Introduction

Over the past 20 years, methicillin-resistant Staphylococcus aureus (MRSA) has been isolated with increased frequency in hospitalized patients as well as in the community. MRSA infections have been associated with greater morbidity, mortality, and hospital costs than their methicillin-sensitive S. aureus (MSSA) counterparts.

Until recently, treatment options for serious infections caused by MRSA have been limited to a few agents, most notably vancomycin. However, with the introduction of new antimicrobial agents, it has become possible to develop new treatment strategies for MRSA, including toxin-producing strains of MRSA that have been identified.

Epidemiology

Gram-positive cocci, in particular S. aureus, account for 20% to 30% of all cases of hospital-acquired pneumonia (HAP).1 Nosocomial strains of MRSA are found worldwide,2 and data from the US National Nosocomial Infections Surveillance System show that MRSA now accounts for more than 55% of S. aureus-related infections in the intensive care setting.3

Traditionally, MRSA has been considered a healthcare-associated organism if it is isolated from a patient at least 72 hours after admission in a healthcare facility (acute-care hospital or long-term care facility) and community-acquired if isolated from a patient at the time of admission or within 48 to 72 hours of hospital admission. However, without the use of sophisticated laboratory techniques, it is often difficult to know if the MRSA was actually acquired in the community or from previous contact with the healthcare system; therefore, some prefer to categorize different types of MRSA as “healthcare-associated” (HA-MRSA), “community-associated (CA-MRSA) with risk factors for healthcare acquisition,” or “community-associated without risk factors for healthcare acquisition.”4

In comparing CA-MRSA with HA-MRSA, Naimi et al found that among MRSA infections, 12% were classified as CA-MRSA; CA-MRSA patients were younger than HA-MRSA patients (average age, 23 years vs 68 years; P<0.001); more CA-MRSA patients than HA-MRSA patients were non-white (32% vs 11%; P<0.001); and CA-MRSA patients generally had a lower median income level than HA-MRSA patients ($25,395 vs $28,290; P=0.02) (Table).5

Virulence

S. aureus strains can express many potential virulence factors, including surface proteins that promote colonization of host tissues, exotoxins and superantigens that cause tissue damage and the symptoms of septic shock, and invasins that promote bacterial spread in tissues (eg, leukocidin, kinases, hyaluronidase).6

Panton-Valentine leukocidin (PVL) is a cytotoxin produced by fewer than 5% of S. aureus strains, and it has been associated with primary skin infections and severe necrotizing pneumonia. In a study in which investigators screened 172 strains of S. aureus, PVL genes were detected in 93% of strains associated with furunculosis and in 85% of strains associated with severe necrotic hemorrhagic pneumonia, both of which were community acquired. PVL genes were not detected in strains associated with other types of infections, such as HAP, toxic shock syndrome, infective endocarditis, or mediastinitis.7,8
Toxin Production

PVL is a synergohemolytic toxin composed of 2 component proteins. PVL creates lytic pores in the cell membranes of neutrophils and induces release of neutrophil chemotactic factors including interleukin-8 and leukotriene B4 (Figure). Adapted from reference 5.

Table. Comparison of HA-MRSA and CA-MRSA

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HA-MRSA</th>
<th>CA-MRSA</th>
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<tbody>
<tr>
<td>Setting</td>
<td>Hospital, nursing home, dialysis clinic</td>
<td>Community, entering hospitals</td>
</tr>
<tr>
<td>Ethnic predominance</td>
<td>White</td>
<td>Non-white (African-American, Asian, Hispanic)</td>
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<tr>
<td>Horizontal transmission</td>
<td>Yes (hospital, nursing home)</td>
<td>Yes (family, day care, military barracks, locker room, prison)</td>
</tr>
<tr>
<td>Predisposing underlying illnesses</td>
<td>Diabetes, head trauma, renal failure</td>
<td>None</td>
</tr>
<tr>
<td>Predominant site of infection</td>
<td>None</td>
<td>Skin and soft tissue</td>
</tr>
<tr>
<td>Tissue necrosis</td>
<td>Uncommon</td>
<td>Common in skin and lung</td>
</tr>
<tr>
<td>Preceding influenza illness</td>
<td>Uncommon</td>
<td>Common with pneumonia</td>
</tr>
<tr>
<td>Waterhouse-Friderichsen syndrome</td>
<td>Absent</td>
<td>Can occur</td>
</tr>
<tr>
<td>mecA gene</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Panton-Valentine leukocidin</td>
<td>Historically not found</td>
<td>Usually present</td>
</tr>
<tr>
<td>Susceptible to non-β-lactam antibiotics</td>
<td>Usually not</td>
<td>Often yes</td>
</tr>
</tbody>
</table>

CA-MRSA, community-associated methicillin-resistant Staphylococcus aureus; HA-MRSA, healthcare-associated methicillin-resistant Staphylococcus aureus.

Adapted from reference 5.

Antibiotic susceptibility among all strains isolated varied significantly. However, the study found that antibiotic therapy was not concordant with the results of susceptibility testing in 57% of patients with MRSA infection who received antibiotics. As a result, the authors recommended that when antimicrobial therapy is indicated for the treatment of complicated skin and soft-tissue infections, clinicians should consider obtaining cultures and modifying empirical therapy to provide MRSA coverage.

In addition, Katayama et al noted that MRSA strains produce a cell-wall penicillin-binding protein with a low affinity for β-lactam antibiotics. The authors added that a notable difference between MRSA and MSSA is that a higher percentage of MRSA strains possess toxins such as PVL. Indeed, when selecting antimicrobial therapy, minimum inhibitory concentrations (MICs) and coverage of the infection and the host are typically considered. Based on findings such as these, however, clinicians may also want to consider the issue of toxin penetration during the selection process.

In addition to antibiotic therapy, alternative treatments may become available for toxin-producing strains of S. aureus. Polyclonal immunoglobulin has been proposed as a therapy for patients with serious CA-MRSA infections. Potential mechanisms of action include neutralization of circulating cytokines and down-regulation of their expression.

Conclusion

The optimal management strategy for toxin-producing strains of S. aureus is still unknown. Pending further clinical investigations, clinicians should consider the use of antibiotics that can inhibit specific toxin production in patients with serious infection.

References