regimen for treatment-naïve patients was prescribed. It included tenofovir, lamivudine, atazanavir, ritonavir, dapsone, and azithromycin. One month later, his CD4+ count was 192 cells/mm³.

S. aureus is an exceptionally versatile pathogen capable of causing human infections that range in severity from impetigo and cellulitis to life-threatening bacteremia and endocarditis. Asymptomatic nasopharyngeal and perineal carriage and uncomplicated skin and soft tissue infections are far more com-
mon than invasive infections (2, 28). Of note, *S. aureus* is a very
infrequent cause of necrotizing fasciitis, with an estimated case
rate of approximately 0.1/100,000 (7, 15, 24, 25). Colloquially
termed the “flesh-eating disease,” necrotizing fasciitis is an
invasive infection characterized by widespread tissue destruction
and significant morbidity and mortality (11). However,
most published cases of *S. aureus* necrotizing fasciitis involve
beta-lactam antibiotic-susceptible strains which progress with a
relatively indolent clinical course (24, 25). Thus, the MRSA
necrotizing fasciitis case presented herein was unusual in that
it was rapidly progressive and nearly fatal. Of further interest,
this infection was the initial presenting illness for an apparently
healthy adult with previously undiagnosed HIV/AIDS.

In an effort to better understand the unusual virulence ob-
erved in this MRSA necrotizing fasciitis case, we analyzed the
peripheral blood isolate by molecular genotyping. Results were
consistent with the USA300 genotype, a strain now causing
epidemic disease in the United States (7, 18, 24, 32, 34, 35).
DNA sequencing of a polymorphic 24-bp variable-number tan-
dem repeat in the staphylococcal protein A (*spa*) gene deter-
mined that this organism was *spa* type 1, which is associated
with multilocus sequence type 8 (20, 31). Multiplex PCR dem-
onstrated that it had the staphylococcal chromosomal cassette
*mec* type IVa element, the arginine catabolic mobile element,
and the genes (*lukS-lukF*) encoding Panton-Valentine leuko-
cidin (PVL) (8, 10, 20, 31, 35). Western immunoblotting con-
ferred that the organism expressed alpha-hemolysin and PVL
Toxin (data not shown).

The USA300 genotype of *S. aureus* is now a common cause of
community-associated skin and soft tissue infection in North
America (7, 18, 24, 32, 34, 35). There are also a few reports of
healthcare-associated sepsis, pneumonia, and endocarditis (13,
30, 33). Furthermore, recent increases in the overall frequency
and severity of MRSA infection, particularly in nontraditional
risk groups, have been noted (21, 30). Thus, there is an emerg-
ing concern about an evolution toward greater virulence of the
MRSA USA300 genotype.

The patient described herein lacked most known risk factors
for invasive staphylococcal disease (19). Although immunosup-
pressive comorbidities such as malnutrition, diabetes mellitus,
and hepatic cirrhosis have been associated with poor prognosis
and increased mortality in necrotizing fasciitis, there is no
evidence that they significantly increase infection susceptibility
(3, 22). Similarly, chronic corticosteroid and nonsteroidal anti-
flammatory therapy are linked to necrotizing fasciitis, but
dose-response relationships are poorly defined (1, 14). HIV/
AIDS is not generally considered to be a substantial predis-
posing risk factor for invasive MRSA infections (27), and nec-
rotizing fasciitis is uncommonly reported from studies of these
patients (4, 24). However, HIV/AIDS is linked to community-
acquired MRSA, and an increased rate of skin infections by
USA300 genotype strains was recently noted for this popula-
tion (6, 30).

We reviewed the English-language literature and identified
19 other reported cases of necrotizing fasciitis caused by
MRSA, but only one patient was HIV positive (9, 16, 23, 26,
37) (Table 2). Molecular analyses documented that the
USA300 genotype caused our case and five others (Table 2,
Cases 1 and cases 2 to 6, respectively). This finding suggests that
the USA300 MRSA genotype should be added to the differen-
tial diagnosis of pathogens that cause necrotizing fasciitis,

TABLE 1. Antimicrobial susceptibility patterns of the MRSA strain
grown from blood

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>MIC (µg/ml)</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clindamycin</td>
<td>&gt;2</td>
<td>Resistant</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>&gt;4</td>
<td>Resistant</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>4</td>
<td>Resistant</td>
</tr>
<tr>
<td>Linezolid</td>
<td>2</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Methicillin</td>
<td>&gt;2</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Rifampin</td>
<td>&lt;0.5</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>&lt;0.5</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Trimethoprim/sulfamethoxazo</td>
<td>&lt;0.5/9.5</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>2</td>
<td>Susceptible</td>
</tr>
</tbody>
</table>

* The MIC of each agent is reported in micrograms per milliliter. The MIC was measured by broth dilution, and susceptibility or resistance was interpreted according to CLSI guidelines (5).

FIG. 1. Representative photomicrographs of necrotic tissue taken
from the patient. (A) Nonviable myocytes and adipocytes are seen in
a background of necrotic tissue (hematoxylin-eosin; original magnifi-
cation, ×10). (B) A thrombosed artery is present within the necrotic soft tissue (hematoxy-
lin-eosin; original magnification, ×40). No organisms were seen upon
performing Gram staining (data not shown).
TABLE 2. Reported characteristics of necrotizing fasciitis cases caused by MRSA

<table>
<thead>
<tr>
<th>Case and reference</th>
<th>Predisposing risk factor(s)</th>
<th>HIV status</th>
<th>MRSA bacteremia test result</th>
<th>Genotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>HIV, SSTI</td>
<td>Positive</td>
<td>Positive</td>
<td>USA300/SPA-1/PVL+</td>
</tr>
<tr>
<td>2 (22)</td>
<td>HIV/AIDS</td>
<td>Positive</td>
<td>Positive</td>
<td>USA300/PVL+</td>
</tr>
<tr>
<td>3 (22)</td>
<td>DM, IDU, homeless</td>
<td>Unknown</td>
<td>Positive</td>
<td>USA300/PVL+</td>
</tr>
<tr>
<td>4 (22)</td>
<td>IDU</td>
<td>Unknown</td>
<td>Positive</td>
<td>USA300/PVL+</td>
</tr>
<tr>
<td>5 (22)</td>
<td>DM</td>
<td>Unknown</td>
<td>Positive</td>
<td>USA300/PVL+</td>
</tr>
<tr>
<td>6 (22)</td>
<td>DM, CVD, homeless</td>
<td>Unknown</td>
<td>Unknown</td>
<td>USA300/PVL+</td>
</tr>
<tr>
<td>7 (22)</td>
<td>None reported</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>8 (22)</td>
<td>None reported</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>9 (22)</td>
<td>HCV, IDU, homeless</td>
<td>Unknown</td>
<td>Negative</td>
<td>Unknown</td>
</tr>
<tr>
<td>10 (22)</td>
<td>IDU, SSTI, homeless</td>
<td>Unknown</td>
<td>Negative</td>
<td>Unknown</td>
</tr>
<tr>
<td>11 (22)</td>
<td>Malignant neoplasm</td>
<td>Unknown</td>
<td>Negative</td>
<td>Unknown</td>
</tr>
<tr>
<td>12 (22)</td>
<td>None reported</td>
<td>Unknown</td>
<td>Negative</td>
<td>Unknown</td>
</tr>
<tr>
<td>13 (22)</td>
<td>HCV, IDU</td>
<td>Unknown</td>
<td>Negative</td>
<td>Unknown</td>
</tr>
<tr>
<td>14 (22)</td>
<td>SSTI</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>15 (22)</td>
<td>HCV, IDU</td>
<td>Unknown</td>
<td>Negative</td>
<td>Unknown</td>
</tr>
<tr>
<td>16 (25)</td>
<td>DM, CVD, postsurgical</td>
<td>Unknown</td>
<td>Positive</td>
<td>Unknown</td>
</tr>
<tr>
<td>17 (8)</td>
<td>None reported</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>18 (8)</td>
<td>None reported</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>19 (36)</td>
<td>DM, corticosteroids</td>
<td>Unknown</td>
<td>Negative</td>
<td>PVL-</td>
</tr>
<tr>
<td>20 (15)</td>
<td>SSI</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

* Data for the reported patient (case 1) are compared to those from 19 other published cases (cases 2 to 20). Abbreviations: DM, diabetes mellitus; IDU, injection drug use; HCV, hepatitis C virus; SSTI, skin and soft tissue infection; CVD, cardiovascular disease. Unknown, testing was either not reported or not performed.

including infections within the HIV/AIDS population. Prevalence studies have not been performed on MRSA strains isolated in Houston, but the USA300 genotype has been previously detected in another local adult hospital (13), and it is the predominant strain isolated from pediatric patients treated for uncomplicated infections (12, 13, 17).

Our report is an important reminder that benign-appearing skin and soft tissue infections caused by MRSA can rapidly progress to potentially fatal illness. The hidradenitis diagnosed in this patient evolved into necrotizing fasciitis and septic shock within a few days of initial clinical presentation. This case also underscores the need for improved early diagnostic procedures and enhanced understanding of the bacterial virulence factors that contribute to necrotizing fasciitis. In recent years, PVL, a leukocyte-lytic exotoxin produced by most USA300 S. aureus strains, has been speculated to be a virulence factor (35). Similarly, the arginine catabolic mobile element encoding multiple gene products that may enable infecting organisms to suppress and/or evade the host immune system also has been thought to contribute to the success of this strain (8, 10). However, patient epidemiological data and experimental infection models have failed to unambiguously demonstrate a direct role in invasive disease (8, 10, 35). Furthermore, there is uncertain therapeutic significance associated with constitutive clindamycin resistance and increased vancomycin MICs (29, 36). This susceptibility profile may have contributed, in part, to the initial treatment failure and subsequent disease progression that occurred in this patient. The USA300 strain may cause more cases of severe necrotizing fasciitis as its prevalence increases in the United States and elsewhere.

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REFERENCES


