

# A Severe Pneumonia due to Methicillin Resistant *Staphylococcus aureus* Clone USA 300: Implications of Vertical Transmission

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## ABSTRACT

*Staphylococcus aureus* is an important pathogen in both community and healthcare associated pneumonia. We describe a case of severe pneumonia caused by the methicillin resistant *Staphylococcus aureus* (MRSA) clone USA 300 in a 44-year old post-partum woman and the subsequent vertical transmission of this virulent organism to her neonate.

**Keywords:** Antibiotic therapy, methicillin resistant *Staphylococcus aureus*, pneumonia, vertical transmission

# Pulmonía Severa debido al Clon USA 300 del Estafilococo dorado Resistente a la Meticilina: Implicaciones de la Transmisión Vertical

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## RESUMEN

El estafilococo dorado (*Staphylococcus aureus*) es un patógeno importante tanto en la atención a las comunidades como en el cuidado de la salud en relación con la pulmonía. Se describe un caso de neumonía severa causada por el clon USA 300 del estafilococo dorado resistente a la metilina (EDRM) en una mujer de 44 años en periodo de post-parto, y la posterior transmisión vertical de este virulento organismo a su neonato.

**Palabras claves:** terapia antibiótica, metilina, estafilococo dorado resistente a la metilina, pulmonía, transmisión vertical

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## INTRODUCTION

It has been well established that methicillin resistant *Staphylococcus aureus* (MRSA) is a predominant cause of healthcare associated infections. Furthermore, there have been several reports of MRSA infections occurring in the community (CA-MRSA). Two major clones of CA-MRSA, USA 300 and USA 400, have been identified in the United States of America (USA) using pulsed field gel electrophoresis (PFGE) and other genotyping characteristics (1). In addition, the USA 300 clone has been reported to be the predominant cause of skin and soft tissue infections in the USA. Studies have reported that CA-MRSA is an increasing-

ly common pathogen in pneumonia (2). The majority of CA-MRSA strains carry the intracellular toxin Panton-Valentine leukocidin (PVL), which is a potent mediator of inflammation and can destroy polymorphonuclear cells by forming pores in their cell membranes.

## CASE REPORT

A 44-year old female presented at the Emergency Department with a one-day history of chest pain, fevers and chills. The patient was six days post-partum, from a spontaneous vaginal delivery complicated by a vaginal tear. The patient had been in hospital since delivery, rooming in with her baby who had hyperbilirubinaemia. There was reduced air entry to the right lung zone with coarse crepitations. Vaginal examination revealed a swollen indurated right labia majora, with normal *lochia rubra* and the perineal sutures were intact. Laboratory studies revealed a white blood cell count of  $17.3 \times 10^3/\text{UL}$  with an absolute neutrophil count of  $16.7 \times 10^3/\text{UL}$ , platelets  $316 \times 10^3/\text{UL}$  and haemoglobin 12.8 g/dL. A computed tomography (CT) scan showed patchy bilateral subsegmental air space disease of bronchopneumonia. The

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patient was screened for MRSA nasal carriage and was found to be positive. In addition, MRSA was isolated from vaginal and perineal screening. Blood cultures, sputum and episiotomy wound cultures were sent to the Department of Microbiology for culture and susceptibility. Empirical antibiotic therapy with azithromycin IV 500 mg every 24 hours (Q24H) and ceftriaxone IV 1.0 g Q24H was initiated. Blood cultures, sputum and wound specimens grew MRSA. Therapy with ceftriaxone and azithromycin was discontinued on day 2 of admission and vancomycin IV 1.0 g Q12H was added. The chest X-ray was repeated which revealed bilateral pleural effusions, with a 2 cm depth of layering on the right lateral decubitus film. Right thoracentesis was carried out and 370 ml of blood-stained exudative viscid fluid were drained. White cell differential count revealed scattered reactive mesothelial cells in a background of predominantly neutrophils, monocytes and lymphocytes. However, no organisms were seen and no growth was detected by culture. Following six days of vancomycin therapy, the patient developed fever, chills, abdominal pain with general body aches despite resolution of her lung condition, and decreasing white cell count. Since there was no clinical improvement, the patient was transferred from Bermuda to the Lahey Clinic, USA, for the management of her condition. After evaluation and consultation at the Lahey Clinic, the patient was started on linezolid 600 mg Q12H and her condition improved after two days of therapy. The patient was subsequently transferred back to Bermuda, where she completed 14 days of oral linezolid with resolution of pneumonia.

The patient's male infant was re-admitted to hospital at age five days for phototherapy because of a serum bilirubin level of 18.3 mg/dL. At 22 hours of age, he had a serum bilirubin of 11.5 mg/dL and he received phototherapy for 58 hours. He did well and was discharged on day four of life. Follow-up bilirubin value was arranged to be done the next day which was 18.3 mg/dL and he was re-admitted to hospital. He was restarted on phototherapy and a nasal swab for MRSA was done, as per hospital policy for patients re-admitted within 30 days of discharge, and was positive. He was then well and a five-day course of nasal bactroban was commenced with the goal of eradicating the carrier state. By day nine of life, the hyperbilirubinaemia had resolved and phototherapy was discontinued. At 15 days of age, he developed a left breast abscess with a purulent discharge which was sent to the microbiology laboratory for culture and sensitivity testing and the patient was started on clindamycin. The culture grew MRSA and therapy with clindamycin was discontinued and vancomycin IV 22.5 mg/kg Q12H was added. The MRSA isolate from the infant had similar susceptibilities to those obtained from the mother and were kept for molecular typing. In addition, the abscess was incised and drained. The vancomycin was continued for three days and the remainder of his hospital stay was uneventful. He would have been able to go home at that point but then his

mother had become ill (she had been rooming in with him) so he was kept in hospital.

The MRSA isolates from mother and infant were identified and antibiotic susceptibility tests were carried out using standard microbiological methods and the automated system Vitek 11. In addition, the isolates were genotyped by PFGE and were performed using a protocol developed in the Division of Medical Microbiology at the Johns Hopkins Hospital. Overnight broth cultures of *S aureus* were pelleted; bacterial DNA was extracted in agarose plugs using a solution containing lysostaphin and lysozyme. Restriction enzyme digestion was performed using *Sma* I. Restriction endonuclease fragments were analysed by PFGE using a contour-clamped homogenous electric field DR-11 apparatus (BioRad Laboratories, Inc, Hercules, CA) set at 14°C; initial switch, 5 seconds, final switch 50 seconds; and time 23.5 hours. After electrophoresis, gels were stained with ethidium bromide. Macrorestriction DNA banding patterns were digitized and analysed using Molecular Analyst DNA Fingerprinting software (BioRad). Patterns were compared and interpreted using the criteria of Tenover *et al* (3).

The isolates from mother and infant had identical antibiotic susceptibility profiles and genotyping analysis demonstrated that the isolates matched the profile of USA 300, the predominant CA-MRSA clone in the USA (Figure).

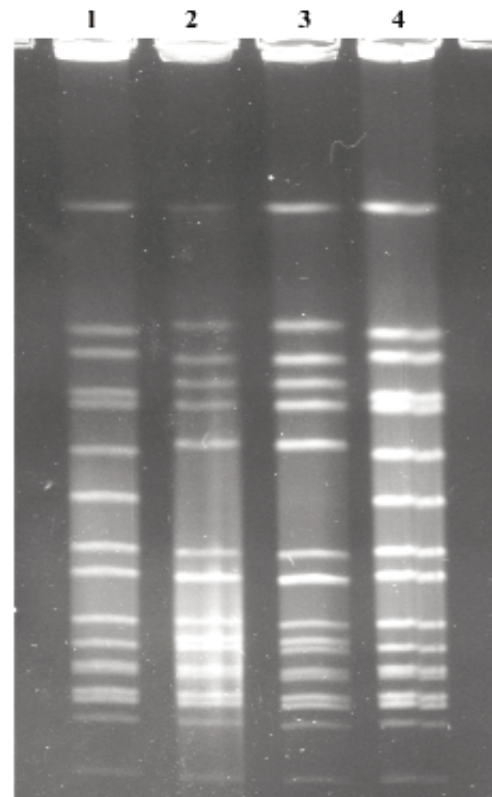


Figure: Pulsed field gel electrophoresis of representative CA-MRSA isolates. Lane 1: molecular weight marker (NCTC 8325); Lane 2: mother; Lane 3: neonate; Lane 4: molecular weight marker (NCTC 8325).

## DISCUSSION

The diagnosis of CA-MRSA was made based on the patient's clinical presentation and culture results being positive for MRSA within 48 hours of admission. The patient was colonized in her nares with MRSA which is a risk factor for developing community acquired pneumonia (CAP). A recent study reported that CA-MRSA as the causative agent of CAP should be considered when pneumonia develops in a person known to be colonized with CA-MRSA or other high risk groups which are known to be carriers of CA-MRSA (4). Once it was established that the patient was colonized and had positive cultures for MRSA, azithromycin and ceftriaxone were discontinued and vancomycin IV 1.0 g was added. However, despite a modification in antibiotic management, there was little improvement in the patient's condition. Although vancomycin is considered by many to be the drug of choice for treating MRSA, several studies have reported high failure rates in the treatment of MRSA pneumonia and one reason for the poor outcomes in some patients is the drug's poor penetration into pulmonary tissue and lung epithelial lining fluid (5). An alternative antibiotic for the treatment of MRSA pneumonia is linezolid and it has been reported that this drug achieves greater levels in lung epithelial lining fluid than in plasma. Initially, the patient was offered linezolid instead of vancomycin when her condition did not improve. However, linezolid was refused by the patient because of fear of drug interaction with fluoxetine which the patient was receiving. The patient was transferred overseas for management because her condition worsened while on vancomycin and later, after consultation with an infectious disease specialist at Lahey Clinic, USA, the patient agreed to be managed with linezolid.

The infant in this report was re-admitted to hospital because he had hyperbilirubinaemia. He did not have any risk factors that are known to be associated with MRSA

infection in paediatric units. Interestingly, there were no other patients who tested positive for MRSA by screening or culture on the maternity and paediatric wards during the time the mother and infant were infected. These findings suggest that it was likely that the infant acquired the infection from the mother rather than the environment, especially since both the vaginal and perineal sites of the mother tested positive for MRSA.

In conclusion, this report illustrates the vertical transmission of CA-MRSA clone USA 300 from a mother to her neonate and highlights the challenges regarding the management of CA-MRSA pneumonia.

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