Family Outbreaks of Invasive Community-Associated Methicillin-Resistant *Staphylococcus aureus* Infection

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Outbreaks of invasive methicillin-resistant *Staphylococcus aureus* infection within families are unusual. We investigated 2 family clusters of invasive methicillin-resistant *Staphylococcus aureus* infection, including 1 in which a young mother died of fulminant pneumonia. Although surveillance via culture of family contacts of patients with invasive methicillin-resistant *Staphylococcus aureus* infection is not currently recommended, such clusters should stimulate reevaluation of preventive measures.

Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is an increasingly common cause of substantial morbidity worldwide [1, 2]. CA-MRSA can cause complicated skin and soft-tissue infections and has been associated with severe necrotizing fasciitis and pneumonia. Transmission of MRSA to household contacts of hospital employees and of persons infected with MRSA has been reported, but this type of transmission has not generally been associated with disease [3]. Intrafamilial spread of CA-MRSA associated with skin and soft-tissue infection has occurred [4], but the clustering of invasive disease within families has been reported rarely; when reported, it has occurred among high-risk persons [5–7]. Although the “ping-pong effect” of transmission of CA-MRSA within families is recognized in clinical practice, it is neither well documented nor highlighted in existing guidance documents [8]. We investigated 2 family clusters of invasive CA-MRSA infection that demonstrate the potentially severe consequences of this means of transmission.

**Methods.** *S. aureus* isolates were confirmed by the presence of the *mec* gene using PCR with previously described oligonucleotide primers [9]. Genomic DNA was extracted and purified via Wizard DNA genomic preparation kit (Promega). Methicillin resistance was confirmed by *mecA* gene amplification, and typing of the staphylococcal cassette chromosome (SCC *mec*) was performed using a multiplex PCR strategy [10]. Testing for the Panton-Valentine leukocidin (PVL) locus was performed using PCR methods described elsewhere [10]. Oligonucleotide primers were obtained commercially (Integrated DNA Technologies) and were added, with genomic DNA, to 1× PCR Master Mix (Promega). Amplification products were visualized in a 2% agarose gel to which ethidium bromide was added. Control strains of *S. aureus* for SCC *mec* typing were graciously provided by Dr. Lisa Plano. Genetic relatedness was assessed with PFGE using an *Sma*I restriction enzyme.

**Outbreak investigations.** In family cluster 1, a previously healthy, 35-year-old mother presented to an emergency department with a 5-day history of cough, fever, myalgias, and shortness of breath. She received a diagnosis of pneumonia and was treated with penicillin. She presented again the following day with worsening symptoms and a dense, left lower lobe infiltrate. The results of a rapid influenza test were negative. She was intubated and received mechanical ventilation, but her condition deteriorated rapidly; despite intensive therapy, including intravenous antibiotics, the patient died the morning after hospital admission. Cultures of blood and pleural fluid grew MRSA.

On the day of the patient’s funeral, her husband presented to a different hospital with a 1-week history of body aches, sore throat, nasal congestion, cough, and pleuritic chest pain. He had been previously well and was taking penicillin that had been prescribed by his physician several days previously. A chest radiograph revealed an infiltrate in the left lower lobe and lingula. Results of a rapid influenza test were positive. Sputum culture grew MRSA with an antimicrobial susceptibility pattern identical to that of his wife’s isolate. He was treated with intravenous vancomycin and doxycycline and experienced resolution of symptoms.

The day after the father’s hospitalization, his 14-year-old daughter was admitted to a third hospital with a several-week history of cough, fever, and nasal congestion. On the day prior to hospital admission, results of a rapid streptococcal antigen test of the throat were positive, a chest radiograph showed a
right middle lobe infiltrate, and the patient was treated with penicillin. A nasopharyngeal culture was positive for influenza A. Results of sputum and blood cultures were negative. She was treated with intravenous vancomycin and azithromycin, was discharged 2 days later, and was given oral antibiotics. Subsequent investigation revealed that 2 more of this couple’s 7 children had had “boils” 1 month before the mother’s death. One child had the lesions lanced and drained; culture of a sample of the fluid from the lesion was positive for MRSA with an antimicrobial susceptibility pattern identical to that of the mother’s isolate.

After the parents’ hospitalizations, all household family members who had contact with them (7 children) had nares cultures performed (specimens were obtained with unmoistened swabs from a single naris) and were treated with trimethoprim-sulfamethoxazole. The anterior nares culture of 1 asymptomatic child grew MRSA.

Antimicrobial susceptibility testing results for *S. aureus* isolates from the mother, from the father, and from the abscess culture for 1 daughter all had identical susceptibility patterns, including resistance to ampicillin, nafcillin, cefazolin, and erythromycin; intermediate resistance to levoquin; and susceptibility to tetracycline, gentamicin, clindamycin, vancomycin, and trimethoprim-sulfamethoxazole. Isolates of *S. aureus* from the mother and father and from the nasopharynx culture of the asymptomatic child had indistinguishable PFGE patterns that matched the patterns of the widely disseminated USA300-0114 clone [11]. The isolates were SCC mec type IV and were positive for the PVL gene locus.

Approximately 1 month later, a second family cluster of MRSA infection that was unrelated to the previous family outbreak occurred. A husband and wife presented at a hospital in the same region as the family in cluster 1. The husband, a 45-year-old man with a history of injection drug abuse and multiple medical problems, including end-stage renal disease, was admitted with a several-day history of cough, shortness of breath, and fever. A chest radiograph revealed a left lower lobe infiltrate and cavitary lesion. He ultimately received a diagnosis of MRSA endocarditis. His 46-year-old wife, who also had multiple underlying medical problems and a history of injection drug abuse, was admitted 4 weeks later with cellulitis, an abscess on the left forearm, left lower lobe pneumonia, endocarditis, purpura, respiratory failure, and septic shock. Culture of the wife’s blood, urine, and sputum specimens grew MRSA. Antimicrobial susceptibility patterns of both the husband’s and the wife’s isolates were identical (resistant to oxacillin, azithromycin, ceftiraxone, ciprofloxacin, levofloxacin, and imipenem and susceptible to trimethoprim-sulfamethoxazole and all other agents tested). The PFGE pattern, available only for the wife’s isolate, was distinct from that of the earlier family cluster.

The isolate was SCC mec type IV and was positive for the PVL gene locus.

**Discussion.** Family clusters of invasive MRSA infection have rarely been reported but have important implications for the treatment of those in close contact with patients. Although 1 cluster involved multiple family members who had had no previous hospital exposure and the other involved a couple with multiple medical problems and substantial exposure to health care settings, both instances demonstrate likely intrafamilial spread of MRSA. Antimicrobial prophylaxis for the family members of patients with CA-MRSA infections has not been recommended, but as additional data are gathered, a discussion of such policies may be warranted for specific circumstances.

MRSA first emerged as a nosocomial pathogen, but community-associated strains have become widespread. The transmission of CA-MRSA skin infections among close contacts, including members of sports teams, military trainees, and persons in correctional facilities, has been well documented [11]. Transmission of nasal colonization within families has also been reported [3, 12, 13], but intrafamilial transmission resulting in skin infection [4, 6] or invasive disease among high-risk contacts [5, 7, 14] has been described only occasionally. Most of these reports involve strains that are often referred to as hospital-associated MRSA, which are typically resistant to a wide range of antimicrobials and are related to nosocomial exposure [11]. A few of the more recent reports of intrafamilial transmission involve what appear to be CA-MRSA strains [4–6, 15], which are typically susceptible to multiple antibiotics and have non–β-lactam susceptibility patterns similar to those of community strains of methicillin-susceptible *S. aureus* [11].

Strains of CA-MRSA that have emerged in recent years are characterized by the presence of an SCC mec type IV element. Two particular strains (USA300 and USA400) have been responsible for a large proportion of CA-MRSA cases in the United States [11]. Many CA-MRSA strains carry the PVL virulence factor, which elicits tissue necrosis and has been associated with epidemic furunculosis and severe, necrotizing pneumonia [11]. Two of the patients in cluster 1 had evidence of concurrent influenza infection, although the findings of influenza testing were negative in the patient who died. The association between influenza and severe staphylococcal infection is well recognized and has been noted with MRSA infection [16].

Overall rates of MRSA carriage in the United States are low [17] but are increasing rapidly. In a recent study in Tennessee, 36% of children presenting to primary care centers were colonized with *S. aureus*, and 9% were colonized with MRSA (a >10-fold increase over 4 years). Of those who were colonized with MRSA, 22% carried the PVL gene [10]. Because nasal carriage is a notable risk factor for staphylococcal infection [18],...
the identification and treatment of high-risk persons or those with exposure to more virulent strains may be of particular concern.

Studies of decolonization of MRSA carriers have not addressed low-risk patients in the community [19], and additional clinical studies are necessary. Current guidelines recommend empirical treatment of minor skin and soft-tissue infections with oral antibiotics and evacuation and drainage of abscesses and inflamed epidermoid cysts [8]. The occurrence of outbreaks of furunculosis among families is acknowledged, with nasal or oral antimicrobial treatment for decolonization noted as “one approach” to controlling recurrent furunculosis [8, p. 1380]. These recommendations do not address testing for carriage of MRSA or decolonization of contacts or patients with minor skin infections or nonrecurrent lesions, but this would not have changed the management of family members in these clusters. It is of note that guidelines for the treatment of community-acquired pneumonia also do not address treatment of contacts or decolonization [20]. Although available records suggest that patients in cluster 1 were initially treated with penicillin for presumed respiratory infections, which is not a recommended treatment of community-acquired pneumonia [20], adherence to current guidelines is unlikely to have affected the carriage status of contacts or the transmission patterns observed in these clusters.

Given the remarkable increase in CA-MRSA colonization and infection in recent years, intrafamilial spread of invasive disease remains a relatively rarely reported phenomenon. A decade ago, it was thought that there was insufficient evidence to support the screening and treatment of family members of patients with invasive MRSA infection to eliminate nasal carriage [14]. There still are no recommendations to do so. Although cluster 2 involved persons with multiple risk factors for severe disease whose infections may have been amenable to limited recommendations targeted to high-risk groups, the first cluster involved persons without traditional risk factors. Any guidelines pertaining to such cases would likely apply to huge numbers of persons, which necessitates careful consideration of the risks and benefits associated with recommendations affecting large populations. As virulent strains of CA-MRSA become more ubiquitous in the community, the question will likely warrant further discussion.

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References