CASE REPORT

Community-Associated Methicillin-Resistant *Staphylococcus aureus* Infective Endocarditis with Panton-Valentine Leukocidin Gene in an Injection Drug User with HIV Infection

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Abstract

Reports of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) isolates carrying Panton-Valentine leukocidin (PVL) gene that causes infective endocarditis in injection drug users (IDUs) with human immunodeficiency virus (HIV) infection are rare in the English language literature. We present a case of CA-MRSA infective endocarditis with bilateral septic lung emboli in a previously healthy 45-year-old IDU. This case suggests that PVL gene-positive CA-MRSA should be considered as a potential pathogen in IDUs with infective endocarditis.

Key words: infective endocarditis, intravenous drugs user, methicillin-resistant, *Staphylococcus aureus*

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Introduction

Increasing rates of methicillin-resistant *Staphylococcus aureus* (MRSA) globally have been accompanied by the increase of MRSA infections among healthy individuals in the community without apparent traditional risk factors (1). Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections are now regarded as a serious public health problem (2). Although infective endocarditis due to CA-MRSA has been reported in a case series (3), none was reported in patients with human immunodeficiency virus (HIV) infection. Herein, we report a 45-year-old HIV-infected man with infective endocarditis caused by CA-MRSA isolates carrying Panton-Valentine leukocidin (PVL) gene. He was treated successfully with linezolid and trimethoprim/sulfamethoxazole without surgical intervention.

Case Report

This previously healthy 45-year-old injection drug user (IDU) presented to our hospital with 1 week of fever, intermittent chills, and left leg pain. He started to inject morphine sulfate intravenously 2 months prior to admission and had not been hospitalized in the past nor had any recent antibiotic usage. He was admitted to another hospital one week prior to admission because of fever, dyspnea and cough after a motor vehicle accident and blood culture revealed presence of MRSA. A transthoracic echocardiogram revealed a 2 cm vegetation over the tricuspid valve. He was transferred to our hospital for further evaluation after he tested positive for HIV, hepatitis B and hepatitis C.

At presentation, his temperature was 39°C. Physical examination revealed a grade 2/6 systolic murmur on the left lower sternal border. Laboratory examination showed a peripheral leukocyte count of 1.2×10^9 cells/mm^3 with 97% polymorphonuclear cells. Chest radiography revealed the
Figure 1. Chest radiography revealed the presence of bilateral septic lung emboli.

Figure 2. A transesophageal echocardiogram showed a vegetation at the anterior leaflet of the tricuspid valve (RV inflow view).

presence of bilateral septic emboli (Fig. 1). Two sets of blood cultures grew MRSA within 24 hours; the blood isolate was sensitive to vancomycin, trimethoprim/sulfamethoxazole, linezolid, minocycline, levofloxacin, chloramphenicol and moxifloxacin. Screening for Panton-Valentine leukocidin (PVL) genes by PCR (4) was positive. The PCR product for PVL was verified by subjecting the sample to gene sequencing using ABI 310 gene analyzer based on the Sanger dideoxy nucleotide triphosphate (ddNTP) terminator method. The isolate was identified to have a type IV staphylococcal cassette chromosome mec (SCCmec) (5). His CD4 lymphocyte count was 320 cells/μL and his HIV viral load was >100,000 copies/mL (Roche Amplicor 1.5). The patient initially received vancomycin and subsequently teicoplanin and rifampin and the regimen was changed to linezolid on hospital day 17 due to the appearance of skin rashes and persistence of MRSA bacteremia. A transesophageal echocardiogram at our hospital also showed a 2 cm vegetation that was fixed to the anterior leaflet of the tricuspid valve (Fig. 2). Mild tricuspid regurgitation was noted. Computed tomography (CT) of the chest disclosed multiple bilateral pulmonary nodules, some of which were cavitary and were suspicious of septic pulmonary emboli. Blood cultures turned negative for MRSA after 7 d of treatment. He received 3 weeks of linezolid and a hemogram performed one day before discharge showed no evidence of thrombocytopenia or mild anemia (HgB 10 g/dL). However, five days after discharge, he was admitted because of fever and diarrhea. Laboratory examination showed a peripheral leukocyte count of 1.13×10⁴ cells/mm³ with 71% polymorphonuclear cells and 22% lymphocytes; hemoglobin of 6.5 g/dL and platelet count of 2.1×10⁵ cells/mm³. Blood culture revealed MRSA with the same antibiotic. He was initially treated with teicoplanin, rifampin and gentamicin for 10 days and shift to linezolid and trimethoprim/sulfamethoxazole due to fever and relapsing MRSA bacteremia. Blood culture turned negative and fever subsided after 5 days of treatment. He was given 4 weeks of linezolid and trimethoprim/sulfamethoxazole and both were discontinued because of pancytopenia (Hgb 8 g/dL, platelet 2.3×10⁴ cells/mm³, white cell count 3,800 cells/mm³). The clinical course of this patient is summarized in Fig. 3. A repeated transthoracic echocardiogram showed partially healed tricuspid vegetations. He was followed up at Out Patient Department with no obvious complications.

Discussion

A Medline search of English language literature from January 1999 to July 2007 for cases with community-associated MRSA (CA-MRSA) infective endocarditis was performed and included the following individual search terms: ‘CA-MRSA’, ‘CO-MRSA’, or ‘community-acquired MRSA’. The above-mentioned terms were combined with ‘endocarditis’. Inclusion criteria were: 1) community-associated MRSA bacteremia, defined as isolate recovered within 48 hours to 72 hours of admission; 2) infective endocarditis fulfilling modified Duke criteria for definite infective endocarditis (6); 3) molecular data available on SCCmec typing, with or without data available on PVL gene testing. There were 8 previously reported cases of CA-MRSA infective endocarditis in patients with IDUs that fulfilled our criteria (Table 1). All 9 patients carried the SCCmec IV gene. However, six of MRSA isolates (66%) were PVL positive. Only the present patient had HIV infection.

A longitudinal study of 282 community-based drug abusers conducted from February 1999 through September 2000 in New York showed high rates of incident S. aureus colonization present in IDUs. Moreover, HIV serostatus was significantly and uniquely associated with S. aureus incidence and persistence and with MRSA colonization (11). No therapeutic or clinical factors of HIV infection were found to increase the risk of colonization (11). The present patient
had no skin lesions to explain the source of MRSA bacteremia and endocarditis. Although we did not test \textit{S. aureus} colonization before the patient became ill, HIV itself may have had some contribution in the \textit{S. aureus} colonization (11).

Community-associated (CA) and health care-associated (HA) MRSA cases differ demographically and clinically (12). Community-acquired strains were characterized by limited antibiotics resistance, with cellulitis and abscess being the major clinical manifestations (4,13). They have a common pulsed-gel electrophoresis (PFGE) pattern, possess different exotoxin gene profiles (e.g., PVL) and harbor type IV staphylococcal cassette chromosome \textit{mec} (SCCmec) (4, 12, 13). In contrast, health care-associated MRSA were mainly type I to III SCCmec (12, 14). Cases of CA-MRSA have been increasing recently (15). In Taiwan, MRSA colonized a substantial proportion of healthy children and accounted for 25\% to 75\% of childhood CA-MRSA infections (15, 16). The most common SCCmec types were type IV and V (15-17). However, in the study of Huang et al (18), they found that SCCmec type IV consisted of 43\% of their hospital-associated MRSA isolates in 2005. Another study also demonstrated that SCCmec type IV was found in 40\% of their patients with hospital-associated MRSA (16). This suggests that SCCmec type IV, which is usually community associated, was closed related to hospital acquired isolates. Although the present patient had no risk factor for hospital-associated MRSA, the possibility of clonal spread of SCCmec type IV MRSA between community and hospital cannot be excluded. The combination of CA-MRSA in skin lesions and skin trauma through intravenous drug injection may represent a new susceptible population for the acquisition of CA-MRSA endocarditis such as in our patient.

The decision to operate on patients with infective endocarditis is determined primarily on the severity of congestive heart failure. Other clinical situations in which surgical intervention should be considered are fungal infective endocarditis, infection with aggressive antibiotic-resistant bacteria or bacteria that respond poorly to antibiotics, left-sided endocarditis caused by Gram-negative bacteria such as \textit{S. marcescens} and \textit{Pseudomonas} species, persistent infection with positive blood cultures after 1 week of antibiotic therapy, or 1 or more embolic events during the first 2 weeks of antimicrobial therapy (19). Our patient refused surgical intervention because of personal economic consideration and lack of family support and his decision was respected.

This case was different from the previously reported cases. First, this is the first case with HIV coinfection. Secondly, the antibiotic susceptibility pattern in this case is different from the others. In Taiwan, the strikingly high prevalence of macrolide resistance in clinical isolates of \textit{Streptococcus pyogenes} appears to be associated with the widespread medical use of these agents. This continuous and widespread utilization may have contributed to the remarkably high incidence of erythromycin and clindamycin resistance among the CA-MRSA isolates from our patient and children in this region (20).

PVL-producing \textit{S. aureus} appeared to be associated with furunculosis, cutaneous abscesses, severe necrotic skin infections and severe hemorrhagic pneumonia (4, 13). But PVL gene is rarely found in other infections such as infective endocarditis. However, PVL gene was frequently detected in CA-MRSA (4, 13). In the study of Huang et al (18), PVL genes were detected in 50\% of their CA-MRSA isolates. The detection of PVL gene in our CA-MRSA isolate with infective endocarditis may only reflect the high prevalence of PVL-producing \textit{S. aureus} in Taiwan or it may be due to a clonal spread of PVL genes between community and hospit-
Table 1. Clinical and Molecular Characteristics of Patients with CA-MRSA Infective Endocarditis in IDUs

<table>
<thead>
<tr>
<th>Patient</th>
<th>Country</th>
<th>Valve involved</th>
<th>SCCmec</th>
<th>PVL</th>
<th>Therapy</th>
<th>Outcome</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Taiwan</td>
<td>Tricuspid</td>
<td>Type IV</td>
<td>Positive</td>
<td>Chloramphenicol, trimethoprim/sulfamethoxazole 8 weeks</td>
<td>Survived (no valvular surgery)</td>
<td>Current case</td>
</tr>
<tr>
<td>2</td>
<td>USA</td>
<td>Tricuspid</td>
<td>Type IVd</td>
<td>Negative</td>
<td>Vancomycin/ rifampin 6 weeks</td>
<td>Survived (TV replacement)</td>
<td>7</td>
</tr>
<tr>
<td>3</td>
<td>Singapore</td>
<td>Tricuspid</td>
<td>Type IVa</td>
<td>Negative</td>
<td>Vancomycin 6 weeks</td>
<td>Survived (TV replacement)</td>
<td>8</td>
</tr>
<tr>
<td>4</td>
<td>Australia</td>
<td>Tricuspid</td>
<td>Type IV</td>
<td>Not tested</td>
<td>Vancomycin/ rifampin 6 weeks</td>
<td>Survived (no valvular surgery)</td>
<td>9</td>
</tr>
<tr>
<td>5</td>
<td>USA</td>
<td>Aortic</td>
<td>Type IV</td>
<td>Positive</td>
<td>Vancomycin 6weeks/ gentamicin 2 weeks</td>
<td>Died 11 months following discharge due to subarachnoid hemorrhage and S. aureus bacteremia (porcine bioprosthetic valve)</td>
<td>10</td>
</tr>
<tr>
<td>6</td>
<td>USA</td>
<td>Tricuspid</td>
<td>Type IV</td>
<td>Positive</td>
<td>Vancomycin 6weeks/ gentamicin 4 days</td>
<td>Loss of follow up, blood culture clear at discharge</td>
<td>10</td>
</tr>
<tr>
<td>7</td>
<td>USA</td>
<td>Between pulmonic valve and tricuspid valve</td>
<td>Type IV</td>
<td>Positive</td>
<td>Vancomycin 6 days/ gentamicin 6 days</td>
<td>Status unknown, leave against medical advice</td>
<td>10</td>
</tr>
<tr>
<td>8</td>
<td>USA</td>
<td>Tricuspid</td>
<td>Type IV</td>
<td>Positive</td>
<td>Vancomycin 39 days/ gentamicin 7 days, changed to daptomycin due to renal failure, discharge on 6 weeks clindamycin</td>
<td>No signs of infection 1 week post-discharge (no valvular surgery)</td>
<td>10</td>
</tr>
<tr>
<td>9</td>
<td>USA</td>
<td>Aortic</td>
<td>Type IV</td>
<td>Positive</td>
<td>Vancomycin 5 weeks</td>
<td>Status unknown, did not return for follow-up</td>
<td>10</td>
</tr>
</tbody>
</table>

SCCmec: staphylococcal cassette chromosome mec; PVL: Panton-Valentine leukocidin; CA-MRSA: community-associated methicillin-resistant Staphylococcus aureus; Therapy: final antibiotic regimen with length of treatment. TV: Tricuspid valve

tal. The clinical significance of PVL gene in IE needs further study. In conclusion, the present case suggests that PVL gene-positive CA-MRSA should be considered as a potential pathogen in IDUs with HIV infection and endocarditis.

References


