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Case Report Open Access

Hematogenous Osteomyelitis in an Adult: From Axilla to Metatarsal-A Case Report

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Abstract

Hematogenous osteomyelitis is an uncommon and often challenging etiology to diagnose and treat. This pathology has a bimodal population spread between children and adults, the former making up majority of the cases. Each population has its own challenges in diagnosis and treatment with specific characteristics found been children and adult hematogenous osteomyelitis. In the adult population, bacterial seeding to the distal extremities is rare. Often the inciting event is traumatic in nature with direct seeding. However, in this paper the authors describe their experience with acute hematogenous osteomyelitis of the forth metatarsal in an adult female who just months before was treated for an axillary abscess. Further, diagnostic criteria from physical exam to laboratory and imaging studies, as well as treatments are discussed.

Keywords: Abscess; Foot; Hematogenous osteomyelitis; Metatarsal; MSSA; Osteomyelitis; Pediatric

Introduction

Presented is a case of hematogenous osteomyelitis (HOM), initially starting from an axillary abscess, and seeding to the metatarsal after a period of suspected asymptomatic bateremia. The case demonstrates not only the importance of complete history and physical taking, but having a high suspicion and wide differential base for each patient that presents to the office from children to the elderly. Additionally, it discusses the challenges in diagnosing and treating hematogenous osteomyelitis with differences between pediatric versus adult HOM, and the importance of complete antibiotic therapy with the need to reassess the situation and plan throughout the course of treatment.

Case Report

Patient permission for print and electronic publication and International Review Board (IRB) approval was obtained before reporting on this case. The patient, a 44 year old female, initially presented to the emergency department (ED) (5/19/14) after an insidious onset of left axillary pain the day prior to presentation. She had a past medical history (PMH) of tension headaches and depression, a twenty-pack year smoking history, and no history of alcohol or intravenous drug abuse. She displayed no systemic signs of infection with all vital signs stable. Review of systems was negative except for pain, swelling, and erythema to the left axillary region. After evaluation, an incision and drainage (I&D) with packing was performed to the axilla. Cultures were taken and sent to the lab for microbiological analysis. She was sent home with a seven day course of Sulfamethoxazole/Trimethoprim (SMX/TMP). Days later the culture resulted Methicillin-sensitive *Staphylococcus aureus* (MSSA). The patient subsequently presented on antibiotic day number two and four (5/21/14 and 5/23/14) for continued pain with packing changes performed in the ED. No changes were made to the antibiotic course during the follow-ups. She had an excision of the cyst by general surgery approximately two weeks after the initial I&D in the ED. Healing of this surgery was uneventful.

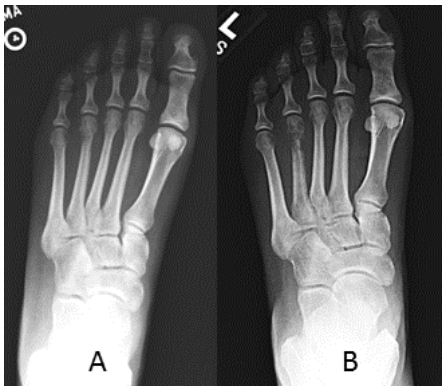

Figure 1: (A) Radiograph from emergency room visit on 6-27-14 for patients initial presentation of left foot pain and swelling. Negative for pathology in the foot per official radiology read. (B) Radiograph from follow-up podiatric evaluation, 7-18-14. Positive for cortical destruction of the forth metatarsal head with osteopenic changes on the cortical margins medially and laterally proximally, consistent with osteomyelitis.

Approximately one month later (6/27/14), the patient presented to the same ED for a new complaint of left foot pain. The patient stated three weeks prior her large, 125 pound dog stepped on her foot. Over the following week after this traumatic incident, the foot developed pain, bruising, and swelling. She went to an urgent care center (6/14/14) for treatment where she had radiographs (XR), reported as negative for any pathology. She was dispensed a surgical shoe for

weightbearing as tolerated and told to take ibuprofen for pain. The pain continued which brought her to the ED one week later. Again, standard foot XRs were taken and read as negative for osseous pathology, only noting soft tissue edema over the dorsal midfoot. (Figure 1A) Vital signs were stable and white blood count (WBC) was 8.5 mg/dL. Assumed to have a deep contusion, she was given medication for pain and told to follow-up outpatient with podiatry.

Three days passed from the ED visit and the patient presented to the senior authors (D.E.S.) office (6/30/14) with unresolved pain, erythema, and edema to the left foot. The patient brought with her the urgent care imagining and it, along with her ED imaging. It was read by the attending physician as a cortical break in the fourth metatarsal neck, assumed to be a fracture from the dog stepping on the foot (Figure 1A). After reviewing her PMH as well as the timeline of recent events starting at the axillary abscess, there was a concern that the traumatic event of her dog stepping on the foot caused a microfracture or inflammatory reaction. The physicians' thought process was while in an asymptomatic bacteremic state, this reaction resulted in a hematogenous seeding from the axillary abscess to the fourth metatarsal. At this initial visit, the patient was started on SMX/TMP and instituted protected weight bearing in a CAM boot to prevent further pathological fracture.

The patient followed up 3 weeks later (7/21/14) after having a new radiograph of the foot taken the week prior (7/18/14). This new image demonstrated radiographic signs consistent with osteomyelitis of the head, neck, and shaft of the forth metatarsal (Figure 1B). What resembled a small cortical break read by the attending physician at the initial podiatric evaluation were possibly the initial manifestations of osteomyelitis. Magnetic resonance image (MRI), blood work, and an Infectious Disease (ID) consult was also ordered. MRI (7/23/14) revealed an "aggressive, destructive process" with marrow edema of the fourth metatarsal with "differential considerations including hematogenously spread osteomyelitis, metastatic disease, multiple myeloma, or a primary bone neoplasm" (Figure 2). To rule out a possible metastatic process, a bone scan was ordered and showed increased uptake on the first three phases of the scan only at the lateral left foot, consistent with the previous two studies for osteomyelitis (Figure 3).

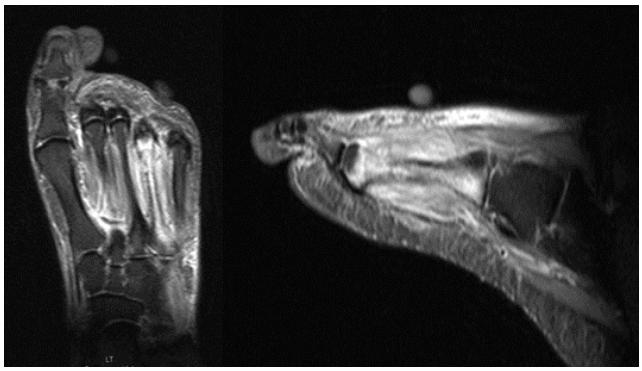

Figure 2: MRI T2-weighted image taken 7-23-14. Positive for enhanced marrow edema throughout the forth metatarsal from head to base. No extension across joint spaces or neighboring metatarsals. Note the soft tissue edema without abscess formation.

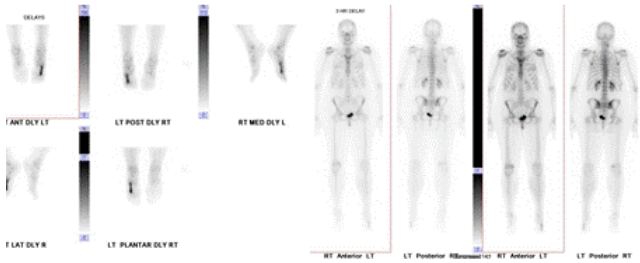

Figure 3: Bone Scan 7-30-14. Delayed phase images with positive uptake in the lateral foot (Left) and delayed phase whole body images, negative for uptake in the body other than the left foot (Right).

The patient was taken to the operating room for bone biopsy of the left forth metatarsal (7/29/14). Soft tissue wound and fungal cultures were negative, but bone cultures grew MSSA and bone pathology was described as tan "bone fragments showing features consistent with chronic osteomyelitis."

The patient was offered both conservative and surgical treatments; conservative being a six-week course of culture-driven intravenous (IV) antibiotics, while surgical was bone removal with possible wedge-ray resection. The patient chose conservative therapy, receiving a course of IV and oral antibiotics. She had a complicated course of treatment due to deep venous thrombosis from the initial peripherally inserted central catheter (PICC) line and a drug fever reaction from her initially prescribed IV cephelaxin. This event resulted in the patient being hospitalized (9/4/14-9/7/14), the PICC line being removed, and being placed on Xeralto (Rivaroxaban, Bayer HealthCare AG, Leverkusen, Germany). The IV cephalexin was converted to oral clindamycin. She was discharged at week 5 of 6 of antibiotic therapy. Levofloxacin was added and the therapy was extended to a total of 8 weeks.

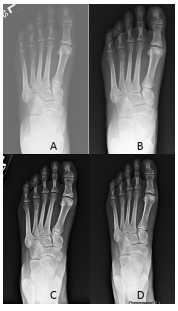

Figure 4: Left foot radiograph from (A) 10/1/14, (B) 12/1/14, (C) 3/3/15, and (D) 7/13/15, demonstrating decrease lucency with increased sclerotic changes to the forth metatarsal with no advancement of infectious process.

Over the course of subsequent months the patient was seen several times by both the ID team and senior author. There was a normal progression in skin healing at the surgical biopsy site. Serial radiographs demonstrated no new periosteal reaction, no new progression of osseous destruction, and no advancement of infection to another bone in the foot. The present lytic lesions slowly improved

with sclerotic changes to the metatarsal. (Figures 4A-D) Clinically there was resolution of the patient foot pain and foot erythema and edema once antibiotic treatments were started and remained under control with no relapse to date after 17 months from the bone biopsy. Concurrent blood laboratory testing normalized as well.

Discussion

Osteomyelitis (OM) is defined as inflammation involving the bone and its marrow, almost exclusively the result of infection due to bacterial seeding into bone, producing a local inflammatory reaction resulting in bone destruction, necrosis, and sequestra formation [1,2]. HOM, described and classified by Waldvogel, occurs when the bone infection is secondary to an infection elsewhere in the body that spreads through the bloodstream to an area predisposed to infection. HOM is always preceded by a period of bacteremia with the infection often being asymptomatic to the host [3,4]. Hematogenous dissemination in a bacteremic patient can be from various sources such as recent UTI, cellulitis, abscess, catheter infection, dental surgery, meningitis, endocarditis, osteomyelitis or open trauma [5,6]. Bone that has been recently traumatized, especially if there is a break in the cortex and results in hematoma formation, can serve as an excellent culture medium for bacteria to seed from the sources stated above [4].

Historically HOM has been a disease of children. Approximately 85% of cases are in patients younger than 17 years of age with one-quarter younger than two years of age and one-half younger than five years old [7,8]. Eighty percent of cases are found in tubular bones with 13% described in the hands and feet [7,9]. HOM is suspected to have higher prevalence in children due to anatomical differences compared to adults such as sluggish and turbulent medullary circulation in the long bones and a thinner cortex with loosely apposed periosteum [1,7,9–12]. Any sort of obstruction due to this vascular and anatomic anomaly, or event of trauma, can result in hematoma, inflammation, and avascular necrosis; all factors leading to a site for bacteria to seed in a bacteremic patient.

In adults, secondary spread from a contiguous focus is the leading cause of OM [13]. When HOM is seen in the adult population, it is most often in patients older than 50 years of age and accounts for 20% of all adult cases of OM [8]. Compared to children, sites of HOM are the vertebra, sternoclavicular, and pelvic bones (the last two most common in intravenous drug users) with a primary presenting symptom of back pain [8,14]. Another high risk adult population are those with joint prosthesis or indwelling catheters, where the infection often attacks [1,8,12]. In patients younger than 40 years of age, intravenous drug abuse (IVDA) is a common culprit [8].

There are three phases to HOM: the acute stage (first three weeks), sub-acute (on average a duration of 6 months), and chronic stage [15]. Acute HOM has an incidence of 2 to 13 cases per 100,000 persons in the developed countries annually, often seen in a bimodal population spread between children and adults [11,15]. Acute infections are typically diagnosed within two weeks of the onset of symptoms upon presentation to the clinicians office while chronic forms may be diagnosed months later [2,9,15]. The chronic or asymptomatic population is often the compromised patient with co-morbidities such as diabetes, cancer, rheumatoid, chronic corticosteroid usage, sickle-cell anemia or peripheral vascular disease. Regardless of age, patients commonly present with an abrupt onset of pain and tenderness to a specific area with or without other signs or symptoms of infection.

Obtaining a complete history and performing a thorough examination with appropriate diagnostic studies is of the utmost importance in diagnosing HOM. Question the patient regarding any potential inciting event such as innocuous trauma to the affected area. Question the patient regarding any recent ear, dental, urinary, skin or pulmonary infections and what the outcome was of that infection. Question the patients' social history or get drug screen if IVDA is suspected. Specifically, find out if the patient had any recent cultures and antibiotic usage, getting the drug, strength, and duration of therapy. This piece of information may help in antibiotic selection if HOM is suspected as the problems with most of these cases are caused by the same organism, as seen here [12]. Laboratory values may be normal or elevated and blood cultures are positive in only around one-half of cases, even if antibiotics have not been started prior to culture [10,14]. This can be increased up to 80% when multiple cultures are taken including blood cultures in pairs, bone cultures, and joint fluid aspirates [9]. The absence of a raised value, such as WBC, erythrocyte sedimentation rate (ESR), or C-reactive protein (C-RP) is not sufficient to rule out the diagnosis of HOM [6]. In one of the largest retrospective studies of calcaneal HOM in children (n = 21), when specific test were performed, WBC count was elevated in 24% (5/21), ESR elevated in 95% (20/21), C-RP elevated in 47% (7/15), positive blood cultures in 20% (3/15), and positive bone cultures in 50% (7/14) of cases [16]. Generally speaking, *Staphylococcus aureus* is the most common organism found in acute and chronic HOM in children and adults, cited upwards of 74% of all cases [3,14]. To further help delineate other potential inoculating organisms, patient age, comorbidities, and mechanism of primary infection are important factors to consider [3,6] (Table 1).

Finding	Organism
• Infants	Beta-hemolytic streptococcus
• Children < 2 years old	*Haemophilus influenza*
• Recent history of urinary tract infection	Streptococcal species Gram-negative organisms (ex. *Escherichia coli)*
• Intravenous drug user • History of puncture wound • Immunocompromised • Male > 9 years old	*Pseudomonas aeruginosa*

• Sickle cell anemia	*Salmonella typhi*

Table 1: Common Infectious Agents in HOM.

XRs are useful for initial diagnosis with MRI or nuclear imaging aiding to back up ones suspicion, but bone biopsy is the preferred modality for diagnosis [13,14]. XRs often have a delay in visual signs (cues) for OM compared to patient symptoms. Early changes (periosteal thickening, lytic lesions, intramedullary abscess, osseous fragmentation) are subtle and may not be obvious until 5 to 7 days after inoculation in children and 10 to 14 days in adults, once up to 50% of bone mineral content has been destroyed [1,14,17]. Pathological fractures are most commonly seen in the sub-acute phase time window, while visualization of sequestrum is a finding of the chronic stage [6,15]. XR changes in the case presented were seen three weeks after an initial negative film, a total of six weeks after the inciting traumatic event. Once the early findings were made, protected weightbearing was instituted to prevent pathological fracture until advanced imaging could be performed to formalize the treatment plan.

MRI is a useful modality in its ability for early detection of marrow edema, a feature seen in OM as early as 3-5 days post inoculation [17]. Bone scans, whether it be the technetium-99-methyl diphosphate (99mTc-mdp) scan, technetium-99-hexamethylpropylenamine oxime (99mTc-HMPAO)-labeled leukocyte scan or the indium-111 (111In)-labeled leukocyte scan, will demonstrate a localized focus of uptake at the affected structure [10]. Due to possible open epiphyseal plates and increased osteoblastic activity in children, it has been recommended that bone scans (99mTc-mdp) should be ordered bilaterally for comparison or avoided altogether to prevent misinterpretation [6]. Regardless of the multiple diagnostic tests that can be ordered, many suggest the gold standard for diagnosis is bone biopsy with microbiology and pathology examination [3,13]. All of the aforementioned tests were performed here to obtain the correct diagnosis.

Differentials are vast when a patient, regardless of age, presents with an erythematous, edematous, painful extremity or area of the foot. The list should include fracture/stress fracture/contusion, apophysitis, enthesopathy, old trauma, non-infected non-unions, Charcot joint, cyst (soft tissue or bone), primary bone tumor (benign or malignant), metastatic disease or disorders of the musculoskeletal (ex. tendon or ligament damage), hematologic or neurologic systems [8,11,16-18]. If suspicion is high for OM, one should see the patient more often than normal for follow-up and monitoring, developing and changing the course of treatment based on clinical response to therapies employed and laboratory analysis as stated earlier.

Treatment for HOM is widely debated. It often consists of some combination of medical antibiotic therapy and surgical debridement. While children often can undergo several (3-4) weeks of antibiotic therapy (oral and IV), in adults surgery is often required in conjunction with culture driven antibiotic therapy [1,14]. Once therapy is initiated, abnormal lab values like ESR (peak by 3-5 days; return to normal by 3 weeks) and C-RP (peak by 2 days; return to normal by 1 week) are helpful to track efficacy of treatments rendered [9]. Despite appropriate surgical debridement and antibiotic therapy, chronic OM in adults has a 30% recurrence rate at 12 months [14].

In reviewing the English literature, to the best of our knowledge, there are only a few cases reported of HOM to the foot and ankle with majority in the pediatric population. This includes children between the ages of 1 month and 13 years with hematogenous seeding to the first and fifth metatarsal (Loder et al.; Goforth et al.), calcaneus (Kelsey et al.; Jaakkola et al.), talus (Narang et al.) [3,6,10,16,19]. One of the largest reported retrospective series of pediatric HOM was performed by Jaakkola et al., identifying 21 cases of calcaneal infection over the 7 years reviewed [16].

There are only a few cases of adult HOM of the foot (and ankle) reported as well. HOM of the adult foot, especially without a history of trauma is rare. In a study by Chandrasekar and Narula et al. (1986), of 45 cases of IVDA HOM (primary or secondary), only 1 seeded to the foot and ankle [4]. Of case reports, one was that of a 48 year old female with HOM developing 18 months after a first metatarsophalangeal replacement [20]. This is a kin to hematogenous infections in other joint replacements such as the hip, knee, and shoulder. A second study was a 26 year old female with a history of daily heroin and cocaine abuse developing in the 3rd metatarsal [4]. Mesgarzadeh et al. (1986) reported on a 63 year old male with HOM of the calcaneus after lung infection [21]. D'Amato et al. (1985) reported a case of a 19 year old female with navicular HOM, misdiagnosed as tibialis anterior tendonitis, which went untreated by antibiotics for twenty-eight days from time of onset of the patients' symptoms [22]. A literature search performed by the same group found only 6 cases reported over a 20 year period, demonstrating the rarity of this condition [22]. Here we add to the literature with a case report of metatarsal HOM after abscess infection in the upper extremity.

Conclusion

The presentation of HOM in the adult population, especially seeding to the foot has been sparsely published in the literature. Because of its uncommon nature, the surgeon needs to be astute in always starting with a wide differential list, considering all possibilities regardless of prevalence. It is important to listen to the history of present illness, perform a complete physical exam, and review all imaging modalities regardless of the previous read, positive or negative. HOM is difficult to diagnose, especially with the pathology presenting and responding differently in the children versus adults. Laboratory studies and the delay in radiographic changes may early diagnosis difficult. Advanced imaging such as MRI, CT, and bone scans may further help, but the bone biopsy is the definitive diagnostic tool. Delay in or incomplete treatment can result in continuation of symptoms, increase in osseous spread, pathological fracture, and growth plate arrest (in children). Treatment is complex in a patient with HOM and often requires multiple modalities and a team approach between podiatric, primary care, infectious disease, and vascular physicians.

In this case, it is suspected that the patient had an incomplete antibiotic therapy (duration or dose or compliance?) of her axillary abscess. This resulted in an asymptomatic bacteremia that after the trauma of her dog stepping on her foot and possibly causing a stress fracture (bone trauma), resulted in the 4th metatarsal being the site of bacterial seeding. After bone biopsy conformation of MSSA, an extended course of IV and oral antibiotics has quelled the infection

after 15 months of radiographic and laboratory follows up. Due to the distal 2/3 of the metatarsal showing evidence of osteomyelitis, we opted to aggressively treat with antibiotics. Surgery would have likely required resection of most, if not all, of the involved metatarsal, leaving potential for incomplete resection, further spread, and altered foot mechanics. This paper, though literature and a real life case, demonstrates the complicated nature of diagnosing and treating HOM in both the pediatric, and in this instance, the adult population.

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