

## CASE REPORT

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### PVL PRODUCING MRSA OSTEOMYELITIS IN NEONATE - A RARE PRESENTATION

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**ABSTRACT:** This is the first reported case of osteomyelitis caused by Panton-Valentine-Leucocidin (PVL) producing (MRSA) Methicillin Resistant Staphylococcus Aureus in a newborn. The presence of multiple abscesses, necrotizing fasciitis, severe leucopenia and thrombocytopenia should prompt one to consider PVL producing Community acquired-MRSA.

**CASE REPORT:** A term male baby was referred to us on Day 15 of life with complaints of 2 day history of fever, poor feeding, reduced urine output and painful swelling of the right leg. The baby had a birth weight of 2.7 kg was born to a primi gravid mother by emergency CS for reduced fetal movements. The antenatal period was normal. The baby was normal until 4<sup>th</sup> day of life when he developed poor feeding. He was treated with Cefotaxime and Gentamicin for 6 days and discharged. He remained well at home for 3 days after which he developed a second episode of poor feeding and activity for which he was referred.

On admission the baby appeared active, had painful restriction of movement and swelling of the right lower limb. There were petechial spots on the chest and abdomen. The HR was 126/min, RR was 68/min, and Spo<sub>2</sub> was 99% in 40% oxygen. He had subcostal recessions and grunting. Hepatomegaly of 3 cm and the spleen tip was palpable. A provisional diagnosis of septicemia with right thigh cellulitis and knee septic arthritis was made.

Hence the neonate was isolated and barrier nursed, commenced on ceftazidime, ampiclox and amikacin. The blood results showed a total count of 4, 100 cells /mm<sup>3</sup>, neutrophil count of 1100 cells/mm<sup>3</sup> and platelet count of 80, 000 cells/ mm<sup>3</sup>. The right lower limb X-ray showed diffuse soft tissue swelling of the right thigh with no bone or joint involvement.

Over the next 2 days he developed worsening hypotension, increasing respiratory distress, abdominal distension, renal failure and hyperkalemia. Multiple cutaneous nodules developed ranging from 0.5 to 1 cms suggestive of pyemic abscess. Fluids were restricted, inotropes escalated and hyperkalemia was managed with salbutamol nebulization and dextrose insulin infusion. On Day 3 following admission because of poor clinical response and thrombocytopenia of 11, 000cells/mm<sup>3</sup> the antibiotics were changed to vancomycin (15mg per kg q 8H) and meropenem (40mg per kg q8H). The same day a fluctuant and pointing abscess was noted above the right knee. Under local anesthesia, after platelet transfusion, 60ml of pus was drained from the suprapatellar fossa. New pyemic abscesses developed on the chest and lower limbs of which large ones were drained. A single volume exchange transfusion was done and intravenous immunoglobulin given. The baby's condition continued to deteriorate. He needed an escalation of inotrope support repeated platelet and packed cell transfusions.

In view of the poor response to antibiotics even after 72 hours, multiple pyemic abscesses and necrotizing nature of the illness, infection with PVL producing MRSA was suspected. Vancomycin was

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stopped, clindamycin (10mg per kg q 8H) and rifampicin (10mg per kg per day) was commenced. The blood and pus culture showed MRSA sensitive only to vancomycin, clindamycin, amikacin and gentamicin. Over the next 72 hours, the baby continued to improve as evidenced clinically and laboratory investigations. Inotropes were stopped and feeds commenced. Pus continued to be drained from the right thigh. A stock of the baby's blood culture for PVL strain typing by PCR was reported as positive. 15 days following admission X-ray showed a dislocated femoral epiphysis for which external fixation and K wire pinning was done. (Fig 1 and 2). The antibiotics were continued for 12 weeks. The external fixator was removed 30 days after application and the K wire 2 months later. On follow-up at one year of age, the child has a shorter right leg with pseudo-arthritis of the right femur for which further surgery has been planned. He has achieved age appropriate fine motor, social and adaptive milestones.

The pus swab of the Caesarean section wound of the mother which had not healed even after 3 weeks showed a heavy growth of MRSA with the same sensitivity as the baby's blood culture. Healing was achieved with rifampicin and amikacin. The nasal swabs of the other relatives did not show MRSA. Hence we suspected that the source of neonatal infection was presumably the mother.

Early isolation, barrier nursing and meticulous hand washing prevented spread in our NICU.

**DISCUSSION:** Septic arthritis and subcutaneous abscesses are relatively common problems in the newborn period. But the presence of septic arthritis and abscesses needing repeated and multiple surgical drainage procedures are uncommon which should prompt the clinician to consider PVL producing MRSA.

Community acquired MRSA commonly harbor the PVL toxin producing genes, Luk S and Luk F responsible for necrotizing fasciitis and abscesses<sup>1</sup>.

Panton-Valentine leukocidin (PVL) is a synergohymenotropic toxin, i.e., it acts through the synergistic activity of 2 non-associated secretory proteins, component S and component F<sup>2</sup>. The toxin first described by Panton and Valentine in 1932 activates human neutrophils before creating lytic pores, thereby damaging the cellular membrane<sup>3</sup>.

Infection with PVL-positive *S. aureus* most commonly causes necrotizing pyogenic skin infections, cellulitis, tissue necrosis<sup>4</sup>. It can also cause septic arthritis, osteomyelitis, pyomyositis, bacteremia, purpura fulminans and community-acquired necrotizing pneumonia.

PVL positive MRSA has been isolated from the pustules in healthy neonates<sup>5</sup>. Necrotizing pneumonia and outbreaks in neonatal intensive care units have been reported<sup>6,7</sup>. But there are no reported cases of neonatal osteomyelitis.

Appropriate clinical samples for culture and sensitivity should be sent. Incision and drainage is the optimal management for abscesses. This should be in conjunction with empirical parenteral antibiotics effective against MRSA together with immunoglobulin (IVIG).

The reason for unresponsiveness to vancomycin in this patient may be that though invitro sensitivity to vancomycin is seen, this drug is ineffective invivo. Our patient showed rapid clinical improvement only when clindamycin was instituted. The drugs of choice are clindamycin, linezolid and rifampicin. There is in-vitro synergy and linezolid and clindamycin can switch off toxin production<sup>8</sup>. The strain of MRSA isolated in this neonate and the mother was resistant to linezolid. Rifampicin has an excellent tissue penetration, reaching intracellular staphylococci, and exhibits synergistic activity. IVIG neutralizes exotoxins and superantigens<sup>9</sup>.

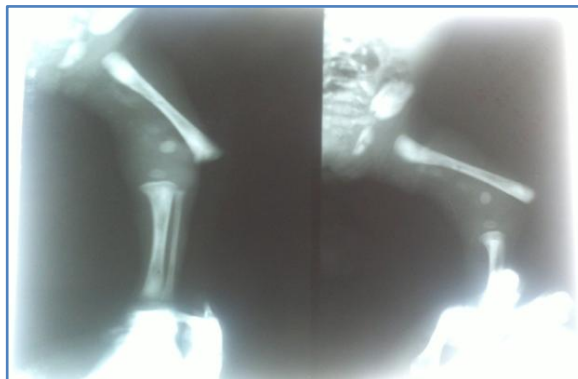
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Decolonization of neonates is difficult and unstandardized. Nasal mupirocin may be used. Screening must include a swab of the anterior nares, throat and any suspicious lesions, including damaged skin.

The diagnosis has also very important implications in terms of infection control in the NICUs. The suspected patient should be isolated, barrier nursed, meticulous screening of caregivers and the treatment of affected caregivers initiated to prevent an outbreak.

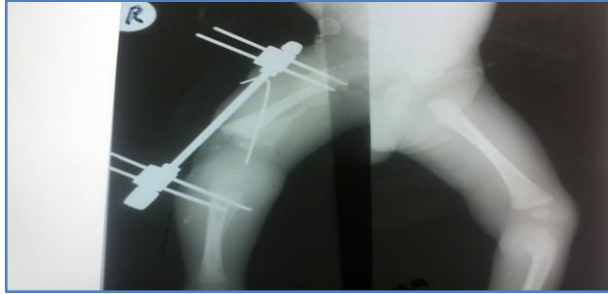
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**Fig. 1: Displaced lower femoral epiphysis**

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**Fig. 2: K wire pinning and external fixation of the displaced femoral epiphysis**

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