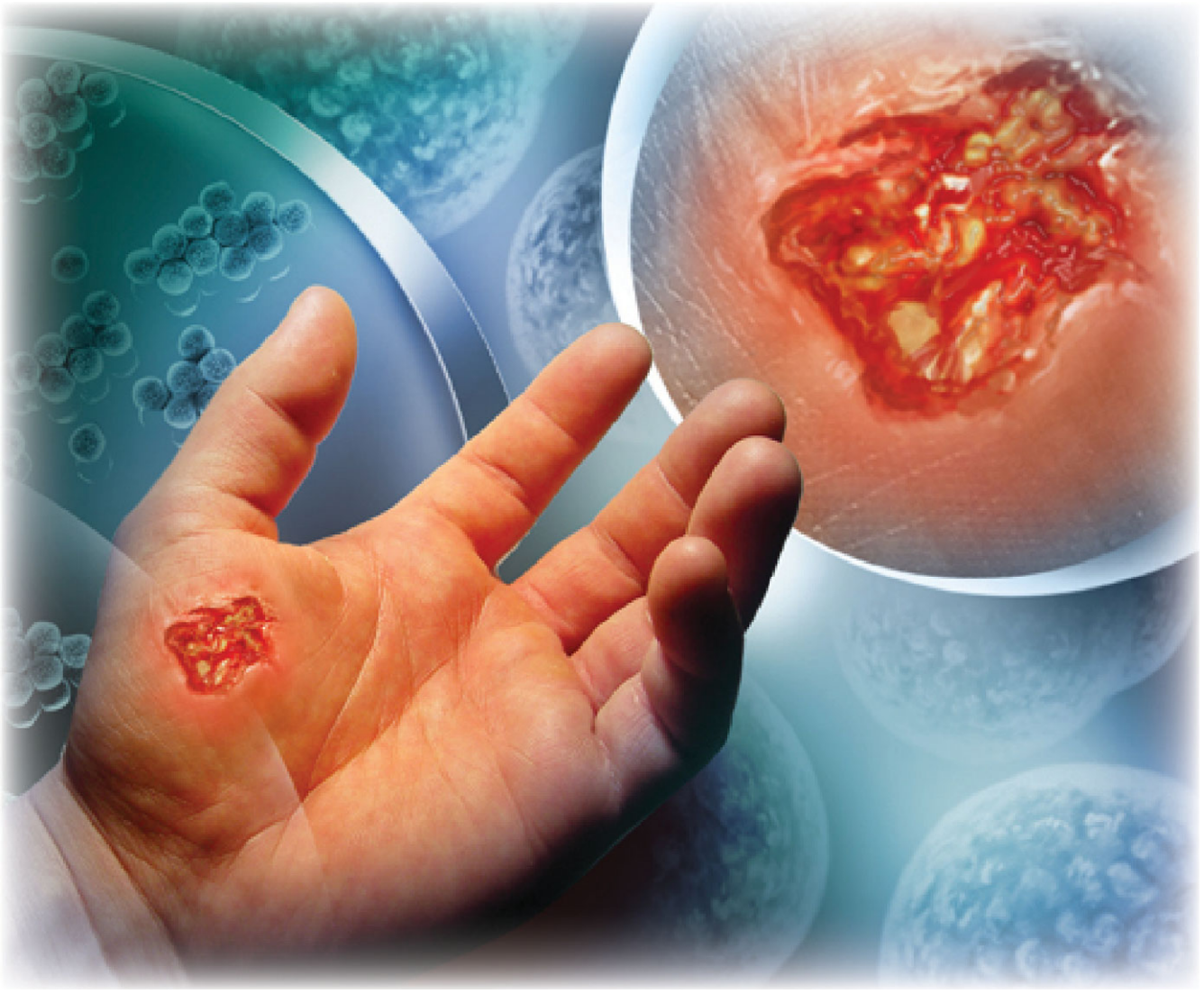

Hospital-Acquired and Community-Acquired MRSA

Two Distinct Infections

Patricia Seymour, MD, MS
Senior Resident

Jeremy Golding, MD, FAAFP
Clinical Professor of Family Medicine

Department of Family Medicine and Community Health
Hahnemann Family Health Center
University of Massachusetts Medical School and
UMass Memorial Health Care
Worcester, Massachusetts

Knowledge of how these illnesses differ is critical to both diagnosis and proper management. The authors use case examples to illustrate clinical features of the two infection types, as well as considerations in treatment and prevention of reinfection.

Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) burst into public view in 2003 when five members of the St. Louis Rams NFL team developed skin abscesses at sites of turf burns.[1] Distinct from health care–associated MRSA (HA-MRSA) infections, which were better known to clinicians, CA-MRSA had been described in injection-drug users as early as the 1980s. The US Centers for Disease Control and Prevention participated in the 2003 investigation, and since then CA-MRSA infections have become both increasingly widespread and somewhat more readily recognized and diagnosed. As urgent care clinicians are encountering these infections more often, it is important to understand MRSA virulence patterns, clinical features, risk factors, and regional resistance patterns when diagnosing infections and selecting appropriate therapies.

DISTINCT PATHOGENS, COMMON ANCESTOR

Historically, CA-MRSA and HA-MRSA have had significantly different clinical features, antimicrobial resistance patterns, and treatment requirements. However, both types of infections cause significant morbidity and are thought to have evolved from methicillin-sensitive *S aureus* (MSSA) via species-specific phage-mediated genome alteration resulting from environmental pressures. Compared with MSSA infections, both types of MRSA infections lead to greater morbidity and mortality, as well as to increased hospital stays and treatment costs, even after controlling for the patient's general level of illness (eg, disease history, hospitalizations, antibiotic exposure).[2,3]

Colonization with MRSA increases the risk for infection by the organism. In fact, in one study, 82% of patients with MRSA bacteremia had identical nasal isolates.[4] *S aureus* colonizes specific areas of the human body, including the anterior nares, axillae, groin, and gastrointestinal tract. Breaches of host integrity caused by shaving, aspiration, catheterization, and surgery potentially lead to infection by colonizing strains.

MRSA produces the cell wall molecule penicillin-binding protein 2′ (PBP2′), which confers resistance to all beta-lactam antibiotics and cephalosporins. The staphylococcal cassette chromosome encodes PBP2′, as well as HA-MRSA and CA-MRSA's differing virulence factors, leading to the clinical differences seen in resultant infections. Panton-Valentine leukocidin (PVL), a molecule expressed primarily in CA-MRSA, is a tissue necrosis factor and causes the organism to be more aggressive than PVL-negative *S aureus*, readily producing pyogenic infections in skin and deeper tissues.[5] Recently, PVL-encoded HA-MRSA strains have been isolated. In fact, PVL-positive HA-MRSA accounted for 12.7% of HA-MRSA isolates in a 2-year study at a Turkish academic hospital.[6] Its presence clearly increases mortality in pulmonary infections.[7] Although both varieties of MRSA are generally susceptible to vancomycin, resistance has been documented and is increasingly problematic.

CASE 1

A 14-year-old boy presents to his primary care provider with a painful red swelling on his medial left thigh. He reports that the swelling began as a pimple and has grown steadily with increasing pain over a 2-week period. He denies any recent history of fever. The patient is a high school student, is not involved in sports, and is not sexually active. He has had no similar skin issues in the past. The patient's family history includes an aunt in the same household who has had similar swellings that were treated with antibiotics.

On exam, the patient is afebrile with a 3- to 4-cm tender, red fluctuant swelling on his midmedial left thigh. A smaller swelling (<1 cm in diameter) is noted distal to this. The larger lesion is draining purulent material. There is no inguinal lymphadenopathy. The clinician performs a culture.

>>FAST TRACK<<

Compared with MSSA, CA-MRSA and HA-MRSA lead to greater morbidity and mortality, as well as to increased hospital stays and treatment costs.

Which organism is more likely to have caused this infection: MRSA or MSSA? If MRSA is responsible, is it more likely to be a community-acquired or a health care–associated strain?

Diagnosis

In making a diagnosis, the clinician should consider some information on MRSA infections. For

instance, in one study, MRSA was found in 59% of all soft-tissue infections in the ED, and 98% of these were CA-MRSA.[8] Furthermore, CA-MRSA comprises 30% of all MRSA infections in the community.[9] A generally aggressive and moderately invasive pathogen, CA-MRSA is significantly more likely than HA-MRSA to cause skin, soft-tissue, and joint infections and deep-seated abscesses.[5,10,11] CA-MRSA patients are typically younger than HA-MRSA patients (median age, 23 vs 68 years, respectively)[12] and are often completely healthy prior to infection. Furthermore, CA-MRSA is associated with better clinical outcomes compared with HA-MRSA. A decade ago, CA-MRSA was seen predominantly in indigenous groups (eg, Native Americans, Australian aborigines) and marginalized populations (eg, IV drug users, homeless persons, and incarcerated individuals); however, it is now clearly established in mainstream society. Due to unclear reasons, CA-MRSA skin infections are frequently misdiagnosed as spider bites.[13]

As for the patient described, the clinician should consider a diagnosis of CA-MRSA if there is a high prevalence of this organism noted in the community. A culture of drainage material or tissue is the gold standard for diagnosis and should be performed if antibiotic treatment is under consideration. In this case, a culture of the patient's spontaneously draining abscess grew MRSA with a CA-MRSA–resistance profile. Although not available in many institutions, polymerase chain reaction assays may provide results in 3 hours; rapid culture results typically take 48 hours.

>>FAST TRACK<<

CA-MRSA is significantly more likely than HA-MRSA to cause skin, soft-tissue, and joint infections and deep-seated abscesses.

Treatment

For skin abscesses, most authorities suggest incision and drainage, as well as soaking and elevation. In general, antibiotics are discouraged, due to their association with increasing resistance. Compared with HA-MRSA, CA-MRSA is generally is less resistant to antimicrobials.[14] First-line oral antimicrobial therapy, if indicated, includes trimethoprim/sulfamethoxazole, tetracycline, or clindamycin. Linezolid remains a second-line agent because of its high cost and the need to preserve its effectiveness against MRSA.[15,16] Erythromycin resistance suggests inducible clindamycin resistance, so the practitioner should avoid using clindamycin if the organism is found to be erythromycin-resistant. Use of the "d-zone" test demonstrates clindamycin resistance and should be standard practice in CA-MRSA–sensitivity testing.[17,18] If oral antibiotics fail or infection severity warrants hospital admission, glycopeptides such as vancomycin or teicoplanin (not available in the United States) may be used.

In this case, the clinician decided not to use antibiotics since incision and drainage is the most effective therapy. The clinician widened and placed a wick in the spontaneous opening in the abscess and advised the patient to soak and elevate the wound. To decrease risk for transmission, the clinician also recommended that the patient cover his wound, practice good hand hygiene, and not share personal care items.

Prevention of Reinfection

In deciding whether additional treatment is warranted to prevent reinfection, the clinician should consider the following: Nasal colonization is less common with CA-MRSA than with HA-MRSA. In fact, in the instance of the St. Louis Rams, health care professionals did not detect nasal colonization in any of the affected players, which suggested other sites of colonization.[1] Heterosexual genital transmission has been offered as a common source of CA-MRSA colonization.[14]

Some authorities do not screen for and treat colonization because of concern about increased resistance,[14] while others support a regimen including nasal mupirocin, oral doxycycline and rifampin, and chlorhexidine washes. A 2007 study found that this regimen cleared carriage in more than twice as many patients as did not treating colonization (74% vs 32%, respectively)[19]; however, it remains unclear how effective treatment of colonization is in preventing long-term reinfection.

A Cochrane review of topical and oral antimicrobial strategies for eradicating MRSA colonization showed mixed results.[20] The most effective strategy, oral rifampin, seemed to eradicate MRSA from colonization sites at 30 days, but these results were no longer statistically significant by 90 days. Importantly, the incidence of ad-

verse events was 20% with all antimicrobials used in the studies reviewed, and these studies also reported antimicrobial resistance. The authors found insufficient evidence and possible harm in attempts at clearance.

CASE 2

A 71-year-old male nursing home resident presents with hypotension and fever. The patient has dementia and is thus limited in his ability to provide a history; however, the nursing home staff reports he has had fever for 36 hours, as well as hypotension and increasing confusion. In addition, they note that the patient recently had an indwelling urinary catheter placed following an episode of medication-induced urinary retention.

On exam, the patient is disoriented and febrile at 39.3˚C, with a systolic blood pressure of 84 mm Hg and a pulse of 104 beats/min. Other pertinent findings include clear lung sounds, suprapubic tenderness, and absence of rash. Head CT, chest x-ray, and cerebrospinal fluid analysis yield normal results, but urinalysis indicates an infection.

Which organism is the likely cause of urosepsis in this patient? In what clinically relevant ways does HA-MRSA differ from CA-MRSA?

Diagnosis

In making a diagnosis, the clinician should consider that HA-MRSA generally affects older patients and is associated with worse clinical outcomes than both MSSA and CA-MRSA. Risk factors for HA-MRSA infection include previous hospitalization, residence in a long-term care facility, prior antibiotic use, prior MRSA infection, and known colonization. In this case, the patient is an elderly man residing in a long-term care facility; thus, he has clear risk factors for HA-MRSA colonization and infection. HA-MRSA is more likely to infect the blood, respiratory system, and urinary tract than the skin.[10] Five major strains of HA-MRSA are known, and their prevalence varies geographically, again suggesting evolution in response to local pressures.[4] Scrupulous attention to antisepsis in insertion of urinary and bloodstream catheters has been clearly shown to reduce subsequent infection and bacteremia.

>>FAST TRACK<<

Although it has been reported, vancomycin resistance has occurred in relatively few strains of HA-MRSA.

When dealing with potential HA-MRSA, a high index of suspicion and early empiric treatment may be lifesaving. Definitive diagnosis requires isolation of the organism in urine, sputum, blood, or tissue culture. The clinicians treating the case patient obtained urine cultures, which grew MRSA with a HA-MRSA profile.

Treatment

HA-MRSA is known to have greater drug resistance than that associated with CA-MRSA. Initial treatment modalities for suspected HA-MRSA include vancomycin, teicoplanin, or linezolid.[15] Although it has been reported, vancomycin resistance has occurred in relatively few strains. Other treatment options include the streptogramins, quinupristin/dalfopristin, and the cyclic lipopeptide daptomycin, which has the advantage of decreased cell lysis and subsequent inflammation.[15,21] The case patient was admitted to the intensive care unit, where he received multiple antibiotics, including those with gram-negative coverage (because he had evidence of urosepsis) and vancomycin for empiric MRSA coverage.

Prevention of Reinfection

The colonization site for HA-MRSA is clearly established as the anterior nares, although other sites, such as the urinary tract and skin, are well known to exist. Twenty percent of the US outpatient population is persistently colonized with HA-MRSA, while another 30% is intermittently colonized.[9] Screening for and clearance of HA-MRSA colonization is controversial, and some authorities do not recommend the practice due to concerns of increasing resistance. Others support the regimen used for CA-MRSA clearance: topical and oral antibiotics, as well as chlorhexidine washes. Of course, good hand hygiene reduces nosocomial rates of MRSA infection and, along with environmental cleaning between patients, is an important prevention strategy.

Screening

Screening for HA-MRSA carriage in hospitals is becoming more common; however, global

screening for HA-MRSA colonization at hospital admission has not decreased nosocomial HA-MRSA infection detectably.[22] Thus, there is little evidence to support this practice.

CONCLUSION

Many, if not most, outpatient *S aureus* skin infections are caused by CA-MRSA, while blood, urinary tract, and respiratory tract infections are more likely to be caused by HA-MRSA. Knowledge of how these infections differ is critical to proper management. Reduction of antibiotic use for conditions that do not benefit from antibiotics (eg, viral upper respiratory infections), and avoidance of overtreatment of skin infections with antistaphylococcal antibiotics may help prevent rapid emergence and spread of MRSA. Practitioners must pay close attention to ever-evolving CA-MRSA and HA-MRSA pathogens and their clinical implications. □

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CORRECTION

In the August 2009 article "Lower Extremity Ulcers: Venous, Arterial, or Diabetic?" (Aydin A, Shenbagamurthi S, Brem H. *Emergency Medicine*. 2009;41[8]:18-24,48), the ankle-brachial index should have been defined as the blood pressure in the ankle divided by the blood pressure in the upper arm.