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CASE REPORT

Community-associated methicillin-resistant *Staphylococcus aureus* necrotizing pneumonia in a healthy neonate



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The number of cases of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) pneumonia has increased since the late 1990s, with skin and soft tissue infections predominant among neonates. Herein, we present a rare case of CA-MRSA necrotizing pneumonia with empyema following respiratory syncytial virus (RSV) infection in a healthy neonate. Despite prompt vancomycin treatment, the disease worsened and finally we had to perform pneumonectomy. This case highlights the possibility of emerging CA-MRSA-related invasive disease among neonates.

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Introduction

The number of cases of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infection has increased worldwide over the last decade.¹ In neonates, a majority of CA-MRSA infections involve skin and soft tissues. Although not often seen, the invasive disease does occur even in previously healthy term or near-term infants. This is an emerging disease that might cause serious

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hazards to the health of newborn infants universally. We present a rare case of CA-MRSA necrotizing pneumonia following respiratory syncytial virus (RSV) upper respiratory tract illness in a healthy term neonate. The severity of her course may be attributed to the Pantón–Valentine leukocidin (PVL) carrying sequence type 59 (ST59) strain.

Case report

A 23-day-old female infant presented to the emergency room (ER) with fever, cough, progressive dyspnea, and lethargy. She was born at 38 weeks' gestation to a 29-year-old woman after uncomplicated pregnancy, and the perinatal course was uneventful. She was discharged home on the 3rd day of life and breastfed with good body weight gain. While the mother and sibling had symptoms of common cold, this infant began to develop cough, rhinorrhea, and fever on the 13th day of life. Her symptoms waxed and waned for a while but she was eventually brought to the ER due to high fever and progressive dyspnea on the 23rd day of life. Her chest X-ray (CXR) showed right lobar pneumonia and pneumatocele formation (Fig. 1). She also had leukocytosis with left shift: white blood cell count $30.8 \times 10^9/L$; with 16% band form; 46% segment; and 18% lymphocyte. C-reactive protein level was 262.5 mg/dL.

She was admitted to the neonatal intensive care unit with oxygen and positive pressure support via nasal prongs. Oxacillin (75-mg intravenous injection every 6 hours) and cefotaxime (150-mg intravenous injection every 8 hours) were empirically administered. However, her respiratory condition rapidly deteriorated while CXR revealed pneumothorax and worsening pneumatocele formation over the right lung. Chest computed tomography scan confirmed necrotizing pneumonia of the right lung with bronchopleural fistula and empyema formation (Fig. 2). Endotracheal intubation and chest tube insertion were performed. Her endotracheal aspirate, pleural effusion, and blood culture all grew methicillin-resistant *S. aureus* (MRSA) that was sensitive to vancomycin. The result of sputum enzyme-linked immunosorbent assay for RSV antigen was positive. Despite starting vancomycin treatment (45-mg intravenous

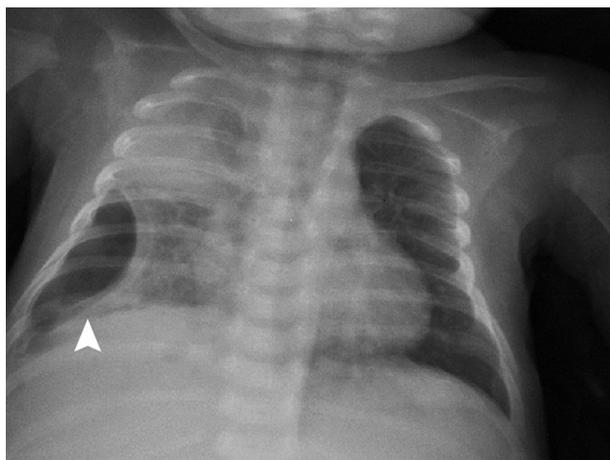


Figure 1. Chest film upon admission showing right lobar pneumonia and pneumatocele formation (white arrowhead).

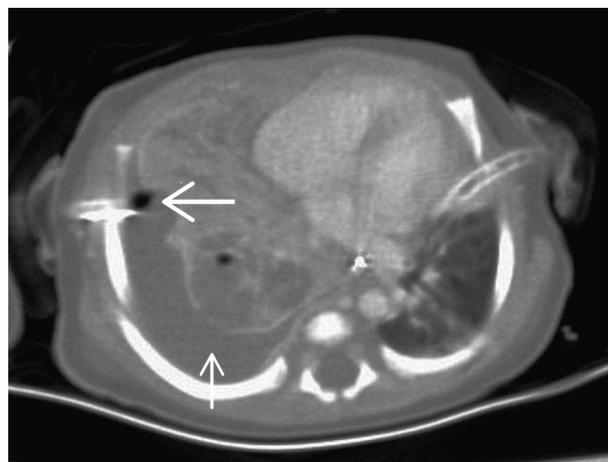


Figure 2. The first chest computed tomography scan of the patient showing necrotizing pneumonia of the right lung with bronchopleural fistula (abnormal air collection; large arrow) and empyema formation (low-density fluid collection with fibrin content; small arrow).

injection every 8 hours) on the 2nd day of admission, her clinical condition continued to deteriorate. She finally underwent partial pneumonectomy of the right upper and lower lobes on admission day 7. Culture of intraoperative pleural fluid still grew MRSA. Her condition improved and the patient came off mechanical ventilation 3 days after the operation. However, even though vancomycin had been given without interruption, she developed fever 3 days later and was reintubated. Her respiratory condition deteriorated to the point that high-frequency oscillatory ventilation with 100% fraction of inspired oxygen could only barely maintain her oxygen levels. Extracorporeal membrane oxygenation was proposed but it was declined by her parents. Because of treatment failure, the patient's antibiotic was switched to linezolid (30-mg intravenous injection every 8 hours) after 18 days of vancomycin therapy.

She developed necrotizing pneumonia again in the remaining right lower lung with bronchopleural fistula and pneumothorax. A second total right lung pneumonectomy was performed on the 40th day of admission. Microscopic examination of the removed tissue showed diffuse atelectasis, fibrosis, bronchitis, and abscess formation. She received linezolid for a period of 3 weeks without inadvertent effects, and the patient eventually came off ventilator support 2 weeks after the second surgery.

This infant was oxygen-dependent until she was 3 months old with normal development at 1 year of age. Her immunological studies including immunoglobulin levels and cluster of differentiation subsets were all normal.

Five MRSA isolates, including two isolates from bloodstream, one isolate each from pleural effusion, sputum, and pus specimen, were collected for microbiological characterization. All the five isolates had the same antibiogram, showing resistance to clindamycin and erythromycin, and susceptibility to trimethoprim/sulfamethoxazole, vancomycin, teicoplanin, tigecycline, and linezolid. All the five isolates also shared common molecular characteristics and

were characterized as pulsed-field gel electrophoresis (PFGE) type D4 (similar to USA1000), ST59 by multilocus sequence typing, carrying staphylococcal cassette chromosome *mec* (*SCCmec*)-type V_T genes, and possessing *PVL* genes, which are typical molecular characteristics of CA-MRSA in Taiwan.²

Discussion

As CA-MRSA becomes more prevalent, it is inevitable that we will encounter CA-MRSA-related invasive disease more often. As our case may imply, CA-MRSA could play an increasingly important role in neonatal pneumonia. As the first case of CA-MRSA pneumonia among neonates in Taiwan, the clinical presentation of neonatal CA-MRSA pneumonia is similar to that in older children with characteristics of respiratory failure, high fever, abnormal CXR from empyema to necrotizing pneumonia.²

The CA-MRSA clones are different in different regions of the world. For example, USA300 strain multilocus sequence type (MLST8) prevails in the United States, Canada, and in some European countries, whereas strains of ST30 clonal lineage are common in Australia, Japan, and Greece, while strains of ST80 clonal lineage are common in Europe.^{3–5} In Taiwan, most of the CA-MRSA clinical isolates have been characterized as ST59/PFGE type D/*SCCmec* V_T /*PVL*-positive, and so are the isolates from our presented case.^{2,6} A majority of CA-MRSA isolates possess *PVL* genes. *PVL* genes, which cause leukocyte destruction and tissue necrosis, are reported to be associated with skin infections and necrotizing pneumonia in both clinical cases and murine models.^{7–10}

A preceding viral infection has been proposed as the initiating event in severe necrotizing pneumonia, and may contribute to the severity of CA-MRSA infection. Hageman et al reported that patients with invasive CA-MRSA pneumonia were frequently preceded by an influenza-like illness.¹¹ After the viral infection, the respiratory epithelium is injured and this enhanced the binding of *PVL*-positive *S. aureus* strains.⁸ The preceding upper respiratory tract infection 10 days before admission and the coinfection of RSV can be attributed to the severity of CA-MRSA pneumonia in our patient.

Treatment of CA-MRSA infections should be stratified according to the site and severity of disease as well as national epidemiology and antibiotic susceptibility pattern.⁶ Although CA-MRSA strains generally retain susceptibility to trimethoprim/sulfamethoxazole, fluoroquinolones, gentamicin, their resistance to clindamycin and macrolides is increasing.¹² In Taiwan, up to 94–97% of the CA-MRSAs are resistant to clindamycin and erythromycin.² Concerning fatality of invasive CA-MRSA infection due to delayed use of effective antibiotics, glycopeptides such as vancomycin are advised to be used empirically and continued until susceptibility test is available for invasive disease.^{2,6} However, if there is no satisfactory response to vancomycin therapy, linezolid, a member of oxazolidinones

that inhibits bacterial protein synthesis, can be considered as an alternative in treating invasive CA-MRSA infection, as in the current case.¹³

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