



Inflammatory markers limitations in the diagnosis of pediatric calcaneal osteomyelitis [☆]

Jared Ingersoll MS4, ENS, MC, USN ^{a,*}, Megan Halliday MD, LT, MC, USN ^b,
Daniel J. Adams MD, Maj, MC, USAF ^b, Jonathan D. Auten DO, CDR, MC, USN ^c,
Daphne Morrison Ponce MD, LCDR, MC, USN ^d

^a Uniformed Services University School of Medicine, Bethesda, MD, United States of America

^b Naval Medical Center Portsmouth, Portsmouth, VA, United States of America

^c Naval Medical Center San Diego, San Diego, CA, United States of America

^d Department of Emergency Medicine, University of Michigan, Ann Arbor, MI, United States of America

ARTICLE INFO

Article history:

Received 16 August 2019

Received in revised form 22 August 2019

Accepted 24 August 2019

Keywords:

Osteomyelitis

Pediatric

Calcaneus

Inflammatory markers

Kingella kingae

ABSTRACT

Calcaneal osteomyelitis is an uncommon, but clinically important emergent condition in the differential of the limping child. Early recognition is paramount to prevent complications from delayed diagnosis like formation of periosteal abscesses or growth plate injury. The diagnosis of pediatric osteoarticular infection relies on a combination of clinical exam, imaging and inflammatory markers. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) have reported sensitivities for osteomyelitis of 94% and 95%, respectively. However, clinicians should be aware that certain clinical factors can decrease the reliability of inflammatory markers in this pediatric condition. Location of infection in small bones like the calcaneus can lead to significantly lower sensitivities than in long bones. Pretreatment with antibiotics prior presentation can also decrease the reliability of ESR and CRP. In this case, we highlight two unique clinical factors that diminish the sensitivity of commonly used inflammatory markers in the diagnosis of pediatric osteomyelitis.

Published by Elsevier Inc.

1. Introduction

Osteomyelitis is a relatively common infection in the pediatric population, with an incidence up to 13 per 100,000 children in developed countries [1]. Although osteomyelitis is a disease most commonly affecting long bones, calcaneal infections make up approximately 8% of pediatric infections [2]. *Kingella kingae*, a microbe found in the flora of the oropharynx, has recently been identified as an increasingly prevalent pathogen in pediatric osteoarticular infections [3,4]. The diagnosis of *K. kingae* osteoarticular infections in children is often delayed, with an average of 5 to 21 days from symptom onset until diagnosis [5]. Traditionally, inflammatory markers such as ESR and CRP are thought to be reliable screening markers for osteomyelitis, given their high sensitivity. The sensitivity of these laboratory values, however, can be significantly decreased in osteoarticular infections of small bones

like the calcaneus. This case illustrates the indolent nature of *K. kingae* osteomyelitis, the difficulty of establishing an early diagnosis, and the limitations of inflammatory markers.

2. Case report

A 12-month-old male presented to the emergency department with his mother for right heel pain and limping for 10 days. Nine days prior, the patient was diagnosed with cellulitis and started on oral clindamycin and ibuprofen. Since that time, the patient's pain and limping worsened. The patient's mother denied any recent trauma or puncture wounds. She endorsed the child had a fever 2 weeks prior that was treated with acetaminophen. On day of presentation, the patient had symptoms of an upper respiratory infection (URI). He had met appropriate developmental milestones and was up to date with recommended vaccinations.

On exam, vitals were within normal limits. He was alert and in no distress. Musculoskeletal exam revealed exquisite tenderness on compression of the right heel, without overlying erythema, warmth, or edema. Labs showed WBC $6.1 \times 10^3/L$, ESR 5 mm/h and CRP <5 mg/L. A right foot radiograph was read as normal

[☆] The authors have no financial or industry affiliations.

* Corresponding author at: Uniformed Services University, 4301 Jones Bridge Road, Bethesda, MD 20814, United States of America.

E-mail address: jared.ingersoll@usuhhs.edu (J. Ingersoll).

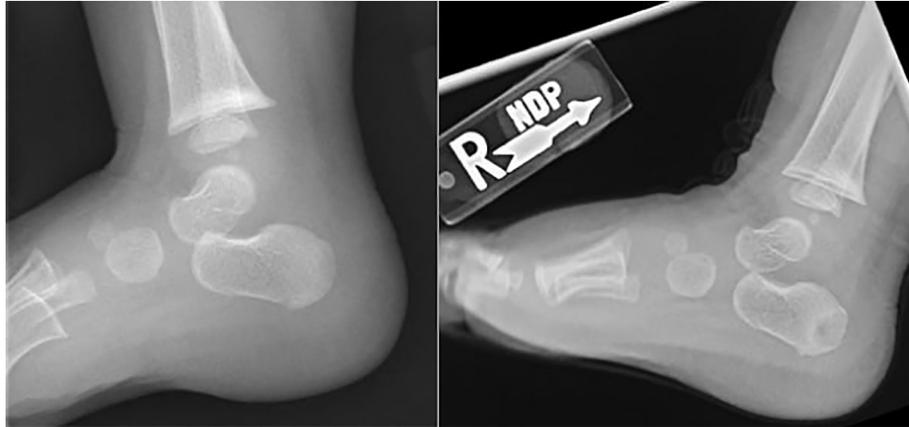


Image 1. Radiograph on day of ED presentation (left) and radiograph on day 22 after surgical debridement (right).

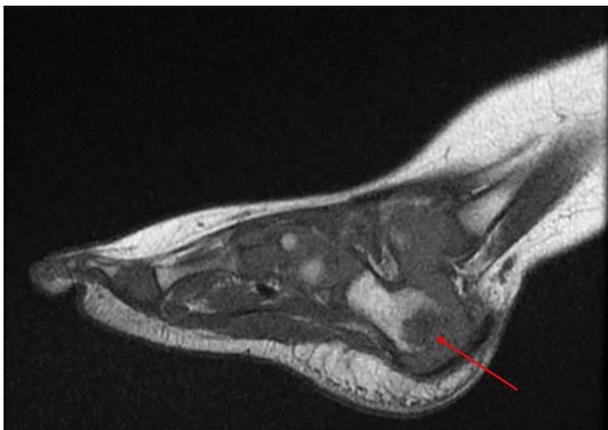


Image 2. T1 weighted MRI of the right foot with hypointense signal in the posterior calcaneus.

(Image 1). The patient was started on empiric intravenous cefazolin and admitted to the hospital for MRI of the right foot, given the concerning physical exam findings. Magnetic Resonance Imaging (MRI) showed a hypointense signal on T1 weighted imaging within the calcaneus, consistent with osteomyelitis (Image 2). *Kingella kingae* grew from intraoperative bone culture. The patient was treated with IV cefazolin and washed out by orthopedics in the operating room. He was subsequently transitioned to oral amoxicillin and sent home. His limp resolved in a few weeks after discharge and he has had no known complications one year after discharge.

3. Discussion

The most common presenting complaint of calcaneal osteomyelitis is a painful foot with a limp, progressing in severity to avoidance of walking [6]. These patients are often not ill-appearing and may only present with vague URI or diarrheal illnesses. Similar to our patient, only 22% of pediatric patients with calcaneal osteomyelitis present with a fever $>38^{\circ}\text{C}$ [3]. There is rarely a history of preceding fall or injury, suggesting hematogenous spread as the most likely source of infection [3,4]. Inflammatory markers such as ESR and CRP have been shown to be highly sensitive laboratory findings in pediatric osteoarticular infections. In one large study, ESR and CRP were found to be elevated in 94% and 95% of patients, respectively. When used together within the first 3 days of infection, 98% of patients had at least one marker

elevated [7]. ESR peaks at 3 days and remains elevated for up to 3 weeks, while CRP peaks at 2 days and returns to normal at one week [7-9]. In contrast, WBC count has been shown to be elevated in only a minority of patients with active infection [8,10]. Despite the reported utility of ESR and CRP, there are important limitations to consider in pediatric osteoarticular infections. The sensitivities of these inflammatory markers decrease in smaller bone infections like calcaneal osteomyelitis with reported sensitivities between 81 and 95% and 47–77% respectively [3,6,11]. Calcaneal osteomyelitis due to *K. kingae* has been shown to independently lead to lower CRP sensitivity [5]. Children being treated with antibiotics prior to presentation can also decrease inflammatory marker levels (10). This is pertinent as our patient had been on a course of clindamycin for over one week prior to presentation. Despite the limitations of inflammatory markers in this case, MRI was able to establish the diagnosis. MRI has been noted to be 100% diagnostic in comparison to X-rays, which were between 14%–71.4% diagnostic [12].

4. Conclusion

This case highlights that prior antibiotic use and small bone location can diminish inflammatory marker sensitivity in the evaluation of pediatric osteoarticular infections. Despite normal ESR and CRP levels, a high clinical index of suspicion based on history and physical exam led to definitive imaging. MRI serves as a highly sensitive imaging modality for osteoarticular infections in scenarios where diagnostic uncertainty exists.

Disclaimers

The views expressed in this case report are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.

We are military service members. This work was prepared as part of our official duties. Title 17 U.S.C. 105 provides that “Copyright protection under this title is not available for any work of the United States Government.” Title 17 U.S.C. 101 defines a United States Government work as a work prepared by a military service member or employee of the United States Government as part of that person’s official duties.

References

- [1] Dartnell J1, Ramachandran M, Katchburian M. Haematogenous acute and subacute paediatric osteomyelitis: a systematic review of the literature. J Bone

- Joint Surg Br 2012;94(5):584–95. <https://doi.org/10.1302/0301-620X.94B5.28523>. May.
- [2] LaMont RL, Anderson MD, Dajani AS, et al. Acute hematogenous osteomyelitis in children. *J Paediatr Orthop* 1987;7:579–83.
- [3] Leigh W, Crawford H, Street M, Huang M, Manners S, Puna R. Pediatric calcaneal osteomyelitis. *J Pediatr Orthop* 2010;30(8):888–92. Dec.
- [4] Arnold JC, Bradley JS. Osteoarticular infections in children. *Infect Dis Clin North Am* 2015;29(3):557–74. Sep.
- [5] Mallet C, Ceroni D, Litzelmann E, Dubois-Ferriere V, Lorrot M, Bonacorsi S, et al. Unusually severe cases of *Kingella kingae* osteoarticular infections in children. *Clin Pediatr (Phila)* 2016;55(14):1328–37. Dec.
- [6] Puffinbarger WR, Gruel CR, Herndon WA, Sullivan JA. Osteomyelitis of the calcaneus in children. *J Pediatr Orthop* 1996;16(2):224–30. Mar-Apr.
- [7] Pääkkönen M, Kallio MJ, Kallio PE, Peltola H. C-reactive protein versus erythrocyte sedimentation rate, white blood cell count and alkaline phosphatase in diagnosing bacteraemia in bone and joint infections. *J Paediatr Child Health* 2013;49(3):E189–92. Mar.
- [8] Pääkkönen M, Kallio MJ, Kallio PE, Peltola H. Sensitivity of erythrocyte sedimentation rate and C-reactive protein in childhood bone and joint infections. *Clin Orthop Relat Res* 2010;468:861–6.
- [9] Unkila-Kallio L1, Kallio MJ, Peltola H. The usefulness of C-reactive protein levels in the identification of concurrent septic arthritis in children who have acute hematogenous osteomyelitis. A comparison with the usefulness of the erythrocyte sedimentation rate and the white blood-cell count. *J Bone Joint Surg Am.* 1994 Jun;76(6):848–53.
- [10] Unkila-Kallio L, Kallio MJ, Eskola J, Peltola H. Serum C-reactive protein, erythrocyte sedimentation rate, and white blood cell count in acute hematogenous osteomyelitis of children. *Pediatrics* 1994;93(1):59–62. Jan.
- [11] Jaakkola J, Kehl D. Hematogenous calcaneal osteomyelitis in children. *J Pediatr Orthop* 1999;19(6):699–704. Nov-Dec.
- [12] Mooney ML, Haidet K, Liu J, Ebraheim NA. Hematogenous calcaneal osteomyelitis in children. *Foot Ankle Spec* 2017;10(1):63–8. Feb.