

CASE REPORT

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Spontaneous tibiotalar arthrodesis as a complication of acute tibial osteomyelitis due to Panton-Valentine leukocidin-producing *Staphylococcus aureus*: a case report

Dimitri Ceroni^{1,2*}, Rebecca Anderson de la Llana¹, Tristan Zand³, Léopold Lamah¹, Denis Dominguez¹, Geraldo De Coulon¹ and Victor Dubois-Ferrière¹

Abstract

Introduction: Strains of Panton-Valentine leukocidin-producing *Staphylococcus aureus* producing a new pattern of disease have emerged worldwide. Infection with these bacteria typically presents as a life-threatening infection of soft tissues and bones, and may cause potentially devastating consequences.

Case presentation: We report a case of osteoarticular infection caused by Panton-Valentine leukocidin-producing *Staphylococcus aureus*. A 12-year-old Caucasian girl presented with acute osteomyelitis of the tibia associated with toxic shock syndrome, which was complicated by an unexpected spontaneous ankle arthrodesis.

Conclusions: Osteoarticular infections due to Panton-Valentine leukocidin-producing *Staphylococcus aureus* appear to be severe, and are characterized by their tendency to evolve towards serious complications. This case highlights the need for early and aggressive surgical procedures in conjunction with appropriate antimicrobial therapy and regular long-term follow-up.

Introduction

Panton-Valentine leukocidin (PVL) is a pore-forming toxin [1], secreted by 2% to 5% of *Staphylococcus aureus* strains. This exotoxin induces polymorphonuclear cell death via necrosis or apoptosis, and the subsequent release of leukocytic cytokines [2]. Induction of leukocyte apoptosis by *S. aureus* may cause extensive tissue necrosis and compromise the antimicrobial response, thereby facilitating bacterial spread [2]. The presence of PVL genes is associated with an increased risk of more severe systemic inflammation and serious infection requiring intensive care [3,4]. PVL-positive staphylococcal infections may lead to life-threatening infections of soft tissues, such as necrotizing hemorrhagic pneumonia,

associated with a high mortality rate [5-7]. Bone and joint infections with PVL-producing *S. aureus* (PVL + SA) are more aggressive, present a different evolution, and have a probably higher rate of orthopedic complications [8]. The purpose of this paper is to report an unusual and severe complication resulting from an osteoarticular infection of PVL + SA.

Case presentation

A previously healthy 12-year-old Caucasian girl was brought to the emergency department of our hospital complaining of a swollen left ankle and fever. She had a history of ankle trauma three days before. Her vital signs included a temperature of 40°C, a pulse rate of 132 beats/minute, a respiratory rate of 22 breaths/minute and blood pressure of 90/55 mmHg. Her left leg and ankle were diffusely tender. There was redness on her foot and the medial aspect of her leg. Laboratory results showed a white blood cell count of 21,000 cells/mm³, an elevated C-reactive protein (200 mg/dL; reference range:

* Correspondence: dimitri.ceroni@hcuge.ch

¹Pediatric Orthopedic Unit, University Hospital of Geneva, Geneva 14 CH-1211, Switzerland

²Department of Child and Adolescent, Service of Pediatric Orthopedics, University Hospitals of Geneva, 6, rue Willy Donzé, Geneva 14 1211, Switzerland

Full list of author information is available at the end of the article

0 to 10 mg/dL) and an abnormal erythrocyte sedimentation rate (78 mm/h).

Initial conventional X-rays were normal (Figure 1), but magnetic resonance imaging (MRI) demonstrated a large osteomyelitis of her left tibia with an increased signal intensity in its bone marrow, spreading up to her mid-tibia (Figures 2 and 3). The MRI of the tibia showed the presence of intramedullary abscesses and significant edema of the surrounding muscles (Figure 3). Our patient was taken to the operating theater, where she underwent multilevel surgery with pus drainage and extensive cleaning of the intramedullary cavity, using 12 liters of saline solution. An intravenous empiric antibiotic therapy was immediately started with flucloxacillin and gentamicin. Abscess cultures were positive for methicillin-sensitive *S. aureus*, and a polymerase chain reaction (PCR) was positive for PVL. Because our patient remained symptomatic, she had revision surgery under general anesthesia four times over a 17-day period. New recurrent abscesses were drained each time, and the tibial diaphysis was thoroughly washed using 12 liters of isotonic saline solution. After the fifth intervention, we finally obtained a resolution of local and biological signs of infection. Intravenous antibiotics were given for four weeks, followed by an oral antibiotic for another four weeks. Six weeks after the onset of the infection, we noted a severe restriction of the range of motion of her left ankle, and an X-ray showed an alteration of the tibiotalar joint line (Figure 4). Two months later, she had total fusion of the ankle, fortunately in a functional position (Figure 5).

Discussion

PVL is an exotoxin that induces cytotoxic and cytolytic changes in leukocytes. Complications of infections with PVL + SA include septic thrombosis, purpura fulminans and a redoubtable necrotizing pneumonia [9]. Clinical and biological signs of pulmonary disease are characterized by a combination of hemoptysis, multilobar alveolar infiltrations and leukopenia [9]. Severe pulmonary infection with PVL + SA has a mortality rate up to 75% despite intensive medical care [10]. In those cases, intensive care, antibiotics, aggressive surgical treatment and the additional application of immunoglobulins is the recommended treatment [9]. It is nevertheless important to keep in mind that the onset of necrotizing pneumonia may happen during the evolution of osteoarticular infection.

Interest in PVL + SA has progressively increased over the last years, probably due to the continuing improvement of PVL + SA detection methods with novel PCR assays. However, to date, only a few papers have focused specifically on the aspect of bone and joint infections [7-9,11-13]. The true incidence of osteoarticular infections caused by PVL + SA is unknown, probably because the number of infections due to this strain is underestimated. Ellington *et al.* found that only 1.6% of *S. aureus* from patients with bacteremia in the UK were PVL-positive [12]. In the USA, the PVL-positive methicillin-resistant *S. aureus* (MRSA) strain is responsible for 20% of bloodstream infections [8], and in Germany, PVL + SA became the second most frequent MRSA isolate [14]. In our department, we noted only two cases of osteoarticular infections due to PVL + SA.



Figure 1 Initial conventional X-ray of the affected tibia. Early frontal and lateral conventional X-rays only reveal discrete peritibial soft tissue infiltration.

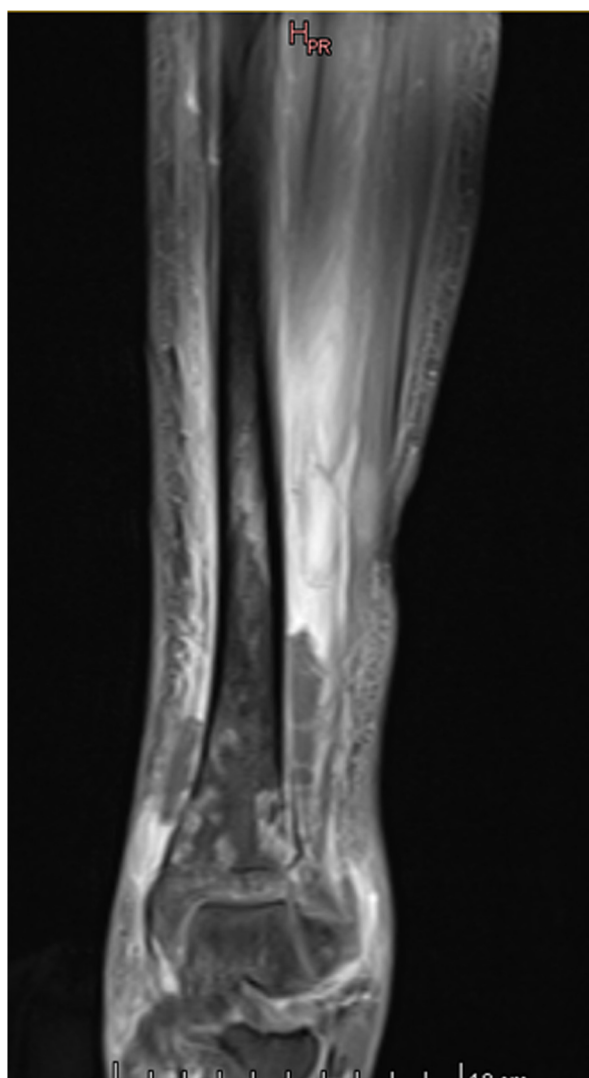


Figure 2 Initial magnetic resonance images of the affected tibia. Overall extension is best understood on magnetic resonance images with extensive heterogeneous medullar and pericortical enhancement on T1-weighted fat-suppressed coronal images.

From an orthopedic point of view, the emergence of osteoarticular infections due to PVL + SA has complicated the conventional management of these infections in children [15]. PVL + SA infections of bone and joints induce more often a concomitant myositis or pyomyositis than PVL negative SA infections [3]. Furthermore, the bone infections are more severe, presenting extended diaphysitis and bone abscesses, and causing more complications [8].

Therefore, osteoarticular infections due to such strains need longer antibiotic courses and various surgical procedures [8,15]. In children, orthopedic consequences may arise if the growth cartilage is involved, or if the articular cartilage is damaged by the infection; unfortunately the early diagnosis of these sequelae is often difficult.

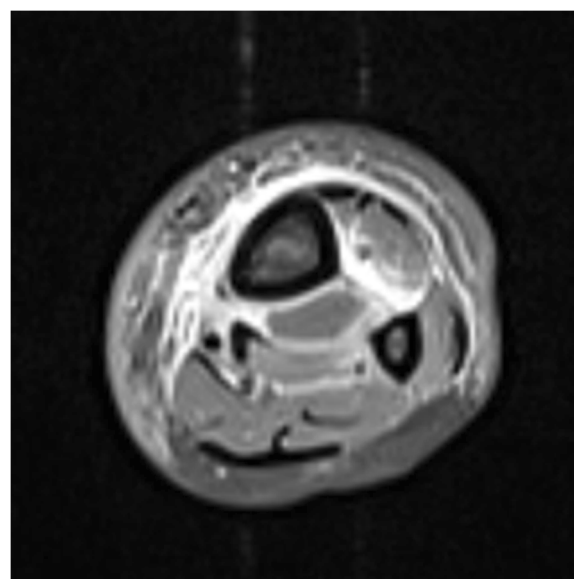


Figure 3 Initial magnetic resonance images of the affected tibia. The peripheral reactive effusion is explicit on liquid sensitive inversion-recovery T2-weighted axial images.



Figure 4 Conventional X-ray of the affected tibia 42 days after surgical drainage and the onset of antibiotic treatment. Frontal X-ray control after pharmacological and surgical treatment illustrates the diffuse bone remodeling and sclerosis. Major narrowing of the tibiotalar joint space illustrates the aggressiveness of the overall infectious process.



Figure 5 Late control X-rays of the affected tibia three and a half months after disease onset. Extensive bone remodeling consisted of cortical thickening, diffuse sclerosis, anatomical deformation and tibiotalar fusion.

In our case, our patient sustained an unusual complication because joint arthrodesis is not commonly encountered after PVL + SA infections. Nevertheless, the biological characteristics of PVL + SA may explain, from a theoretical point of view, the onset of spontaneous arthrodesis after an osteoarticular infection. In fact, PVL specifically interacts with and lyses polymorphonuclear leukocytes, and thus contributes to the inhibition of infection clearance by the host immune system, thereby enabling staphylococcal species to persist [16]. If the infection is not quickly cleared by the host, the potent activation of the immune response, in association with high levels of cytokines and reactive oxygen species, increase the release of host matrix metalloproteinases and other collagen-degrading enzymes, which in conjunction with bacterial toxins lead to joint destruction [17]. The polymorphonuclear response with subsequent release of these proteolytic enzymes can lead to permanent destruction of the intra-articular cartilage and subchondral bone loss in as little as three days [17]. In addition, metalloproteinases and the antigen-induced inflammatory response may persist and continue to damage the joint architecture even after the infection has been cleared [18-20].

Conclusions

PVL + SA seems to be an emerging and dangerous pathogen of osteoarticular infections in children. Its evolution is more aggressive, treatment more difficult, and complications more severe. Even if infections caused by PVL + SA are currently still uncommon, a PCR-based assay for toxin gene profiling should be performed in cases of severe and extended osteoarticular infections or when severe sepsis occurs. Orthopedic surgeons must be aware of the possible future changes in the evolution

and behavior of osteoarticular infections in children. There is probably a subtle balance between an effective immune response, which eliminates the infecting organism from the host, and the overactivation of this response that causes the majority of infection-related joint destruction. For this reason, it is now unanimously recognized that a surgical approach is mandatory for the management of PVL + SA osteoarticular infections, in conjunction with an appropriate antimicrobial therapy, and long-term follow-up of the affected children is necessary to recognize late-onset sequelae.

Consent

Written informed consent was obtained from the patient's legal guardian for publication of this manuscript and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

CD was the major contributor in writing the manuscript. AR drafted and critically revised the manuscript. TZ realized the interpretation of the radiological materials. LL drafted and critically revised the manuscript. DD operated on our patient and critically revised the manuscript. DCG operated on our patient and critically revised the manuscript. DFV contributed toward the study by preparing the photographs, by revising the manuscript and by performing the editorial work. All authors read and approved the final manuscript.

Author details

¹Pediatric Orthopedic Unit, University Hospital of Geneva, Geneva 14 CH-1211, Switzerland. ²Department of Child and Adolescent, Service of Pediatric Orthopedics, University Hospitals of Geneva, 6, rue Willy Donzé, Geneva 14 1211, Switzerland. ³Department of Radiology, University of Geneva Hospitals (HUG), Geneva 14 CH-1211, Switzerland.

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References

1. Pantan P, Valentine F: **Staphylococcal toxin**. *Lancet* 1932, **1**:506–508.
2. Genestier AL, Michallet MC, Prevost G, Bellot G, Chalabreysse L, Peyrol S, Thivolet F, Etienne J, Lina G, Vallette FM, Vandenesch F, Genestier L: **Staphylococcus aureus** Pantan-Valentine leukocidin directly targets mitochondria and induces Bax-independent apoptosis of human neutrophils. *J Clin Invest* 2005, **115**:3117–3127.
3. Bocchini CE, Hulten KG, Mason EO Jr, Gonzalez BE, Hammerman WA, Kaplan SL: **Panton-Valentine leukocidin genes are associated with enhanced inflammatory response and local disease in acute hematogenous Staphylococcus aureus osteomyelitis in children**. *Pediatrics* 2006, **117**:433–440.
4. Sdougkos G, Chini V, Papanastasiou DA, Christodoulou G, Tagaris G, Dimitracopoulos G, Spiliopoulou I: **Methicillin-resistant Staphylococcus aureus** producing Pantan-Valentine leukocidin as a cause of acute osteomyelitis in children. *Clin Microbiol Infect* 2007, **13**:651–654.
5. Gillet Y, Issartel B, Vanhems P, Fournet JC, Lina G, Bes M, Vandenesch F, Piémont Y, Brousse N, Floret D, Etienne J: **Association between Staphylococcus aureus** strains carrying gene for Pantan-Valentine leukocidin and highly lethal necrotising pneumonia in young immunocompetent patients. *Lancet* 2002, **359**:753–759.
6. Holmes A, Ganner M, McGuane S, Pitt TL, Cookson BD, Kearns AM: **Staphylococcus aureus** isolates carrying Pantan-Valentine leukocidin genes in England and Wales: frequency, characterization, and association with clinical disease. *J Clin Microbiol* 2005, **43**:2384–2390.
7. Lina G, Piémont Y, Godail-Gamot F, Bes M, Peter MO, Gauduchon V, Vandenesch F, Etienne J: **Involvement of Pantan-Valentine leukocidin-producing Staphylococcus aureus** in primary skin infections and pneumonia. *Clin Infect Dis* 1999, **29**:1128–1132.
8. Moumille K, Cadilhac C, Lina G, Berche P, Glorion C, Ferroni A: **Severe osteoarticular infection associated with Pantan-Valentine leukocidin-producing Staphylococcus aureus**. *Diagn Microbiol Infect Dis* 2006, **56**:95–97.
9. Mitchell PD, Hunt DM, Lyall H, Nolan M, Tudor-Williams G: **Panton-Valentine leukocidin-secreting Staphylococcus aureus** causing severe musculoskeletal sepsis in children. A new threat. *J Bone Joint Surg Br* 2007, **89**:1239–1242.
10. Salliot C, Zeller V, Puechal X, Manceron V, Sire S, Varache N, Etienne J, Desplaces N, Ziza JM: **Panton-Valentine leukocidin-producing Staphylococcus aureus** infections: report of 4 French cases. *Scand J Infect Dis* 2006, **38**:192–195.
11. Dohin B, Gillet Y, Kohler R, Lina G, Vandenesch F, Vanhems P, Floret D, Etienne J: **Pediatric bone and joint infections caused by Pantan-Valentine leukocidin-positive Staphylococcus aureus**. *Pediatr Infect Dis J* 2007, **26**:1042–1048.
12. Ellington MJ, Hope R, Ganner M, Ganner M, East C, Brick G, Kearns AM: **Is Pantan-Valentine leukocidin associated with the pathogenesis of Staphylococcus aureus** bacteraemia in the UK? *J Antimicrob Chemother* 2007, **60**:402–405.
13. van Duikeren E, Wolfhagen MJ, Heck ME, Wannet WJ: **Transmission of a Pantan-Valentine leukocidin-positive, methicillin-resistant Staphylococcus aureus** strain between humans and a dog. *J Clin Microbiol* 2005, **43**:6209–6211.
14. Witte W, Strommenger B, Cuny C, Heuck D, Nuebel U: **Methicillin-resistant Staphylococcus aureus** containing the Pantan-Valentine leukocidin gene in Germany in 2005 and 2006. *J Antimicrob Chemother* 2007, **60**:1258–1263.
15. Martinez-Aguilar G, Avalos-Mishaan A, Hulten K, Hammerman W, Mason EO Jr, Kaplan SL: **Community-acquired, methicillin-resistant and methicillin-susceptible Staphylococcus aureus** musculoskeletal infections in children. *Pediatr Infect Dis J* 2004, **23**:701–706.
16. Shirtliff ME, Mader JT: **Acute septic arthritis**. *Clin Microbiol Rev* 2002, **15**:527–544.
17. Roy S, Bhawan J: **Ultrastructure of articular cartilage in pyogenic arthritis**. *Arch Pathol* 1975, **99**:44–47.
18. Riegels-Nielsen P, Frimodt-Moller N, Sorensen M, Jensen JS: **Antibiotic treatment insufficient for established septic arthritis**. *Staphylococcus aureus* experiments in rabbits. *Acta Orthop Scand* 1989, **60**:113–115.

19. Smith RL, Schurman DJ: **Bacterial arthritis**. A staphylococcal proteoglycan-releasing factor. *Arthritis Rheum* 1986, **29**:1378–1386.
20. Smith RL, Schurman DJ, Kajiyama G, Mell M, Gilkerson E: **The effect of antibiotics on the destruction of cartilage in experimental infectious arthritis**. *J Bone Joint Surg Am* 1987, **69**:1063–1068.

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