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CASE REPORT

Infective endocarditis caused by community-associated methicillin-resistant *Staphylococcus aureus* in a previously healthy preschool child

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Community-associated methicillin resistant *Staphylococcus aureus* (CA-MRSA) has been increasingly reported recently and has become an emerging pathogen of infective endocarditis (IE) in adults, but still rarely reported in children. A previously healthy preschool child without any heart anomaly developed IE and pneumonia with pleural effusion. Blood cultures repeatedly yielded MRSA and did not become negative until 13 days after a teicoplanin-containing regimen was administered. In total, a 4-week intravenous antibiotic therapy and an additional 8-week oral antibiotic therapy were given. The patient recovered uneventfully. All five MRSA blood isolates were molecularly characterized and shared common characteristics, which were consistent with those of the endemic CA-MRSA clone in Taiwan. This case highlights that physicians should be aware of the growing role of CA-MRSA in childhood IE and should meticulously choose an appropriate empiric antibiotic regimen for such a severe disease.

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Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) is usually considered a nosocomial pathogen, but is increasingly acquired in the community. The term "community-associated" (CA) MRSA infection was defined to describe a community-onset infection without any risk factor for acquisition of MRSA,[1,2] which include a history of hospitalization, surgery, dialysis, a permanent indwelling catheter or percutaneous medical device, and a history of residence in a long-term care facility within the past 12 months.

CA-MRSA strains have been recognized as novel pathogens which are genetically different from hospital-acquired-MRSA strains.[1,2] They are usually characterized by limited antibiotic resistance (except to β-lactams) and carry type IV or V staphylococcal cassette chromosome (SCC*mec* IV, V); major clinical manifestations are usually cellulitis and abscess.[1–4] However, CA-MRSA clones vary in different continents, countries, and even areas.

Aside from skin and soft tissue infection, CA-MRSA has also been implicated in many invasive diseases, including bacteremia, osteomyelitis, septic arthritis, and necrotizing pneumonia.[4] Since the epidemic of CA-MRSA worldwide, there have been increasing reports of infective endocarditis (IE) caused by CA-MRSA in adult patients; however, only a few cases have been reported in children.[5–7] In this paper, we report a previously healthy preschool child with IE caused by CA-MRSA carrying Panton–Valentine leukocidin (PVL genes.

Case report

A 2-years-8-month-old previously healthy boy presented to the Chang Bing Show Chwan Memorial Hospital with an intermittent spike fever, irritability, and generalized itching with erythematous rashes for at least 5 days. There were no other associated symptoms including cough, rhinorrhea, or diarrhea. The patient had hand–foot–mouth disease 2 weeks before this episode. Otherwise, his mother denied any underlying diseases or history of allergies.

At presentation, the boy was febrile and irritable. His body temperature was 37.5°C, his blood pressure 121/71 mmHg, pulse rate 150/min, respiratory rate 35/min, and peripheral oxygen saturation 90–92% in room air (air conditioned). Physical examinations revealed mild to moderate respiratory distress, erythroderma over trunk, desquamation of both soles and two crusty unhealed fissures of both big toes, and a grade 2–3/6 systolic murmur on the left sternal border. Laboratory investigations revealed a white blood cell count of 10×10^9/L, with 74% neutrophils, 3% lymphocytes, 15% band form; hemoglobin 10.6 g/dL, and a platelet count of 70×10^9/L. The serum C-reactive protein level was 19.3 mg/dL (normal, <0.5 mg/dL). A chest radiograph demonstrated some faint patches over both lung fields, but more marked on the right side. He was admitted, and subsequently received intravenous cefazolin and clindamycin therapy. Spike fever, irritability, and progressive tachypnea were noted on the 1st hospital day. Two sets of blood cultures grew MRSA within 24 hours. Under the suspicion of sepsis or toxic shock syndrome, he was referred to a medical center for intensive care on the 2nd day.

On admission there, the repeated laboratory examinations showed a peripheral leukocytes count of 15.8×10^9/L, hemoglobin of 10.7 g/dL, and platelet count of 29×10^9/L. Right-side pneumonia patches with pleural effusion were found. He received intravenous teicoplanin and cefotaxime therapy initially. A chest tube was inserted on hospital day 4 due to progressive tachypnea. Pleural fluid analysis was consistent with exudates but was sterile. Transthoracic echocardiography disclosed mild tricuspid regurgitation, normal LV function, and two vegetations found on the right ventricle: one at tricuspid valve with a size of 16.1 × 8.2 mm and another at interventricular septum with a size of 96.9 × 4.7 mm (Fig. 1). IE was confirmed. On hospital day 7, one episode of generalized tonic seizure was recorded. No embolic event or focal lesion was found by brain magnetic resonance image. Cerebrospinal fluid analyses were within normal limits. Blood cultures obtained on the 2nd, 4th and 7th hospital days all grew MRSA with the same antibiogram. The isolate was susceptible to vancomycin, teicoplanin, linezolid, rifampin, levofloxacin, and trimethoprim-sulfamethoxazole but resistant to clindamycin and penicillin. The antimicrobial regimen was switched to intravenous teicoplanin plus intravenous trimethoprim-sulfamethoxazole on the 10th hospital day. The chest tube was removed on the 11th hospital day. Blood cultures turned negative since the 13th hospital day. Finally, his fever subsided on the 17th hospital day. He then received a 4-week course of intravenous teicoplanin with the addition of a 2-week course of intravenous trimethoprim-sulfamethoxazole while hospitalized. A follow-up echocardiography showed that both vegetations decreased in size. He was discharged on hospital day 30. He received sequential oral trimethoprim-sulfamethoxazole for an additional 8 weeks. Echocardiography performed 3 months after discharge showed no signs of vegetations. No disease recurrence was noted at a half-year follow-up.

All five MRSA isolates from the patient were molecularly characterized. The detection of PVL genes, staphylococcal chromosome cassette (SCC*mec*) typing, multilocus sequence typing, and pulsed-field gel electrophoresis were performed and determined using methods described elsewhere.[4] All isolates shared common characteristics and were characterized as multilocus sequence type (ST) 59, SCC*mec* type V_T, and PVL genes-positive. The pulsed-field gel electrophoresis type belonged to type D in our previous classification. These characteristics were consistent with those of CA-MRSA isolates in Taiwan.

Discussion

IE is a rare but severe illness in children. *S aureus* was the predominant pathogen and accounted for 40–57% of pediatric IE cases.[8,9] Although pre-existing congenital heart diseases remained as the major risk factor for childhood IE, there were growing indications of a continuous shift of IE among children without cardiac anomaly.[8,9] Childhood IE without congenital heart diseases was more often seen in older children, compared with those who have heart diseases.[9,10] Clinically, there are no distinct differences in terms of symptoms and signs between those caused by *S aureus* and non-*S aureus*.[6,11] The morbidity is significant,

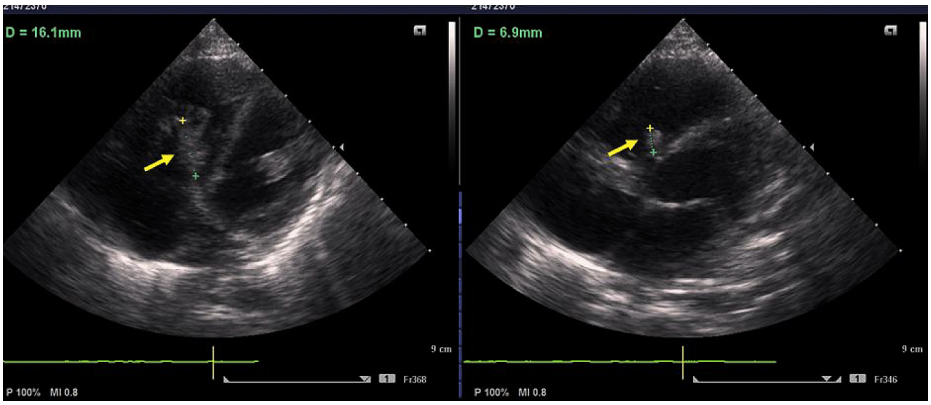

Figure 1. A transthoracic echocardiogram showed two vegetations in the right ventricle (yellow arrow): one at the tricuspid valve (right, 16.1 × 8.2 mm) and another one at the interventricular septum (left, 96.9 × 4.7 mm).

especially among the cases caused by *S aureus*.[10,11] Early identification of a probable case is crucial for a good outcome.

Since it was identified, CA-MRSA has been a recognized emerging pathogen for IE.[6] Most reported cases of IE caused by CA-MRSA occurred in adults without valvular anomaly and without any known predisposing factors for IE. Preexisting skin lesions and intravenous drug abuse were the major risk factors. Tricuspid valve was the most common involved site, followed by mitral and aortic valves. Events due to embolisms were seen in 68.4% of the reported cases.[6] In the present case, the patient had no preexisting cardiac anomaly. Two crusty partially healed fissures on both his big toes were found. It was presumed that *S aureus* invaded through these skin defects and led to IE. Both cardiac vegetations were found at the right ventricle, with one at the tricuspid valve. Pulmonary embolism was found, but no documented intracranial vascular embolism was identified despite an episode of seizure attack.

According to the guidelines for antimicrobial therapy for IE, at least 4—6 weeks of intravenous vancomycin therapy is recommended.[12,13] Most reported CA-MRSA IE cases were treated with vancomycin, frequently combined with a second antimicrobial agent such as rifampicim, gentamicin, linezolid, trimethoprim-salfamethozaxole, and clindamycin. However, there are no sufficient data to support the combination therapy involving gentamicin or SXT for childhood IE.[13] The mortality rate of CA-MRSA IE was 13%, which was markedly lower than that of methicillin-sensitive *S aureus* IE and hospital-acquired MRSA IE.[6] Although CA-MRSA-associated infections are quite common in children, only a few cases of CA-MRSA IE have been reported in the literature.[6,14]

Consistent with worldwide trends, CA-MRSA was epidemic in Taiwan and accounted for 40—70% of clinical isolates from children with CA *S aureus* infections.[3] Most cases caused by CA-MRSA presented as skin and soft tissue infections.[3] CA-MRSA was also associated with invasive diseases including bacteremia, septic arthritis, osteomyelitis, and necrotizing pneumonia.[4] The endemic CA-MRSA clone in Taiwan was characterized as multilocus ST 59, and carries type V_T SCC*mec* element and PVL genes.[3,4] Chi et al[15] showed that CA-MRSA accounted for 36% (8/22) of community-associated *S aureus* bacteremia and IE in southern Taiwan. Multilocus ST59 is the major clone of CA-MRSA isolates. The antibiogram of ST 59 CA-MRSA clone showed a multiresistant pattern. Most isolates were only susceptible to vancomycin, gentamicin, trimethorpim-sulfamethoxazole, and ciprofloxacin,[3,4,16] which made it more difficult to deal with invasive CA-MRSA infections.

In conclusion, we presented a rare case of CA-MRSA IE in a previous healthy preschool child. The MRSA isolate belonged to the endemic CA-MRSA clone in Taiwan. Since *S aureus* remains as the predominant causative pathogen of childhood IE, it is expected that CA-MRSA will have a growing role in childhood IE.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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