

Methicillin-resistant staphylococci presenting as rare hospital-acquired infections: A case series

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ABSTRACT

Even though *Staphylococcus aureus* is present as normal flora on the skin, it is a pathogen when present in otherwise normally sterile body fluids such as cerebrospinal fluid and blood. Methicillin-resistant *S. aureus* (MRSA), presumed to originate from a patient or carrier, is responsible for both community-acquired as well as hospital-acquired infections (HAIs). Coagulase-negative staphylococci (CoNS) are present as normal flora on skin but cause vegetations on valve leaflets in subacute bacterial endocarditis and surgical site infection. MRCoNS arises from the skin flora of hospitalised patients and can contribute to similar infections in the hospital setting. We present three cases of Methicillin-resistant staphylococci causing HAI, MRSA causing meningitis with obstructive hydrocephalus, MRCoNS causing bacteraemia in a child with congenital cyanotic heart disease and MRCoNS causing surgical site infection on an amputation stump.

Key words: Meningitis, Methicillin-resistant coagulase-negative staphylococci, Methicillin-resistant *Staphylococcus aureus*, valve leaflet vegetation

INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) can result in hospital-acquired infections (HAIs) that usually originate from an intermittent carrier present at the health-care setting. This can result in serious infections such as bacteraemia and meningitis in susceptible populations such as infants, elderly and intravenous (IV) drug abusers. In such situations, there is increased risk of complications, confusion in choosing the ideal antibiotic and poor response to treatment.

Coagulase-negative staphylococci (CoNS) are present as normal flora on the skin but act as opportunistic pathogens in acute bacterial endocarditis where it may cause vegetations on heart valve leaflets. When the strain is resistant to Methicillin, there is increased possibility of it having originated in the health-care setting. Such MRCoNS are increasingly being isolated in blood cultures from cases with fever as well as swabs from skin and surgical sites.

CASE REPORTS

Case 1

A 47-day-old male infant was admitted in the Paediatric Intensive Care Unit with complaints of fever and signs of meningitis of one-day duration. He showed tonic posturing of limbs and a staring look. He has no history of prior hospitalisation but had taken immunisation with pentavalent vaccine and inactivated Polio vaccine, three days ago and was therefore referred from that private hospital as a case of adverse event following immunisation.

The cerebrospinal fluid (CSF) appeared turbid, and Gram's smear of CSF showed pus cells 0–2 and Gram-positive

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cocci singly and in small groups of 3–4/OIF. Culture on sheep blood agar showed colonies 2 mm in diameter, convex, golden yellow, beta haemolytic and opaque. MacConkey agar showed small pink colonies. The isolate was positive for catalase, slide and tube coagulase, DNase, urease and phosphatase and it grew yellow colonies on Mannitol Salt agar. It was resistant to Cefoxitin and hence identified as MRSA. The isolate was resistant to Penicillin, Ampicillin and Cephalexin and sensitive to Vancomycin, Linezolid, Rifampicin and Clindamycin. Subsequently, two CSF cultures were sterile. Nasal, hairline and axillary swab of the mother who had been working as a staff nurse abroad grew only MRCoNS.

He was given Ceftriaxone but on culture report of MRSA, was started on IV Vancomycin 100 mg 8th hourly. He developed Red Man syndrome, and therefore, therapy was changed to IV Linezolid 55 mg 8th hourly along with IV Amikacin 37.5 mg 12th hourly and IV Metronidazole 37.5 mg 8th hourly.

On neurosurgery consultation and magnetic resonance imaging (MRI) scan of the brain, two microabscesses were detected at the posterior midbrain and region of the aqueduct of Sylvius. A diagnosis of acute meningitis with obstructive hydrocephalus was obtained. Figure 1 shows MRI of the brain showing meningitis with obstructive hydrocephalus and Figure 2 shows MRI of normal infant brain.

During the following days, signs of meningitis did not recur, but the head circumference showed a steady increase. On the 20th day, the infant showed loss of all activity; MRI scan revealed coning or herniation of the brain stem through the foramen magnum and an external ventricular tap was done immediately. The clinical report of the infant's condition

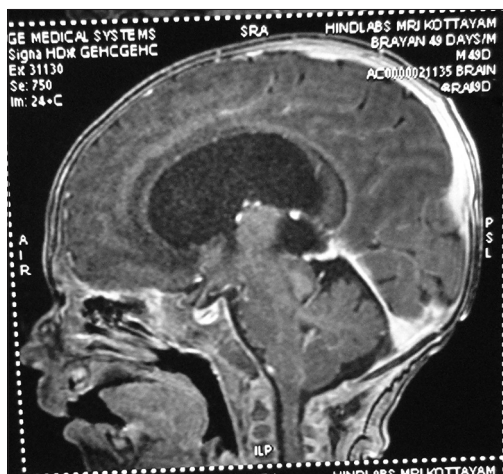


Figure 1: Magnetic resonance imaging of brain showing meningitis with obstructive hydrocephalus in 47-day-old infant with Methicillin-resistant *Staphylococcus aureus*

was discussed with neurosurgeons at Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, a super speciality centre for neurosciences under the Government of India. Following this, the infant was referred to a private hospital to be put under the care of a paediatric neurosurgeon. A week later, after CSF protein reduced to 80 mg/dl, he was continued on Linezolid, Amikacin and Metronidazole, and a ventriculoperitoneal shunt was inserted. He was discharged after 10 days with oral Linezolid and Metronidazole for three weeks. He had come for review and follow-up, and up to the sixth month, MRI was normal and no neurological sequelae have been reported so far.

Case 2

A one and a half-year-old male child was admitted with complaints of fever, cyanosis and clubbing. The child was a known case of double outlet right ventricle with pulmonary stenosis and atrial septal defect with ventricular septal defect. Five months ago, he developed left-sided hemiplegia due to middle cerebral artery infarction for which a bidirectional Glenn shunt had been inserted.

Two samples of blood were sent for automated blood culture. The first sample grew non-haemolytic colonies, 2 mm in diameter, convex, white and opaque on sheep blood agar and small lactose fermenting pink colonies on MacConkey agar. The isolate was positive for catalase and negative for slide and tube coagulase and resistant to Cefoxitin. It was identified as MRCoNS. It was resistant to Penicillin, Ampicillin and Cephalexin and sensitive to Vancomycin, Linezolid, Teicoplanin and Clindamycin. Blood culture of the second sample was sterile. However, IV Vancomycin 120 mg 6th hourly was started. The child showed left-sided weakness and cellulitis of the left foot. IV Amikacin 60 mg 12th hourly was added to the treatment regimen to be continued for six weeks.

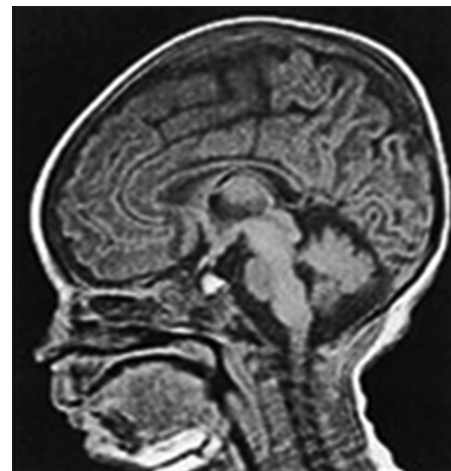


Figure 2: Magnetic resonance imaging of normal infant brains

Echocardiography done as part of evaluation revealed an echogenic freely mobile structure attached to the anterior mitral valve leaflet measuring 7 mm × 3 mm. The case was reviewed in cardiothoracic and vascular surgery department at the third subsequent week. The cellulitis subsided, the shunt was functioning well and the second set of follow-up blood cultures remained sterile.

Case 3

A 34-year-old male was admitted in the surgery department with complaints of pain in the right leg of one-day duration. He was a chronic smoker for the past 20 years and was advised amputation three months ago, but since he refused, an embolectomy was done, and he was put on warfarin. On the fifth day following admission, below knee amputation of the right leg was done for which he was administered IV Cefotaxime, Penicillin and Metronidazole as prophylaxis. On the fourth post-operative day, he complained of pain in the surgical site, discharge, and fever. A swab was sent to the microbiology laboratory, which yielded MRCoNS sensitive to Vancomycin and Linezolid. A repeat sample was requested for confirmation and MRCoNS isolated again. Based on the above report, all three antibiotics were stopped, and patient was put on oral Linezolid 600 mg twice daily along with surgical debridement of the wound. Patient responded well to the treatment and was discharged from the hospital after five days.

DISCUSSION

Penicillin-resistant *S. aureus* (PRSA) was present even before the introduction of Penicillin as stated by Alexander Fleming himself. In the 1940s, the prevalence of PRSA rose steadily throughout the world by 90% as the resistance is mediated by plasmids.^[1]

In the 1960s, following the introduction of beta-lactamase-resistant Penicillins such as Methicillin (Cloxacillin and Oxacillin), the prevalence of MRSA rose but only gradually to 40% as the resistance is chromosomally mediated.^[2] Methicillin resistance is encoded by *mecA* gene locus which is expressed as a unique penicillin binding protein (PBP) 2a. MRSA is presently classified as community acquired, hospital acquired and livestock acquired according to the review done by Hafsat *et al.*^[3]

The studies on *mecA* gene by Musseur and Archer in the 1990s suggest that MRSA arose by horizontal transfer of *mec*-encoding DNA between *S. aureus* and CoNS at some point(s) in the past.^[4-6] Studies by Wu *et al.*, Coutu *et al.* and Piras *et al.* reveal that MRSA PBP2a has a high degree of homology with PBP molecules of *Staphylococcus sciuri* and *Enterococcus hiriae*.^[7-9]

In the case of MRSA in the male infant, causing meningitis with hydrocephalus described here, MRSA caused bacteraemia in the infant resulting in the formation of two microabscesses (presumably due to MRSA) in the brain, the rupture of which resulted in meningitis and subsequent development of ventriculitis and hydrocephalus. Similar reports of bacteraemia and meningitis in preterm and term infants have been documented in other countries,^[10,11] and these are all associated with complications of the primary condition, prolonged hospital stay and increased expenditure. In the study by Joe Dylewski, the mother of the infant was a health-care worker and culture of her nasal swab yielded MRSA.

Huebner and Donald have done an annual review of cases presenting with native valve endocarditis, and their study concludes that CoNS are the most common cause of bacteraemia associated with an indwelling device and this is commensurate with the findings in the study by Mark and Gordon.^[12,13]

CONCLUSION

This case series demonstrates that the identification of MRSA and MRCoNS in the laboratory from CSF, blood culture and wound swab is important in prompt diagnosis of HAIs. MRSA has the potential to spread and the identification of MRSA from nasal swab of mothers who are health-care workers poses an additional risk of subsequent MRSA infection in their infants. These cases have responded successfully to treatment with IV Vancomycin and oral Linezolid.

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Conflicts of interest

There are no conflicts of interest.

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