Community-Acquired MRSA Pericarditis and Mediastinitis in a Previously Healthy Infant

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Abstract

Keywords

- methicillin-resistant *Staphylococcus aureus*
- CA-MRSA
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- children

Invasive community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections disproportionately affect children, but there are few pediatric reports of pericarditis and mediastinitis caused by CA-MRSA in previously healthy children. Here we report a severe case of CA-MRSA pericarditis with extension to the mediastinum and carotid sheath in a previously healthy 8-month-old infant who was successfully treated with surgical interventions and with a combination of daptomycin and vancomycin. The relatively indolent clinical course in this patient was notable given the significant extent of infection. This case highlights the potential virulence of CA-MRSA in previously healthy children and the importance of early diagnosis, prompt drainage, and appropriate antibiotic coverage.

Introduction

Purulent pericarditis is a potentially fatal infection that requires prompt recognition and treatment. In the antibiotic era, it has become relatively rare and typically presents in children with immune dysfunction or history of trauma or instrumentation rather than in previously healthy children. While there are several reports describing staphylococcal purulent pericarditis in the pediatric literature, only a few identify community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) as the culprit in children.^{1,2} The previously reported pediatric cases of CA-MRSA purulent pericarditis were immunocompetent

children from the community who presented with severe shock and multi-organ failure.^{1,2} Here, we report a severe case of CA-MRSA pericarditis with extension to the mediastinum and carotid sheath in a previously healthy immunocompetent 8-month-old infant who was successfully treated with surgical interventions and daptomycin in the setting of suboptimal vancomycin levels. The relatively indolent clinical course was notable given the significant extent of infection. Multiple studies have demonstrated that invasive CA-MRSA infections disproportionately affect the pediatric population and are increasing in incidence.^{3–6} Because these children are often previously healthy and may present to general pediatricians, rapid identification

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and management of potentially life-threatening manifestations of CA-MRSA are critical.

Patient Presentation

A previously healthy 8-month-old female presented with a 10-day history of fever with leukocytosis that was unresponsive to outpatient treatment with amoxicillin. Complete blood counts prior to admission were significant for leukocytosis on the fourth day of fever with a white blood cell count (WBC) of 20,000/mm³, which decreased to 9,900/mm³ 2 days later, and then rose to 34,800/mm³ on the day of admission. A urine culture was positive for *Klebsiella pneumoniae*, and a blood culture was negative. She was transferred to our institution for further management.

On arrival, she was afebrile having received acetaminophen 2 hours earlier, tachycardic, and tachypneic, with an oxygen saturation of 94% on room air. She was noted to be grunting with mild subcostal and suprasternal retractions. Her abdomen was distended and diffusely tender, with her liver edge palpable 4 cm below the right costal margin. Her initial laboratory work was significant for leukocytosis (WBC: 28,500/mm³), with a neutrophilic predominance (69% neutrophils and 8% bands). She also had thrombocytosis (platelet count, 1200 × 10³ cells/μL) and elevated inflammatory markers (C-reactive protein, 237 mg/L and procalcitonin, 2.07 ng/mL). Vancomycin and piperacillin-tazobactam were initiated for concerns of an abdominal infection. A chest X-ray revealed significant cardiomegaly with mild bilateral interstitial pulmonary edema (►Fig. 1). A transthoracic echocardiogram revealed a large, complex circumferential pericardial effusion with multiple fibrinous strands and loculations (►Fig. 2).

To address the extensive pericardial effusion, a surgical pericardial lavage and window creation were performed for both diagnostic and therapeutic purposes although there was

no evidence of tamponade physiology. Approximately 100 mL of purulent fluid was drained, adhered fibrinous exudate was removed, and pericardial and pleural drains were placed. Multiple cultures from the pericardial fluid collection and tissue biopsies of the fibrinous material grew MRSA, sensitive to vancomycin, linezolid, clindamycin, and doxycycline. Piperacillin-tazobactam was changed to ceftriaxone for treatment of the *Klebsiella pneumoniae* urinary tract infection.

On the third day of admission, the patient remained febrile, and the vancomycin trough was subtherapeutic at 10.7 μg/mL despite several dose adjustments.⁷ Daptomycin was added at a dose of 6 mg/kg daily. Magnetic resonance imaging of the chest revealed a large superior mediastinal collection tracking along the left common carotid and internal carotid arteries and internal jugular vein to the skull base and from the superior mediastinum to the left upper lung lobe (►Fig. 3). A decision was made to proceed with an anterior mediastinotomy, and mediastinal abscess drainage was performed. Intraoperative cultures collected during both drainage procedures of the pericardial fluid, mediastinal collection, and tissue biopsies all grew MRSA with matching resistance profiles.

Because of the extensive infection and indolent presentation of this patient, an immunologic workup was performed, with no identified immunodeficiency. Humoral responses to previous vaccines, immunoglobulin panel, T cell subsets, and dihydrorhodamine test for chronic granulomatous disease were all within normal limits. Human immunodeficiency virus polymerase chain reaction (HIV PCR) and respiratory viral panel were negative. Last, a workup for interleukin-1 receptor associated kinase 4 deficiency (IRAK-4) that presents with severe, recurrent staphylococcal and pneumococcal infections, including pericarditis, meningitis, arthritis, and sepsis, was also negative.⁸

After the drainage of the mediastinal abscess, the patient defervesced and clinically improved, and the WBC and C-reactive protein (CRP) began to decrease. She had been treated with vancomycin for 14 days total with the addition of daptomycin for 5 days until vancomycin troughs were above 15 μg/mL, and the patient clinically stabilized. There was no re-accumulation of her pericardial effusion on serial transthoracic echocardiograms. She was discharged on oral linezolid to complete ~4 weeks in total of antimicrobial treatment. By 1 week after discharge, the patient was at her baseline and had no evidence of pericardial effusion recurrence or post-infectious restrictive cardiomyopathy.

Fig. 1 Initial chest X-ray showing cardiomegaly. This chest X-ray obtained at the time of admission demonstrates moderate cardiomegaly with mild bilateral interstitial edema.

Discussion

In children, purulent pericarditis caused by *S. aureus* generally presents with signs of sepsis or shock in patients with predisposing factors, such as previous cardiothoracic surgery, concurrent pneumonia, or penetrating injury to the chest. Surprisingly, our patient had no predisposing factors and presented with mild respiratory distress and no hemodynamic compromise after 10 days of fever. We suspect that our patient had a preceding viral infection because of the 10 days of fever preceding admission with initial leukocytosis that decreased. Upper respiratory illnesses can compromise the mucosal barrier

Fig. 2 Complex, loculated pericardial effusion seen on 2D-echo. (A) This transthoracic echocardiographic two-dimensional subcostal long-axis image demonstrates a complex large pericardial effusion concentrated leftward and posterior (asterisk), with multiple fibrinous strands and loculations. The cardiac apex appears adherent to the pericardium by a large fibrinous strand (caret). (B) Sweeping inferior to the heart demonstrates multiple loculated pockets of pericardial effusion (asterisk), with a large centrally located fibrinous complex (arrow) with multiple strands attaching to the periphery. LA, left atrium; LV, left ventricle; RA, right ventricle.

Fig. 3 Large, communicating fluid collection in the superior mediastinum extending to the carotid space up to the base of the skull. (A) This magnetic resonance black blood axial plane image demonstrates a circumferential pericardial effusion with communication to the left lung located at the leftward and posterior aspect of the pericardium (asterisk). The consolidation extends into the left upper lung lobe. (B) This contrast-enhanced magnetic resonance coronal plane image reveals the extension of the consolidation across the superior mediastinum (asterisks) in close proximity to the brachiocephalic vessels, tracking along (arrows) the left brachiocephalic vein (LBCV) and left internal jugular vein (LIJV) to the base of the neck. LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

in the nares and can lead to transient bacteremia and subsequent invasive disease. Cultures from the anterior nares in our patient confirmed that she was colonized with MRSA. Typing of all isolated MRSA strains from the anterior nares, blood, pericardial fluid and tissue, and mediastinal abscess was performed by deoxyribonucleic acid (DNA) sequence analysis of the protein A gene variable repeat region (*spa* typing), *SCCmec* element subtype, and the presence of the Pantón–Valentine leukocidin and arginine catabolic mobile element genes.^{9–11} This typing, t008-*SCCmec* IVa-PVL(+)-ACME(+), identified all of the isolates including the colonizing strain as genotypically isogenic clones of USA300, the most common epidemic CA-MRSA strain in the United States.¹² There are limited reports of MRSA pericarditis in children, and only two case reports of CA-MRSA;^{1,2,13–17} neither of these studies report management involving with daptomycin and surgical interventions.

Based on adult studies and the Infectious Diseases Society of America (IDSA) guidelines, the recommended vancomycin trough levels for severe MRSA infections are 15 to 20 µg/mL.⁷ However, reaching this trough in children often requires very high doses; our patient reached target levels with 25 mg/kg/dose every 6 hours. Linezolid or clindamycin were not chosen as alternative therapeutic agents because of their bacteriostatic rather than bactericidal activity. With the challenge of attaining therapeutic troughs and potential for renal toxicity with vancomycin, alternative therapies for MRSA are necessary in children. In our case, daptomycin was added to increase confidence in antimicrobial coverage, while vancomycin troughs remained below recommended levels.⁷ We favored a bactericidal agent that has potential synergy with vancomycin based on in vitro studies.¹⁸ Although there are limited reports of daptomycin use in infants, a dose of

6 mg/kg daily was chosen based on one pharmacokinetic study of 20 infants, demonstrating more rapid drug clearance in infants compared with adults.¹⁹

In children, daptomycin is generally not considered as the first-line therapy due to limited data on efficacy, pharmacokinetics, and adverse events. However, in the era of MRSA, there is a renewed interest in daptomycin as an alternative to vancomycin. One prior case study reports effective treatment of MRSA endocarditis with daptomycin in a child,²⁰ but there are no similar reports of daptomycin use in children for pericarditis. Several recent studies report retrospective data on daptomycin use in children, demonstrating favorable treatment outcomes with limited adverse events.^{21–24} The first randomized trial of daptomycin for complicated skin infections in children, which included nearly 100 children with MRSA, reported clinical success rates of 91%, similar to that of the standard-of-care antimicrobial agent.²⁵ Adverse events in all of these studies were minimal and included diarrhea and elevated creatine phosphokinase.^{19,21–28} Eosinophilic pneumonia is a reported adverse event in adults, but has not been reported in children.^{7,29} A wide gap remains between antibiotic regimens available to adults and children, demonstrating a need for further studies in the pediatric population.

The surgical interventions for our patient involved a multi-disciplinary team, including pediatric cardiology, pediatric cardiothoracic surgery, and pediatric surgery. The approach to draining the effusion was surgical as opposed to a pericardiocentesis due to adherence of the cardiac apex to the pericardial sac by the fibrinous strands and the mostly posterior location of the loculated pericardial effusion. When the mediastinal collection was discovered, an anterior mediastinotomy for abscess drainage was chosen over a sternotomy and chest washout as a less invasive option. It is unclear whether the mediastinal fluid collection was present on admission or developed subsequently. Also, the mediastinal abscess drainage was pursued concurrently with optimizing the antibiotic regimen with daptomycin; therefore, it remains unclear which, if either, of these interventions was more beneficial for this patient's clinical improvement.

Conclusion

CA-MRSA pericarditis is a life-threatening condition that can be seen in immunocompetent children without any risk factors. Our case highlights the virulence of CA-MRSA pericarditis and the importance of early diagnosis, prompt drainage, and appropriate antibiotic coverage. A multi-disciplinary approach is required to address the acute critical care, cardiac, surgical, and antimicrobial management issues associated with such complicated cases.

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Conflict of Interest

None.

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