# Panton-Valentine leukocidin *Staphylococcus aureus* osteomyelitis of the femur in a Saudi child

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## ABSTRACT

تؤدي بكتيريا المكورات العنقودية البرتقالية المنتجة لليوكسيدين بانتون– فالانتين إلى التهابات في الجلد والأنسجة، إلا أنه لوحظ مؤخراً تسببها في حدوث التهابات مميته في العظام والعضلات. لقد قمنا سابقاً بنشر مقالة عن 3 أطفال مصابين بالمكورة العنقودية البرتقالية المقاومة للميثيسيلين. ونستعرض في هذا التقرير حالة طفل سعودي أُصيب بالتهاب شديد في عظم الفخذ بسبب هذه الجرثومة.

*Staphylococcus aureus* producing Panton-Valentine leukocidin (PVL) is well recognized to cause severe skin and soft tissue infections. Recently, it has been increasingly recognized as causing life-threatening musculoskeletal infection. We reported previously 3 children who had osteomyelitis caused by methicillin resistant *Staphylococcus aureus*. We report and discuss a case of *Methicillin sensitive staphylococcus aureus* encoding the PVL genes isolated from a child with acute osteomyelitis from Saudi Arabia.

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*Staphylococcus aureus* (*S. aureus*) is the major cause of acute hematogenous osteomyelitis in children. Multiple virulence factors have been identified as important to the pathogenesis of *S. aureus* infections. One such factor is Panton-Valentine leukocidin (PVL), a bicomponent cytotoxin that destroys leukocyte by pore-forming activity and is encoded by pvl genes, luk-S-PV and luk F-PV. The PVL genes are more common in community acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA)) than in community acquired methicillin-sensitive *Staphylococcus aureus* (CA-MSSA).[1] Musculoskeletal infections caused by (PVL) secreting *S. aureus* (CA-MRSA) in children have been previously reported.[2,3] It is increasingly recognized world-wide that PVL positive *S. aureus* is associated with a highly aggressive form of musculoskeletal infection.[4] Here, we investigate the case of a PVL secreting CA-MSSA musculoskeletal infection in a child in Saudi Arabia.

**Case Report.** A 9-month old girl presented to the pediatric emergency with history of a 2-day history of fever, vomiting, and swelling of left thigh one day after administering Measles, Mumps, Rubella ( MMR) vaccine in the same side. Examination on admission revealed sick looking, febrile child (temperature: 38.9°C). Her left leg had a huge swelling involving the entire left thigh with hotness, tenderness, and limitation of the hip and knee joints movement. The rest of the examination was normal. The white cell count (WCC) was 13.7 x $10^9$/L (Normal range: 6-18 $10^9$/L) and the erythrocyte sedimentation rate (ESR) was 117 mm/hour (Normal range: 8 mm/hour). X-ray of the femur bone was carried out and the finding was normal. Empirical antibiotics were started with ceftriaxone (75 mg/kg/day intravenously [IV] every 12 hours) and cloxacillin (150 mg/kg/day IV every 6 hours). Magnetic resonance imaging was carried out 4 days after admission and it revealed extensive involvement of the subcutaneous tissue with abscess formation and osteolytic lesions of the proximal and middle part of left femur and subtrochanter bone (**Figure 1**). The result of the echocardiogram was normal. As the pulse of the femoral artery was not felt, Doppler ultrasound was carried out and shows a left ileofemoral thrombosis. She started on Warfarin. Blood culture on admission grew *S. aureus,* which was highly sensitive to methicillin (MSSA). Accordingly, ceftriaxone was stopped and

clindamycin (40mg/kg/day IV every 8 hours) was added to cloxacillin. She was sick and continued to be febrile with high grade temperature that reached up to 39°C. Repeated blood culture after 48 hours of empiric treatment showed no growth. On day 6, after stabilization of her hemodynamic status and coagulation profile, she underwent surgical debridement of the infected tissue and drainage of the abscess. Pus from the thigh abscess grew MSSA. The fever and swelling decreased 2 days after the surgical intervention. Doppler ultrasound was repeated and revealed resolution of the deep vein thrombosis (DVT). Four days postoperatively, repeated femur x-ray showed periosteal reaction involving the whole femur (**Figure 2**). She required second surgical intervention and approximately 30-40 cc of pus was aspirated from the femur. Because of the severity of the infection, a high suspicion of MSSA carrying PVL gene was raised and the isolated organism was sent to King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia for PCR for PVL testing. The MSSA isolate was positive for both genes pvl (luk F) and pvl (luk S) (**Figure 3**). Immunological assays including Quantitative immunoglobulins, lymphocyte sub-types, and phagocytic function were requested and found to be normal. Eight days after the surgical debridement the swelling was decreased and the size was normal. Movement of the hip joint was improved. She was treated with another 4 weeks course of intravenous cloxacillin and clindamycin by the end of 2 months, she was discharged with a normal WBC and

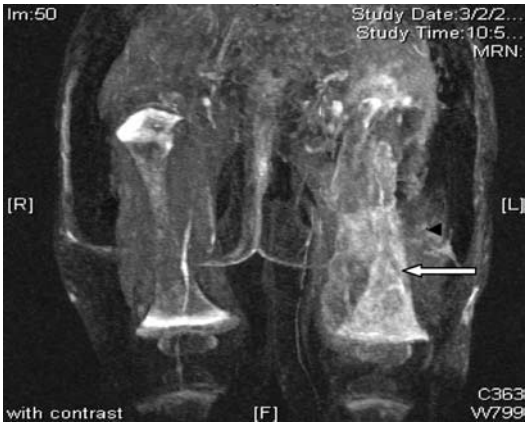


**Figure 1 -** Magnetic resonance Imaging (MRI) of both femur bone showing extensive involvement of the subcutaneous tissue with swelling and abscess formation (black arrow), and multiple osteolytic lesion of the proximalans middle part of left femur and subtrochanter bone (white arrow).

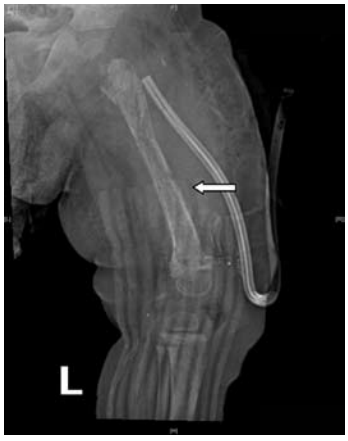


**Figure 2 -** X-ray of the left femur bone (7 days after surgical debridment) showing osteopenia of the left femur bone with osteolytic lesion and destruction of the proximal and middle part of the femur bone, drain is located near the proximal part of the femur bone within the subcutaneous tissue.

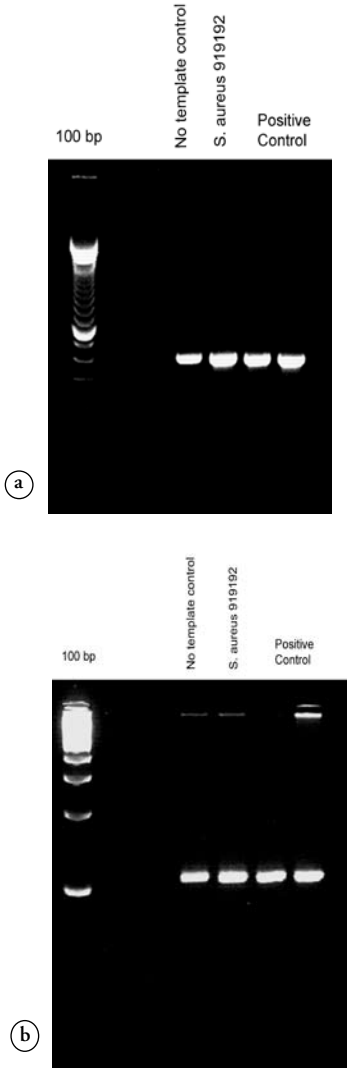


**Figure 3 -** Polymerase chain reaction test. *Staphylococcus aureus* was tested for pvl (lukF) and pvl (lukS). Our results show that this isolate is positive for both genes **a)** pvl (luk F) and **b)** pvl (luk S), PVL - Panton-Valentine leukocidin.

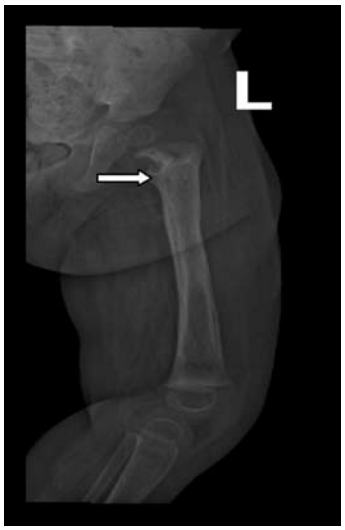


**Figure 4 -** X-ray of the left femur (after 6 month of treatment) showing evidence of healing of the osteolytic lesion of the proximal part of the femur with sclerosis of the neck of the femur.

ESR. Follow up appointment was given in the clinic after 2 weeks from discharge then after 4 weeks then every 2 month. During her follow up, she showed a remarkable improvement in her clinical condition and was able to walk normally without limping. Her x-ray (**Figure** 4) showed improvement with no evidence of chronic osteomyelitis apart from sclerosis of the neck of the femur.

**Discussion.** *Staphylococcus aureus* is the most common pathogen causing osteomyelitis, and MRSA is emerging as a new causative agent.[1,2] Although the spectrum of clinical infections caused by CA-MRSA is similar to that caused by MSSA, primarily skin and soft tissue infections, over the past decade CA-MRSA has been increasingly responsible for invasive infections among children, the most common of which was osteomyelitis. Community acquired methicillin-resistant *Staphylococcus aureus* and MSSA producing PVL as causative agents of osteomyelitis was first described by Dougkos et al.[3] Panton-Valentine leukocidin is a bacterial exotoxin produced by fewer than 2% of clinical isolates of *S. aureus* that leads to leukocytes destruction and tissue necrosis.[4] Its toxic effects results from synergistic action of 2 distinct exoproteins, coded for lukS-PV and lukF-PV genes carried on bacteriophages within the staphylococci. Panton-Valentine leukocidin *S. aureus* is associated with a highly aggressive and fatal infections.[4,5] This child is considered to be a severe and unusual case of osteomyelitis. Invasive infection is demonstrated by positive blood culture along with severe inflammatory response (including ESR and WCC) and extensive local disease seen on MRI requiring several surgical intervention. We believe that our *S. aureus* isolate is behaving aggressively because it encodes the PVL gene. Panton-Valentine Leukocidin has been found to be an associated factor that contribute to the severity of osteomyelitis caused by community acquired *S. aureus*. In a recent retrospective analysis[6] in children with musculoskeletal *S. aureus* infections, children with osteomyelitis caused by pvl+ *S. aureus* were more likely to have complications such as deep venous thrombosis or to develop chronic osteomyelitis than children with osteomyelitis caused by pvl-*S. aureus*. Positive PVL strains of *S. aureus* are associated with difficult treatment and require early MRI to demonstrate the extent of bony involvement.[7] In a study, conducted among children with community-acquired *S. aureus* osteomyelitis prospectively identified at Texas Children's Hospital between August 2001 and July 2004. Children with pvl+*S. aureus* isolates remained significantly ($p$=0.0004) more likely to have an *S. aureus*-positive blood culture (70% versus 12.5%), a more severe inflammatory response (including ESR, CRP level), and more extensive local disease (with more subperiosteal/intraosseal abscesses seen on MRI).[5] A global analysis of PVL positive MSSA showed that, the most predominant genetic background of PVL positive MSSA are pandemic and are phylogenetically related to CA-MRSA.[8]

In conclusion, this case describes a severe unusual presentation of a PVL secreting strain of *S. aureus*. Physicians particularly orthopedic surgeons are encouraged to request testing all *S. aureus* isolated from aggressive cases of osteomyelitis for PVL exotoxin. This will allow them to anticipate the need for early surgical intervention and management.

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## Related topics

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