Community-Associated Methicillin-Resistant *Staphylococcus aureus* Causing Chronic Pneumonia

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A young woman presented with pneumonia of a 3-month duration with predominantly nodular pulmonary infiltrates. Methicillin-resistant *Staphylococcus aureus* was identified in multiple cultures of sputum specimens. According to findings of pulsed-field gel electrophoresis, the isolate was identical to USA 300 and carried a type IV *Staphylococcus* cassette chromosome *mec* type IV gene and the genes for Panton-Valentine leukocidin.

Community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) has emerged as a significant cause of community-acquired lung pneumonia over the past several years. Strains of community-associated MRSA are distinct from hospital-acquired MRSA strains from an epidemiological, genetic, and clinical perspective [1, 2]. They tend to be less resistant to antimicrobial agents than hospital-acquired MRSA strains, and they almost always contain a type IV *Staphylococcus* cassette chromosome *mec* type IV gene (SCC *mec* IV) and the genes for Panton-Valentine leukocidin (PVL), an extracellular cytotoxin that is a virulence factor for primary skin infections and pneumonia [3, 4].

Although pneumonia caused by these strains is uncommon, early recognition is important because of the high mortality rate associated with it [5]. Present treatment guidelines for community-acquired pneumonia do not recommend empirical coverage for MRSA [6]. Infections due to community-associated MRSA are increasingly prevalent in the Detroit area [7] and may cause pneumonia that is typically characterized by a short duration of illness and focal necrotizing infiltrates [8].

We present a case of chronic pneumonia due to community-associated MRSA in an otherwise healthy individual.

**Case report.** A healthy 27-year-old African American woman presented with a 3-month history of low-grade fever, night sweats, and 9-kg weight loss. The patient also had a persistent dry cough during this period that had progressed 1 week prior to admission, with the development of hemoptysis. The patient worked as a home-health aide, and cared for a patient with a history of MRSA infection 1 month prior to the development of her symptoms. On examination, her temperature was 38.4°C, her pulse was 102 beats/min, her systolic/diastolic blood pressure was 106/52 mm Hg, her respiratory rate was 22 breaths/min, and her weight was 69 kg. The patient appeared to be mildly tachypneic. There were crackles and diminished air entry at the right lung base. Laboratory evaluation revealed a WBC count of 14,400 cells/µL (79% neutrophils), a hemoglobin count of 10.1 mg/dL, a platelet count of 333,000 platelets/L. A chest x-ray demonstrated bilateral nodular infiltrates, a right lower lobe infiltrate, and small right-sided pleural effusion. A chest CT scan confirmed these findings as well as extensive cavitition within the lesions, which is consistent with multiple abscesses (figure 1). The patient was initially placed in isolation; however, results of her PPD skin test and test results for 3 sputum specimens were negative for acid-fast bacilli. Blood cultures and tests for serum angiotensin converting enzyme, cytoplasmic and perinuclear antineutrophil cytoplasmic antibodies, and HIV antibody were negative. All Gram stains of sputum specimens demonstrated numerous polymorphonuclear lymphocytes and gram-positive cocci in clusters. Three sputum cultures grew MRSA. Echocardiography (transthoracic and transesophageal) demonstrated no evidence of vegetations or a normal-appearing tricuspid valve. The patient’s condition improved rapidly on receipt of intravenous vancomycin. She was discharged and after receiving 3 days of vancomycin on high-dose oral trimethoprim-sulfamethoxazole (dosage, 2 tablets twice daily), to complete a total of 6 weeks of therapy. The patient had an excellent clinical response, with a weight gain of 8 kg, no residual respiratory or systemic symptoms, and resolution of radiographic abnormalities, as observed by chest x-ray.

**Methods.** The MRSA recovered from the patient’s sputum was analyzed using PFGE. *S. aureus* was recovered from routine sputum culture performed in the clinical microbiology lab. Identification was determined by catalase production and staphaurex latex agglutination testing. Susceptibility testing was performed using a Vitek 2 (bioMérieux), and methicillin re-
resistance was confirmed by growth on Mueller Hinton agar containing 6 μg/mL of oxacillin. \textit{S. aureus} DNA was extracted using a Contoured Clamped Homogeneous Electric Field (CHEF) Genomic DNA Plug Kit (Bio-Rad Laboratories) then digested with \textit{Sma I} restriction endonuclease (Invitrogen). PFGE was performed on the CHEF-DR III (Bio-Rad Laboratories), with switch times of 1–20 s, at 6 V/cm for 21 h. Gel was stained with ethidium bromide, destained in water, and photographed with a Chemilager 4000 (Alpha Innotech). The SCC\textit{mec} types were determined by a previously described PCR-based multiplex assay [9]. PCR amplification of the cassette chromosome recombinase gene was performed using the primers described by Okuma et al. [10]. Positive controls for each assay included \textit{S. aureus} HPV 107/ATCC BAA-44 (type I), NYBK 2464/ATCC BAA-41 (type II), HUSA 304/ATCC BAA-39 (type III), and HDE 288/ATCC BAA-42 (type IV). The \textit{mec} A gene served as an internal control for the multiplex assay. Polymerase chain amplification of the genes encoding PVL luk-PV and lukf-PV was performed using primers described elsewhere [11]. The positive control for the PVL assay was ATCC 49775, and sterile water served as the negative control.

**Results.** The resulting band pattern of the patient’s isolate was compared with other community-associated soft-tissue MRSA isolates, and it confirmed that the isolate was a strain identical to the strain of community-associated MRSA that causes skin and soft-tissue infections in our community [7]. This isolate is type IV \textit{mec}, carries the genes for PVL, and has been confirmed by PFGE to be identical to USA 300, a frequently identified strain in community-associated outbreaks [12].

**Discussion.** MRSA is a well-known cause of nosocomial infections and is now emerging as an important pathogen in the community. Community-associated MRSA infection is defined as being illness compatible with staphylococcal disease, in which MRSA is cultured from the site of infection in an outpatient or <48 h after hospital admission and with none of the following health care risk factors: hospitalization, surgery, dialysis, or residence in a long-term care facility <1 year before the onset of illness; history of treatment with a permanent indwelling catheter or a percutaneous medical device; or having a previous culture result positive for MRSA [13]. These strains are globally distributed and clonally disseminated and may carry additional virulence genes (besides PVL), compared with hospital-associated MRSA isolates, which may result in increased mortality [14]. There is an increased number of reports of community-associated MRSA pneumonia among children and adults [4, 5]. Patients who contract infection are typically healthy, illness is usually of short duration and often follows an episode of influenza, and the infection is associated with a high mortality rate.
We describe a previously healthy woman who lacks any of the traditional risk factors for hospital-associated MRSA infection and who presented with chronic pneumonia characterized by multiple necrotizing nodular and lobar infiltrates. Her case differs from other cases of community-associated MRSA pneumonia by both clinical and radiographic presentation. The slow progression, the absence of preceding influenza-like illness, and the predominance of nodular infiltrates observed by chest imaging should alert clinicians to consider community-associated MRSA as a cause of chronic pneumonia. The absence of echocardiographic findings suggestive of tricuspid-valve endocarditis, positive blood culture results, and venous thrombosis excludes the possibility of a persistent endovascular source of infection. Although MRSA was not identified in the blood, the presence of MRSA as a sole pathogen observed on repeated sputum Gram stains and cultures confirmed its role in our patient’s infection. In addition, the patient’s response to antibiotic therapy supports its role as a pathogen. Another case of chronic pneumonia due to S. aureus was described in 1995 in a patient with AIDS who presented with multiple lung abscesses [15]. This presentation is uncommon in healthy individuals and has not been described among patients with community-associated MRSA infection.

Our patient’s MRSA isolate was confirmed by PFGE to be identical to the strain of community-associated MRSA strain causing skin and soft-tissue infections in our community, as well as to USA 300. The presence of PVL production and SCCmec type IV is consistent with previous reports of community-associated MRSA infection [3, 4].

As community-associated MRSA pneumonia becomes more common, the most effective therapeutic approach will need to be determined. In general, these strains are usually susceptible in vitro to vancomycin, linezolid, trimethoprim-sulfamethoxazole, doxycycline, and fluoroquinolones. In addition, they are often susceptible to clindamycin, but the erythromycin induction test (the D-test) should be performed on such isolates to determine the presence of in vitro inducible resistance [16]. The initial choice in most published series has been intravenous vancomycin, although linezolid appears to be at least equivalent to vancomycin in the treatment of nosocomial MRSA pneumonia [17]. The efficacy of treatment with trimethoprim-sulfamethoxazole in systemic infections due to MRSA was comparable to vancomycin [18] and it has been effective alone and in combination with rifampin in patients with soft-tissue infections due to community-associated MRSA [7, 19].

Our patient was treated with and improved rapidly on receiving intravenous vancomycin. She was discharged from the hospital and given high-dose oral trimethoprim-sulfamethoxazole, to complete a total of 6 weeks of therapy. An extended duration of antibiotic therapy was prescribed on the basis of the presence of cavitary infiltrates and the duration of symptoms. The optimal duration of antibiotic therapy also remains unknown. As with other causes of chronic pneumonia, therapy may need to be prolonged because of the extended duration of infection.

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Potential conflicts of interest. L.B.J. has served on speakers’ bureaus for Pfizer, Gilead, and Aventis; L.S. has served on speakers’ bureaus for Teravance and Pfizer and as a consultant for Schering. All other authors: no conflicts.

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