Case Reports and Series

Delayed diagnosis and treatment of pediatric calcaneal acute hematogenous osteomyelitis: A case report

Nicole A Bauerly, DPM, FACFAS1, Kimberly L Bobbitt, DPM, FACFAS1, Stephanie P Kvas, DPM, AACFAS2, S.P. Kvas, DPM, AACFAS1, Michelle Winder, DPM, AACFAS1

1 Hennepin Healthcare, Minneapolis, MN, USA
2 Mayo Clinic Health System, 301 2nd St NE New Prague, MN 56071 USA

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Introduction

Pediatric calcaneal acute hematogenous osteomyelitis (AHO) is a rare condition with a reported annual incidence of 2-13 children per 100,000 in well developed countries. Hematogenous spread during an episode of bacteremia is the most common etiology for osteomyelitis in pediatric patients. This condition most often affects young males between the ages of 2-9.1,2,3,4 Pediatric calcaneal AHO has a high incidence of misdiagnosis attributable to nonspecific symptoms that mimic more common, benign calcaneal pathology. This delay in diagnosis can result in devastating complications. Diagnosis is based on history, clinical examination, laboratory values and imaging studies. Once confirmed, treatment should commence immediately and varies depending on severity.

We present a case report of a severely progressive calcaneal AHO in a 12-year old African American male, previously misdiagnosed twice at other facilities. Treatment consisted of a 45 day course of IV nafcillin, 20 HBOT sessions and 8 serial operative debridements involving calcaneal biopsies, placement of antibiotic beads and spacers and eventual filling of calcaneal wall defect with ProDense™ bone filler. This case is unique considering the patient’s slightly older than average age, as well as the 63 day time lapse between initial onset of symptoms and diagnosis of AHO, is what makes this case report stand out from previous. To our knowledge, this is the longest reported delay in diagnosis and treatment of pediatric calcaneal AHO to date.

A 12-year old otherwise healthy African American male, accompanied by his mother, presented to our emergency department on August 12th, 2018 for evaluation of worsening left heel pain with two associated posterolateral draining sinuses (Fig. 1A and 1B). Further history revealed the initial onset of symptoms occurred 63 days prior when the patient experienced heel pain after striking his heel on a hard object. Five days after initial symptom onset, the patient was evaluated at an unaffiliated emergency department for left heel pain. During this visit, he was febrile to 38.5°C and tachycardic to 109 beats per minute. Both patient and guardian denied any history of recent illness. Physical examination was unremarkable except for localized warmth, tenderness to palpation, erythema and palpable pulsation in the posterior calcaneal region. No lymphadenopathy was noted.

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documented as unremarkable with the exception of moderate pinpoint tenderness to the medial and plantar calcaneus and slight localized edema and ecchymosis. Left foot radiographs were obtained and read as negative for any acute osseous pathology. The patient was again diagnosed with a deep heel contusion and discharged to home with previous instructions and crutches as needed.

Sixty-three days after initial onset of symptoms, the patient arrived to our emergency department with symptoms mentioned previously. Clinical examination revealed a healthy appearing 12-year old male in no acute distress with stable vital signs. His lower extremity examination revealed two posterolateral draining sinuses overlying the posterior calcaneus, measuring 1.0 cm x 1.0 cm and 0.5 cm x 0.5 cm. Both wounds were actively draining serous and purulent discharge. Edema and ecchymosis were noted to the medial plantar arch. Significant palpatory tenderness was present to the left medial plantar arch and posterior and inferior heel. Neurovascular status was intact to the left foot. Plain radiographs were obtained and revealed significant lucency within the calcaneus and erosion of the plantar tubercle with high suspicion for intraosseous abscess (Fig. 2A and 2B). Laboratory tests revealed a white blood cell (WBC) count of 8.15 and an elevated c-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) of 13.6 and 46, respectively.

The patient was diagnosed with calcaneal osteomyelitis based on physical examination, radiographic findings and elevated inflammatory markers. He was admitted to the pediatric service with Podiatric Surgery, Infectious Disease and Hyperbaric Medicine consulting. An MRI of the left foot with and without contrast was obtained upon admission with evidence of extensive calcaneal osteomyelitis with serpiginous intraosseous abscess formation (Fig 3A-D). He was immediately scheduled for incision and drainage (I&D) of the left foot with intra-operative bone biopsy the following morning. Antibiotic therapy was delayed until bone biopsy was obtained, per Infectious Disease recommendations. After consultation with Hyperbaric Medicine, the patient was deemed appropriate for HBOT with a planned course of 20 daily hyperbaric oxygen treatments at maximum pressure of 2.4 atmospheres (ATA) for a total time of 115 minutes per session.

The following morning, the patient was taken to the operating room for debridement. He was placed on the operating table in the supine position, general anesthesia was administered and an ankle block was performed with 2.0% plain lidocaine. A thigh tourniquet was placed; however, it remained deflated throughout the entirety of the case. A single incision was made along the lateral heel, completely excising the...
two draining sinuses. A subcutaneous abscess was encountered along with a large cavernous defect in the lateral calcaneal wall measuring approximately 0.75cm x 1.0cm, tracking 5.0cm across the body of the calcaneus. A curette was utilized to remove all soft, non-viable bone of which a sample was sent to pathology and microbiology for culture and antibiotic sensitivities. A second incision was made along the plantar medial calcaneus, revealing a deep soft tissue abscess which communicated with the laterally based sinuses. The area was then copiously irrigated with sterile saline, incisions partially closed with retention sutures and packed with betadine soaked packing strips. A sterile dressing was applied with Xeroform™, 4 × 4 gauze, an abdominal pad and contour gauze wrap, to be changed twice daily. The patient was instructed to be strictly non-weight bearing on the left lower extremity.

Intraoperative bone cultures grew methicillin sensitive Staphylococcus aureus (MSSA) and patient was initially started on IV Vancomycin. Once sensitivities returned, therapy was changed to IV nafcillin for a 42 day duration, per Infectious Disease. During hospitalization, the patient underwent 7 additional operative I&Ds which included placement of vancomycin antibiotic impregnated beads, tobramycin antibiotic spacer and eventual placement of ProDense™ bone filler to occupy the large cavernous defect in the lateral wall of the calcaneus (Fig. 4 and 5). A calcaneal biopsy was performed during each procedure, with the exception of the third I&D, all which grew MSSA up until the 6th procedure. Cultures from the 6th through the 8th I&Ds produced no growth with the exception of Staphylococcus hemolyticus which was isolated from the 7th calcaneal biopsy. This, however, was determined to be a contaminate (Fig. 6). Inflammatory markers were trended throughout treatment, with both ESR and CRP normalizing to 15 and 0.7 respectively, prior to discharge.

After completing a 42 day course of IV nafcillin, 20 HBOT sessions and three consecutively negative calcaneal biopsies, the patient was discharged to home. Radiographs prior to discharge revealed early

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**Fig. 3. (A, B, C and D)** MRI images of the left foot T2 fast spin echo (A), T1 fast spin echo (B), proton dense (C), T1 fast spin echo with gadolinium contrast (D) demonstrate evidence of extensive calcaneal osteomyelitis with serpiginous intraosseous abscess formation.
incorporation of ProDense™ bone filler with no new cortical irregularities of the calcaneus (Fig. 7A and 7B). He was kept non weight bearing in a posterior splint for an additional 6 weeks past the date of last surgery. He followed up in the Podiatric Surgery Clinic until complete incisional and osseous healing was obtained. His postoperative course was complicated only by slightly delayed incisional healing, which resolved with local wound care. Follow up radiographs obtained 8 months after initial presentation revealed full incorporation of ProDense™ bone filler with no acute osseous pathology (Fig. 8). At 12 month follow up the patient had returned to all previous activities, including basketball, without pain or functional disability. He denied any sensory deficits, was ambulating pain free and all incisions remained healed.

Discussion

Pediatric acute hematogenous osteomyelitis is a rare condition with an estimated incidence between 2-13 per 100,000 children annually in high-income countries. This is higher in developing countries, approaching 43 per 100,000. Prior to introduction of systemic antibiotic therapy, mortality rates were reported as high as 30% and 50% for pediatric femoral and tibial osteomyelitis, respectively. Today, the mortality rate has decreased to nearly zero.1,2,3

Hematogenous spread during an episode of bacteremia is the most common etiology for pediatric patients; however, acute osteomyelitis can develop secondary to direct inoculation from penetrating trauma or contiguous spread, which are more common among adults.1,3 During an episode of bacteremia, microorganisms enter the bloodstream, traveling to the metaphyseal bone where they enter via the nutrient artery. These then become lodged in the rich, sluggish metaphyseal capillary loops, resulting in localized infection.1

In a systematic review published in 2012, Dartnell et al. reported that the calcaneus is the 7th most frequently affected bone at 4.6%, preceded by the femur (26.9%), tibia (26%), pelvis (9.2%), humerus (8.1%), foot excluding calcaneus (7.7%), and forearm (4.8%).2 Additional studies have shown similar incidence in the calcaneus, ranging from 3-12%.3,4,5 Staphylococcus aureus (S. aureus) is the most commonly isolated organism in cases of AHO worldwide, cultured in upwards of 80% of culture-positive cases.1,6 Due to its prevalence, antibiotic therapy should be targeted against S. aureus while awaiting culture results and culture negative cases, which account for 33-55% of all cultures.1,3 Additional organisms should be considered in the presence of unique risk factors (animal or human bites, farm animal proximity or immunocompromised host), neonates or sexually active adolescents.1

The mean age at presentation is between 2-9 years of age, with a 2:1 male predominance.1,2,3,4 Time from symptom onset to presentation for medical care has been reported between 1 to 34 days, with an average of 6.8 days.3,4 Diagnosis is often delayed due to the insidious onset of symptoms, with a diagnosis >5 days from symptom onset defined as
late. Delayed diagnosis can be detrimental to the patient and result in devastating complications including angular deformity, joint disruption, growth arrest, chronic osteomyelitis, pathologic fractures, toxic shock, and rarely death.3,9

Due to the insidious nature of symptoms, many patients are initially misdiagnosed with deep heel contusions, Severs apophysitis or Achilles tendinitis. Although differential diagnoses including the aforementioned, trauma, malignancy, bone infarction, metabolic disease and avascular necrosis should be considered, a high suspicion for acute osteomyelitis must be present in a child presenting with localized bone pain. Clinicians should be mindful of the most common clinical features in patients with AHO, including pain (81%), localized signs/symptoms (70%), fever (62%), reduced motion (50%) and reduced weight bearing (49%). Absence of fever or known risk factors (recent blunt or penetrating trauma, blisters, scratches or twisting injuries) does not eliminate the possibility of AHO since nearly 40% of all patients will be afebrile and up to half will not have any known risk factors.1,2,3,4

Once diagnosis is suspected, laboratory and imaging studies should be immediately obtained for confirmation. Recommended laboratory tests include WBC, CRP and ESR. When simultaneously elevated, ESR and CRP are the most sensitive laboratory markers for diagnosis of AHO. At time of presentation, WBC, ESR and CRP are abnormal 13-45%, 81-95% and 47-98% respectively, with average values of 10.6, 48.3 and 41.5.2,4,7 All three are more likely to be elevated in instances where
methylene resistant Staphylococcus aureus (MRSA) is the causative pathogen or concurrent septic arthritis is present. Given the insidious onset of symptoms often resulting in delayed medical treatment, ESR may be more reliable for initial diagnosis of calcaneal AHO. Due to the shorter duration to normalization compared to ESR, CRP is often trending to monitor response to treatment.

Imaging studies should begin with plain radiographs to rule out other potential etiologies and assess for acute osseous pathology, including lytic lesions or periosteal reaction. Radiographic findings can be delayed up to two weeks; therefore, MRI imaging should also be obtained if there is a high clinical suspicion for AHO with negative radiographs. A retrospective review of 60 pediatric patients with calcaneal AHO published by Leigh et al. in 2010 reported only 24% of patients had positive findings on their initial radiograph, compared to 100% with signal abnormality consistent with osteomyelitis on MRI imaging. MRI is the gold standard imaging technique for AHO with a reported sensitivity of 97-100% and specificity of 92%. Signal abnormalities can be present within 2-5 days of disease onset, allowing for earlier diagnosis than radiographs. Outside of diagnostic capabilities, MRI is also useful for surgical planning. Technetium radionuclide bone scanning has also been described for early diagnosis of AHO and is a viable alternative in patients who are unable to have MRI imaging due to contraindications including, but not limited to, implantable pediatric sterilum devices, retained metallic foreign bodies, insulin pumps or transvenous pacing leads.

Once diagnosis has been established and bone/joint and blood cultures obtained, antibiotic therapy based on regional susceptibility and directed against S. aureus should be started empirically. Recommendations regarding duration and route of administration vary vastly in literature and depend on multiple factors including infecting pathogen, disease severity, concomitant septic joint and host factors. The general consensus appears to be a short course of parenteral antibiotics followed by transition to an oral agent for a 3-4 week total course for uncomplicated osteomyelitis and a 2-3 week duration of parenteral antibiotics followed by transition to an oral agent for a total duration of 4-6 weeks for complicated cases. Despite some authors advocating for courses less than 20 days in uncomplicated cases, duration of therapy less than 21 days has been found to have a higher risk of developing chronic osteomyelitis.

Surgical debridement has historically been controversial. While some recent evidence has emerged demonstrating that early aggressive surgical source control may be beneficial, other authors have shown higher rates of chronic osteomyelitis following aggressive primary surgery. Various surgical techniques have been described in the literature including abscess drainage and debridement, osseous drilling and the split-heel technique. In complicated cases, such as this case report, serial debridements are often necessary to ensure removal of all necrotic tissue.

In a recent study published by Collins et al. in 2018, the authors found that pathogenesis of AHO in children is related to the virulence capability of the S. aureus genome. Forty genes were discovered to be significantly associated with the severity of the illness. They concluded that this difference in bacterial virulence behavior may contribute to the reason why some otherwise healthy, immunologically competent children undergo multiple surgical procedures, experience prolonged hospitalization and receive long-term antibiotic therapy. The S. aureus genome of our patient was not identified; however, it is possible that he possessed a virulent strain contributing to the severity of his condition.

Our case report substantiates many portions of the previously published literature on pediatric calcaneal AHO. For example, our patient was male, his bone cultures grew S. aureus, he initially sought medical care within 5 days of symptom onset, had a fever at initial presentation and reported a history of blunt trauma to the left heel. His laboratory values were consistent with AHO and ESR was the most significantly elevated. He had plain radiographs obtained at 5 and 22 days post symptom onset which were negative for acute pathology and he was misdiagnosed with a deep heel contusion at two separate facilities prior to AHO diagnosis at our facility.

What is unique about this case is the patient’s slightly older than average age as well as the 63 day lapse between initial onset of symptoms and diagnosis of AHO. To our knowledge, this is the longest reported delay in diagnosis and treatment of pediatric calcaneal AHO to date. There are multiple contributing factors that led to such a significant delay in diagnosis and treatment, first of which is the patient’s complicated social history. The patient’s primary and secondary clinical evaluations took place within two different medical systems in neighboring states. He was also accompanied by the patient’s visits by two separate guardians, who admitted lack of communication with one another about patient’s condition and medical treatment. Lack of advanced imaging also led to a delay in diagnosis of this case. MRI imaging should have been obtained if not at initial presentation, most certainly at second presentation when the patient was reporting worsening symptoms including inability to bear weight secondary to pain, localized tenderness and increased edema.

This patient’s case was complicated in nature due to delayed diagnosis with large intra-calcaneal and deep soft tissue abscesses and cutaneous draining sinus tracts. Due to the advanced stage of the condition, aggressive serial operative debridements were required along with a 6 week course of IV nafcillin and 20 sessions of HBOT. Minimal research has been conducted on the efficacy of HBOT and pediatric AHO. Waisman et al. published a report in 1998 on utilization of HBOT in pediatric patients. The authors retrospectively reviewed 139 pediatric patients, 5 of whom were treated for refractory osteomyelitis. All patients participated in an average of 32 HBOT sessions at 2.5 ATA twice daily in conjunction with standard treatment including antibiotics and surgical intervention. They observed a 93% favorable outcome in all pediatric patients who received HBOT and advocated for the use of HBOT in the treatment of certain conditions in the pediatric patient. Consultation to Hyperbaric Medicine has become an important cornerstone in treatment for pediatric AHO at our facility. In this case, we believe adjunctive HBOT did play an important role in our patient’s ultimately successful outcome, and also advocate for the use of HBOT if indicated for pediatric conditions including AHO. Limitations of this particular case study include the inability to obtain a detailed history of presenting illness due to poor family historians as well as lack of twelve month follow up imaging.

In conclusion, pediatric calcaneal AHO is a rare condition, often initially misdiagnosed. Delayed diagnosis can result in devastating complications with lifelong impacts. High clinical suspicion should exist when any child presents with localized bone pain with or without history of recent illness or inciting event. Advanced imaging should be considered when suspicion exists and even more so upon development of any worsening symptoms. Approach to treatment should be multidisciplinary and include pediatricians, Infectious Disease specialists, surgeons, pathologists and radiologist. Standard care including bone/joint and blood cultures followed by initial IV antibiotic therapy targeted against S. aureus is well established. In complicated cases, addition of aggressive surgical intervention and HBOT may be indicated. It is our hope that the publication of this paper will prevent such a significant delay in diagnosis for any child presenting with similar symptoms hereto forward.

Declaration of Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Patient Informed Consent Statement

Complete informed consent was obtained from the patient for the publication of this study and accompanying images.

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