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CASE REPORT

Community-associated methicillin-resistant *Staphylococcus aureus* bacteremia and metastatic infection in a pediatric patient

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Abstract

Introduction: *Staphylococcus aureus* (SA) is a gram-positive bacterium that can cause serious infections, from bacteremia to invasive infections such as pneumonia, infective endocarditis, osteomyelitis, septic arthritis and soft tissue and central nervous system infections. Objective: To report the case of a pediatric patient who had bacteremia and metastatic infection by community-associated methicillin-resistant *Staphylococcus aureus*. **Case report:** Female patient, 9 years old, previously healthy, started with periorbital edema on the left, acutely and with the presence of high fever. She used amoxicillin-clavulanate with no clinical response, requiring hospitalization. Pustular lesions were identified on the scalp close to the retroauricular region on the left, and oxacillin was associated with treatment with ceftriaxone. The patient evolved with persistent fever and signs of myositis in the left thigh, and a thick liquid collection with a volume of 5 ml was identified on ultrasound. Multiple lung abscesses were also identified in both of the patient's lungs by CT scan. The BioFire BCID2 panel test identified the methicillin-resistant *Staphylococcus aureus* bacteria, therefore, the therapeutic scheme was changed to vancomycin. The treatment was carried out for six weeks, after which the patient's clinical and laboratory improved. **Conclusion:** We report the case of a patient who had bacteremia and metastatic infection by community-associated methicillin-resistant *Staphylococcus aureus*, in which a favorable outcome was obtained, without sequelae, due to the institution of adequate antimicrobial coverage early.

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INTRODUCTION

Staphylococcus aureus (SA) is a gram-positive bacterium that can cause serious infections, from bacteremia to invasive diseases such as pneumonia, infective endocarditis, osteomyelitis, septic arthritis, and soft tissue and central nervous system infections. The definition for community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) used by the Centers for Disease Control and Prevention (CDC) since 2000 encompasses cases of methicillin-resistant *Staphylococcus aureus* (MRSA) infection in persons without the following risk factors for MRSA infection: isolation of MRSA more than 48 hours after hospital admission; history of hospitalization, surgery, dialysis or admission to a nursing home within one year of the MRSA culture date; use of an indwelling catheter or percutaneous device at the time of culture; or history of isolation of MRSA.¹

The first well-documented descriptions of CA-MRSA infection emerged between 1997 and 1999 in children living in the Midwest United States, with cases of death by sepsis and severe pneumonia.² Research has revealed that strains of CA-MRSA have increased virulence compared to hospital-associated methicillin-resistant *Staphylococcus aureus* (HA-MRSA) strains, probably due to combinations and acquisitions of new genes, as well as adaptations in gene expression, resulting in greater expression of toxins.³

A study conducted at a university hospital in Brazil concluded that CA-MRSA is an emerging pathogen in the country, responsible for approximately a third of all strains of *S. aureus* isolated from children with severe community-associated infections.⁴

This article reports the case of a pediatric patient with bacteremia, metastatic infection, and CA-MRSA.

CASE REPORT

A previously healthy 9-year-old girl without a history of hospitalization developed acute left periorbital edema associated with high fever and local redness, heat, and erythema. She was taken to a clinic and was prescribed amoxicillin-clavulanate. After five days, since her symptoms did not improve, she was taken to a hospital and was prescribed intravenous ceftriaxone. Physical examination revealed that in addition to left periorbital cellulitis, she also had pustular lesions on the scalp close to the left retroauricular region and perichondritis in the ipsilateral ear, in addition to pediculosis, which prompted the prescription of oxacillin with ceftriaxone and ivermectin. Computed tomography of the orbits was ordered, which revealed minor left periorbital thickening without post-septal involvement. The patient remained febrile, with tachycardia and tachypnea, despite the addition of a new antibiotic drug. Laboratory tests showed she had microcytic, normochromic anemia, leukocytosis (white blood cell count: 29,800; rods: 298; and segmented: 28,012), and a C-reactive

protein level of 298 mg/L (RV: < 5 mg/L) were identified. Two peripheral blood samples were taken and cultured.

After 48 hours of hospitalization, the patient developed edema, pain, erythema, and stiffness in the left thigh in the posteromedial area close to the knee. Ultrasound examination revealed a thick liquid collection dissecting the muscle-adipose interface of the posterior region of the left thigh, associated with signs of panniculitis, with an estimated volume of 5 ml. MRI scans of the left thigh showed a collection with an estimated volume of 6.5 ml and prominent inguinal lymph nodes measuring up to 0.8 cm (Figure 1). The two blood culture samples were positive for gram-positive cocci. A BioFire Blood Culture Identification 2 (BCID2) Panel (multiplex PCR) ordered subsequently found the bacteria *Staphylococcus aureus* and the *mecA/C* and *MREJ* genes seen in MRSA.

With bacteremia confirmed, the hypothesis of metastatic MRSA infection was raised, and intravenous vancomycin was started at a dose of 60mg/kg/day. Twenty-four hours after the bacteria was identified, a conventional antibiogram confirmed the strain was resistant to oxacillin and sensitive to clindamycin, doxycycline, and trimethoprim-sulfamethoxazole, as characteristically seen in CA-MRSA. Chest x-ray images showed a cavitation in the middle third of the right lung. A subsequently ordered contrast-enhanced chest computed tomography revealed multiple lung abscesses of different sizes with a predominant subpleural/peripheral distribution in both lungs' upper and lower fields (Figure 2).

After four days of treatment with vancomycin, the frequency and intensity of the episodes of fever decreased. The patient's phlogistic signs on the left thigh improved gradually, and her leukocyte count and C-reactive protein levels decreased. Two control blood cultures performed after the start of treatment were negative.

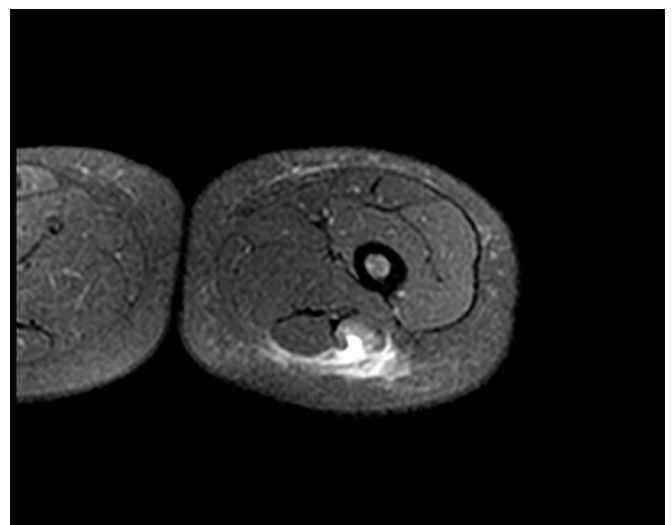


Figure 1. Axial view of the left thigh - MRI (T2). Caption: fluid collection with peripheral contrast enhancement.

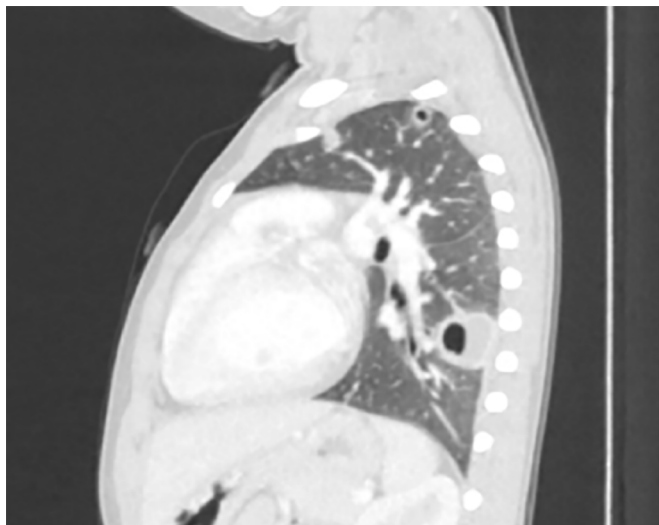


Figure 2. Sagittal view of the chest – computed tomography scan. Caption: Lung abscesses of different sizes in the upper and lower fields of both lungs, with liquefactive necrosis and parietal contrast uptake.

Given the suspicion of infectious endocarditis, the patient underwent a transthoracic echocardiogram in which a Chiari network was seen. It was not possible to differentiate the finding from a lesion suggestive of endocarditis, which prompted the start of preemptive therapy for the condition. Screening tests for primary immunodeficiencies were performed concomitantly with treatment. In at least two moments (15 days apart), low IgM antibody levels ($< 3^{\text{rd}}$ percentile) and cyclic neutropenia were observed in serial tests. After six weeks of antibiotic therapy, the patient underwent a chest tomography, which showed only small residual consolidations. She was then discharged without symptoms.

The Research Ethics Committee of our institution approved this case report for publication (certificate 64631122.5.0000.5040). Consent was obtained from the child's legal guardian.

DISCUSSION

CA-MRSA infections are a common problem and generally involve the skin.⁵ Healthy individuals may have their skin colonized by bacteria from the *Staphylococcus* and *Streptococcus* genera, which generally become pathogenic once skin integrity is compromised.⁶ Pediculosis capitis is a significant risk factor for skin infection in children. Sores from itching and scratching may cause complications such as bacterial infection, mycosis, and myiasis.⁷

A study including pediatric patients hospitalized between 2009 and 2012 in the United States revealed that of 411 episodes of bacteremia due to *S. aureus*, 86% were community-associated (34% CA-MRSA, 59% methicillin-sensitive or CA-MSSA and 7% unknown sensitivity) and 14% were hospital-associated (35% HA-MRSA, 63% methicillin-

sensitive or HA-MSSA, and 2% of unknown sensitivity).⁸ Another study enrolling patients hospitalized in ten pediatric care centers in Argentina between 2012 and 2014 found 1,141 patients with community-associated *S. aureus* infection, 79.2% of which had CA-MRSA infection and 20.8% had CA-MSSA and *S. aureus* infection with unknown antimicrobial susceptibility. The most frequent clinical findings in patients with CA-MRSA infection were skin and soft tissue infection (66.2%), pneumonia (11.5%), and sepsis (8.5%).

Metastatic infections may occur in patients with *S. aureus* bacteremia. A study with pediatric patients admitted to a hospital in Argentina between 2008 and 2009 found a rate of 15.8% of secondary foci of infection in patients with positive blood cultures for *S. aureus*. The leading risk factor was the persistence of positive blood cultures for more than 48 hours.¹⁰ Another study including pediatric patients hospitalized between 2010 and 2016 in another center in Argentina underlined some traits related to the appearance of secondary foci of infection in pediatric patients with *S. aureus* bacteremia, namely female sex, MRSA bacteremia, higher number of positive blood cultures, persistence of bacteremia after the fifth day of treatment, and sepsis.¹¹

As seen in our case, culture results played a fundamental role in the therapy adjustments made due to the lack of response from the previous antibiotic regimen and the suspicion of endocarditis. The BioFire BCID2 panel gave a positive result for MRSA infection within a few hours, faster than the blood culture and the definitive antibiogram. This panel is based on a multiplex PCR technique and detects some of the most common pathogens associated with bacteremia and resistance genes.¹²

Present in about 2% of the population and observed in our patient's echocardiogram, the Chiari network consists of embryonic remnants of the venous sinus valves. Reports indicate that it may be involved in the pathogenesis of thrombotic diseases, endocarditis, and arrhythmia.¹³ As described in the literature, this structure may occasionally be a focus of infection.¹⁴

As in the case described, primary immunodeficiency testing is required primarily in the presence of severe clinical manifestations of prolonged evolution, inadequate response to antibiotic therapy, and high risk of complication and hospitalization.¹⁵

CONCLUSION

The case described showed how localized cutaneous CA-MRSA infection may spread metastatically in a pediatric patient. Thorough physical examination combined with early detection of the resistant microorganism can prompt the start of early treatment and decrease the chances of morbidity and mortality. Healthcare workers must consider CA-MRSA antimicrobial coverage when dealing with children with pyogenic skin and soft tissue infections who do not respond to initial beta-lactam therapy.

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