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# Nosocomial Chronic Osteomyelitis of the Tibia in an Otherwise Healthy Adolescent: A Case Report

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## Learning Point of the Article:

Osteomyelitis may arise from nosocomial infections. Special attention should be paid to the presence of organisms uncommonly seen in community-acquired infections, particularly when detected after operative intervention.

## Abstract

**Introduction:** Pseudomonas osteomyelitis in otherwise healthy children is rare but may present following puncture wounds to the foot or involve the skull following mastoiditis. We present a case of nosocomial chronic osteomyelitis of the tibia caused by Pseudomonas in a previously healthy adolescent following surgical debridement of a non-pseudomonal chronic osteomyelitis in the same location 18 months prior. To our knowledge, such a case has not previously been described.

**Case Report:** A 17-year-old previously healthy young man presented with several month duration of pain in the right leg below the knee with no prior trauma, overlying a site of chronic, culture-negative osteomyelitis which was successfully treated with anti-staphylococcal therapy 1 year prior. Magnetic resonance imaging of the affected area revealed findings consistent with chronic osteomyelitis at his prior surgical site, while operative culture demonstrated growth of a multidrug-resistant Pseudomonas aeruginosa. An extensive immunological evaluation was unremarkable. He demonstrated clinical and radiographic improvement following 4 months of intravenous antimicrobial therapy.

**Conclusion:** Given the extreme rarity of P.aeruginosa in community-acquired osteoarticular infections, as well as the antimicrobial resistance profile demonstrated and the localization to a prior surgical site, this is felt to be the first description of a nosocomial osteoarticular infection with this organism in an otherwise healthy child. Providers should be aware of the potential for osteoarticular infection with atypical organisms in the post-operative patient.

**Keywords:** Chronic osteomyelitis, nosocomial, Pseudomonas.

## Introduction

Nosocomial osteomyelitis is uncommon in children, particularly nosocomial chronic osteomyelitis [1, 2]. Such infections are typically confined to post-operative infections following placement of orthopedic implants and often in children with numerous medical comorbidities [3]. Osteomyelitis associated with Pseudomonas aeruginosa is also rarely described in children and is most often reported following complications of localized infections with the organism, such as mastoiditis, or in post-traumatic or implant-associated infections [3, 4]. We describe the first case of a

nosocomial chronic osteomyelitis due to P.aeruginosa in an otherwise healthy adolescent.

## Case Report

A 16-year-old previously healthy young man presented to the Pediatric Infectious Disease Clinic in September of 2015 1 week after arriving in the United States from a refugee camp in Mozambique with a 3-month history of pain and swelling in the upper leg just below the knee. He had no fever noted, no erythema over the knee, and his symptoms had not changed

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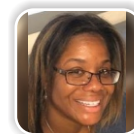
## Author's Photo Gallery



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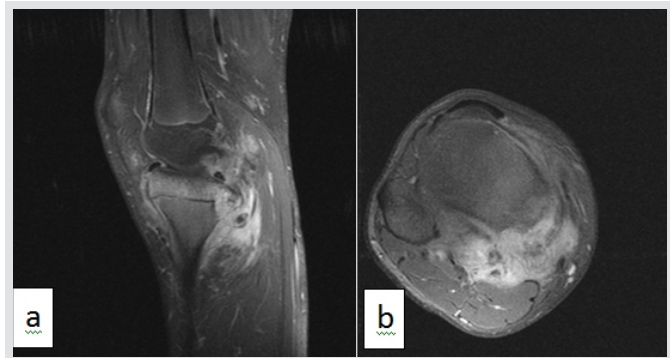


**Figure 1:** Anteroposterior radiograph of the right knee at the time of presentation (a) demonstrating heterotopic bone formation and increased density along the medial side of the proximal tibia indicative of osteomyelitis. Lateral radiograph of the right knee at the time of presentation (b) demonstrates increased density of the proximal tibia with a lucent area in the center consistent with osteomyelitis.

appreciably since arrival in the United States. He had not received any antimicrobial therapy for this condition. His erythrocyte sedimentation rate (ESR) at presentation was 40 mm/h with a C-reactive protein (CRP) level of 0.9 g/dL and a leukocyte count of 6,900 cells/ $\mu$ L (50% polymorphonuclear cells, 37% lymphocytes, 11% monocytes, 1% eosinophils, and 1% basophils). On examination, his affected knee was slightly swollen with mild tenderness over the medial aspect. No discharge or erythema was noted. His range of motion for his knee was slightly decreased for flexion and extension, and an antalgic gait was present. At that time, a plain radiograph demonstrated concerns of chronic osteomyelitis of the right proximal tibia although tumor or subacute fracture was also considered (Fig. 1). Contrasted magnetic resonance imaging (MRI) demonstrated findings consistent with chronic osteomyelitis along the medial aspect of the proximal tibial epiphysis and metaphysis, however, with a cloaca extending from a cortical disruption of the posteromedial tibial

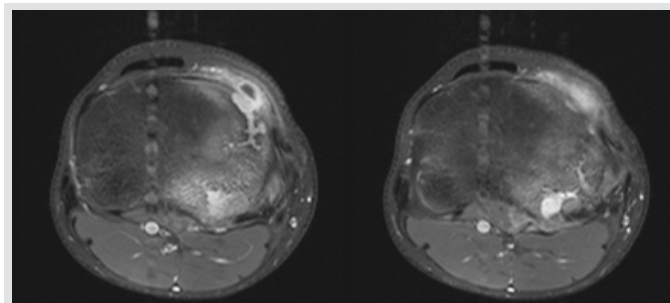


**Figure 3:** Anteroposterior radiograph of the right knee at the time of recurrence (a). There are 3 lucent areas on the medial side of the proximal tibia, and the physes are now closed, likely due to infectious involvement. Lateral radiograph of the right knee at the time of recurrence (b). One of the lucent areas can be seen in the posterior aspect of the proximal tibia, likely a nidus of infection. There is possible erosion through the posterior aspect of the tibia. No involucrum, sequestrum, or periosteal abnormalities were noted.



**Figure 2:** T2 sagittal magnetic resonance imaging (MRI) of the right knee at the time of presentation (a). Signal change posterior to the proximal tibia can be seen indicating the location of infection and surrounding inflammation. T2 axial MRI of the right knee at the time of presentation (b). The same signal change is seen posterior to the proximal tibia showing the location of the infection.

metaphyseal cortex (Fig. 2). Given a desire to pursue potential debridement and obtain cultures simultaneously, he underwent surgical debridement of the area the following day, cultures from which were sterile. Given his recent exposure to a refugee camp in Africa, the resulting potential for infection with an unusual organism was also felt to justify the need for an open biopsy with cultures. A cortical window was not created although extensive debridement of the area was performed. The joint space was not entered during the surgery. No orthopedic hardware or antimicrobial-impregnated beads were placed. Post-operatively, his wound healed well, with resolution of a serous drainage after several days. Given a non-reactive QuantiFERON gold assay for *Mycobacterium tuberculosis* and the frequency with which *Staphylococcus aureus* is implicated in osteoarticular infections in otherwise healthy children, we pursued empiric therapy for methicillin-susceptible *S. aureus* with nafcillin (chosen for its potent activity against this pathogen and ability to administer as a continuous infusion at home). He demonstrated marked improvement after completing 6 weeks of parenteral therapy, and his ESR and CRP normalized approximately 8 weeks into treatment. Per our local practice guidelines, he completed 6 months of total therapy with cephalexin in April of 2016. Given involvement of the growth plate with his infection, follow-up imaging was obtained



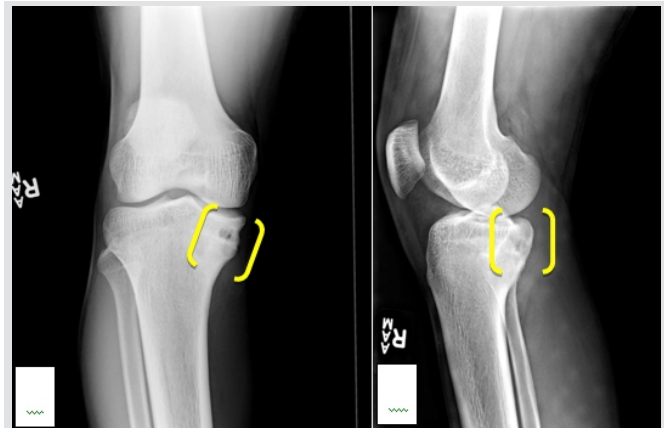
**Figure 4:** T2 axial magnetic resonance imaging (MRI) of the right knee at the time of recurrence. These axial images demonstrate recurrent infection posterior as well as new signs of infection anterior on the proximal tibia. There is edema that can be seen posteriorly as well as a fluid collection posteromedial. The MRI further demonstrates likely erosion through the posteromedial proximal tibial cortex with some signal change subperiosteal. No signal change within the medial head of the gastrocnemius. The neurovascular structures are not involved.



**Figure 5:** T2 coronal magnetic resonance imaging of the right knee at the time of recurrence. There is signal change throughout the proximal tibia and likely a collection of infection on the medial aspect of the proximal tibia (seen as a white fluid collection, marked by arrow).

10 months post-operatively, which revealed a 1.3 cm leg length discrepancy (right leg shorter than his left). He was seen again in the infectious disease clinic 3 months after antibiotic completion and was back to his normal baseline, with plain radiographs demonstrating no concerns of recrudescence disease. A follow-up MRI was not obtained. He played a season of varsity soccer for his local high school that fall without incident.

In April of 2017, approximately 1 year after completing therapy, he was seen in the infectious disease clinic again. At that time, the patient reported a 7-day history of pain, redness, and swelling along the inner aspect of the right upper leg below his knee overlying his prior surgical site. However, his father reported that he had complained of these findings for several months. A firm, tender erythematous mass over the medial aspect of the proximal tibia was noted on examination, underlying his surgical scar, although no drainage was present and the range of motion of his knee was normal. He had been a febrile and denied any recent trauma to the area. His ESR and CRP were normal at this time, as was his total leukocyte count and his differential leukocyte count. Plain radiographs demonstrated concern of recrudescence chronic osteomyelitis in the proximal tibia, with worsening sclerotic changes compared with his most recent radiograph (Fig. 3). A contrasted MRI demonstrated abnormal signal intensity in the proximal tibial metaphysis and epiphysis, with an abscess connected to a nidus of presumed chronic osteomyelitis through a fistula tract running inferior to the physis (Fig. 4 and 5). He was taken to the operating room shortly after this, where an abscess eroding through to the posterior aspect of the proximal tibia was noted.



**Figure 6:** Final anteroposterior radiograph of the right knee taken 3 months after surgery (a) showing no signs of recurrence, closed physes, and the empty area of resected infected bone. Final lateral radiograph of the right knee (b) showing no signs of recurrence, closed physes, and the empty area of resected infected bone (in brackets).

The superficial portion of the abscess was drained, with drilling through the affected bone into the posterior aspect of the tibia followed by curettage of the entire area. A cortical window was not created nor was periosteal elevation noted. His post-operative wound healing was uneventful. Operative cultures produced monomicrobial growth of *P.aeruginosa*, which, given the heavy growth in the primary streaks on the agar plate, was not felt to be a contaminant. This isolate demonstrated intermediate resistance to piperacillin-tazobactam (minimum inhibitory concentration (MIC)=32/4 mg/L), resistance to gentamicin (MIC>2 mg/L), aztreonam (MIC>16 mg/L), and ciprofloxacin (MIC>2 mg/L). The isolate was susceptible to meropenem (MIC of 1 mg/L), ceftazidime (MIC of 8 mg/L), ceftolozane and tazobactam (MIC=1.5 mg/L), and ceftazidime (MIC of 4 mg/L). Ceftazidime and ceftazidime MICs were confirmed with E-testing. No improvement was seen after 72 h of empiric cefazolin, but he did improve following transition to meropenem. Immunological evaluation revealed normal levels of natural killer cells, immunoglobulins (IgG, IgA, IgM, and IgE), tetanus, and pneumococcal antibodies. A lymphocyte subset panel was normal. He also demonstrated a normal lymphocyte proliferation response to phytohemagglutinin and pokeweed mitogen and a non-reactive serology to human immunodeficiency virus. Given the absence of an oral treatment option, he was treated initially with several days of ceftazidime, followed by 49 days of meropenem. He was then transitioned back to ceftazidime for 14 days followed by 56 days of ceftazidime. A contrasted MRI performed 7 weeks and plain radiographs performed 3 months into treatment demonstrated no recrudescence of disease (Fig. 6). He maintained normal inflammatory markers during treatment. At the end of 4 months of therapy, his physical examination was normal and his antibiotic therapy was discontinued. He denied any persistent symptomatology and was participating in soccer again without difficulty.

## Discussion

*Pseudomonas* osteomyelitis is rare in otherwise healthy children but may arise as a result of breaches in bone integrity or overlying soft tissues in contact with moist, colonized skin (e.g., osteomyelitis of the skull arising from mastoiditis or osteomyelitis in the bones of the foot secondary to adjacent puncture wounds) [4, 5]. However, isolated cases from other locations have rarely been reported in otherwise healthy children. Hatakenaka described a 15-month-old previously healthy boy with septic arthritis of the elbow and acute osteomyelitis of the capitellum due to *P. aeruginosa* following trauma [6]. Narang reported a 13-year-old previously healthy girl with chronic *Pseudomonas* osteomyelitis of the talus in the absence of reported trauma, while Yousef described chronic osteomyelitis of the clavicle in an otherwise healthy child [7, 8]. *Pseudomonas* will also occasionally be reported in large case series of pediatric osteomyelitis, usually comprising a very small percentage of the total pathogen burden and without accompanying descriptive clinical data [9]. Although reports of nosocomial osteoarticular infections may be increasing, *Pseudomonas* is rarely reported and almost exclusively follows placement of orthopedic implants [1, 2, 3]. To our knowledge, this is the first case thought to have arisen from a nosocomial infection in an otherwise healthy child with no orthopedic implants. Approximately 1 year after completing therapy for his first episode of chronic osteomyelitis, our patient presented with recrudescence signs and symptoms in the same location as his prior chronic osteomyelitis. Given the good clinical response seen with nafcillin and cephalexin during treatment for his first episode of osteomyelitis, it is unlikely that this initial infection was due to *Pseudomonas*. The heavy monomicrobial growth seen in the primary streaks on his operative culture, as well as the lack of clinical response seen with his initial empiric cefazolin argue against the organism acting as a contaminant. The results of his immunological evaluation as well as his otherwise good health before his osteomyelitis argue against the infection arising as a result of an occult immunodeficiency. The multidrug resistance profile of the organism was also more in keeping with a nosocomial source [10]. Finally, the recurrence at his prior surgical site also argued for a role as a nosocomial pathogen. The timing of the infection is unclear; however, it may have been introduced at the time of his initial surgery, lying quiescent as an indolent infection that ultimately became symptomatic. However, he presented with his second episode of osteomyelitis nearly 18 months after this operation. Chronic osteomyelitis with prolonged and indolent courses due to *Pseudomonas* has been described although not with latency periods of 18 months [7, 8]. However, the exact timing of his

illness was unclear, as his father stated that he had been symptomatic for several months at the time of presentation, which contrasted with what was reported by the patient. Hence, the latency period may actually have been in a more typical range for such an infection. Alternatively, the organism may have colonized his skin following his hospitalization and gained access to the operative site through minor cutaneous trauma and/or transient bacteremia sometime following discharge. With either scenario, the organism most likely arose from a nosocomial source.

The absence of an oral option for therapy also complicated his treatment and required the use of a prolonged parenteral regimen. Although an increasing number of multidrug-resistant Gram-negative organisms are appreciated in community-acquired infections in children, such infections are still generally unexpected [11]. The presence of resistance to aminoglycosides, fluoroquinolones, and piperacillin-tazobactam is unusual in a community-acquired isolate and is more often seen in hospital (particularly intensive care) settings, likely due to the accumulation of multiple different resistance mechanisms over time [12]. Based on antimicrobial susceptibility testing data from our children's hospital for the year 2015, when the patient initially presented for care, 2.9% of all pseudomonal isolates were resistant to gentamicin, 11.4% were resistant to ciprofloxacin, and 14.3% were resistant to piperacillin-tazobactam. Of note, he did not spend any time in the intensive care unit during either of his admissions. Concern did exist regarding the potential for his pseudomonal isolate to develop resistance while on therapy, given the high MICs demonstrated for many of the antimicrobial agents (particularly cefepime), the potential for suboptimal concentrations of antibiotic in the bone, and the proclivity of *Pseudomonas* to develop resistance while on prolonged therapy [13]. This in part led to our decision to rotate his antibiotics, as well as a desire to avoid prolonged therapy with the broad coverage provided by meropenem, with its attendant risk of adverse effects. However, he demonstrated consistent clinical and radiographic improvement while on therapy. Given the difficulty treating such infections, however, a focus should be kept on prevention. Appropriate antimicrobial stewardship interventions in hospitals are imperative to decrease the burden of such multidrug-resistant organisms in the inpatient setting, as is meticulous attention to sterile technique intraoperatively and wound care post-operatively.

## Conclusion

We believe that this is the first case of a nosocomial osteomyelitis in an otherwise healthy child due to *P. aeruginosa* in the literature. Although rare, when faced with children

presenting with concerns of recrudescence or recurrent osteomyelitis, clinicians should consider the possibility of nosocomial infections with multidrug-resistant organisms acquired while hospitalized.

### Clinical Message

Although rare, recurrent osteomyelitis at the previous site of disease should raise a suspicion of a nosocomial infection. As such, culture of the affected area is imperative to help identify and guide treatment of potentially multidrug-resistant organisms.

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