Delay in Diagnosis of Femoral Hematogenous Osteomyelitis in Adults: an Elusive Disease with Poor Outcome

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ABSTRACT: **Background:** Hematogenous osteomyelitis of long bones is rare in adults, especially in the immune competent host. Only a few cases have been described to date.

Objectives: To present a case series of femoral hematogenous osteomyelitis in adults, a rare condition that is difficult to diagnose and may cause major morbidity and mortality.

Methods: We reviewed three cases of femoral hematogenous osteomyelitis that occurred between 2007 and 2009. The course of the disease, physical findings, imaging modalities, laboratory analysis, culture results and functional outcomes were recorded.

Results: In all cases the diagnosis was delayed after symptoms were first attributed to radicular-like pain or lateral thigh pain due to an inflammatory non-infectious source. In all cases infection was caused by an unusual or fastidious bacterium. The pathogen was *Haemophilus aphrophilus* in one case, and Streptococcus specimens were found in the other two. Pathological fracture occurred in two of the cases despite culture-specific antibiotic treatment and a non-weight bearing treatment protocol. It took five surgical interventions on average to reach full recovery from infection, but residual disability was still noted at the last follow-up.

Conclusions: Clinicians should be aware that although femoral hematogenous osteomyelitis is a rare condition in adults, its ability to mimic other pathologies can result in delayed diagnosis and major morbidity. In our series the pathogen was different in each case and was cultured only from the infected site. Pathological fracture is a devastating complication but we do not recommend prophylactic stabilization at this point.

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Femur osteomyelitis in adults is usually caused by open fractures or local spread of soft tissue infection. Femur osteomyelitis can cause significant morbidity and even escalate to be a limb- or life-threatening condition. Hematogenous osteomyelitis, though more common in children, is rare in adults, especially in the immune competent host. Only a few reports have been published on femur hematogenous osteomyelitis in adults in the English-language medical literature [1-3].

The common presentation of osteomyelitis includes dull pain of insidious onset with or without signs of fever, tenderness, swelling and erythema. The formation of a soft tissue abscess, fluctuation or discharge appears late in the course of the disease. Since this condition is rare, the diagnosis is somewhat difficult and may often be delayed or mistaken for more common conditions, resulting in further morbidity and complications.

The most common differential diagnosis for pain along the thigh and leg is probably radicular pain. Unlike osteomyelitis, it is a common condition in adults. The lifetime incidence of radicular pain ranges from 13% to 40% and the annual incidence of a sciatic episode from 1% to 5% [4,5]. The etiology for radicular-like pain is usually related to pathologies involving the lumbar spine, such as intervertebral disk disease, stenosis, infection or malignancy.

We present three cases of femoral hematogenous osteomyelitis in adults. Thigh pain that was first interpreted as radicular pain turned out to be an aggressive infectious disease. Approval for the study was obtained from our local Institutional Review Board

CASE 1

A 56 year old man presented with a 2 week history of severe low back and left thigh pain. Previous medical history was notable for ischemic heart disease, diabetes mellitus and hypertension, as well as a former combined laminectomy, namely, discectomy surgery at the L4–5 level 7 years previously. His physical examination revealed minimal motor weakness of the iliopsoas and quadriceps muscles. Sciatic and femoral nerve stretch tests were negative. Blood analysis was within normal limits, but C-reactive protein and erythrocyte sedimentation rate were not analyzed. Magnetic resonance

Figure 1. Lateral radiograph demonstrates a lesion in the medullary and cortical portions of the femoral diaphysis with bone distraction and soft tissue involvement

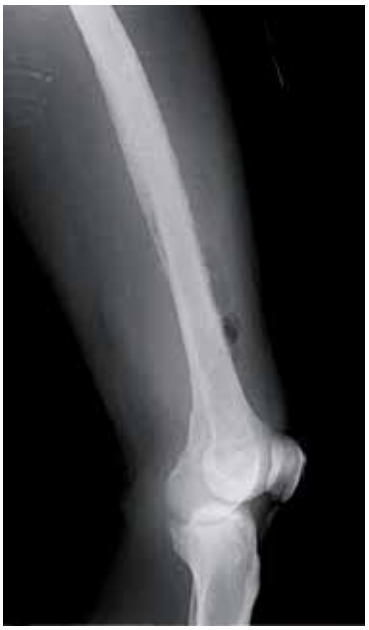
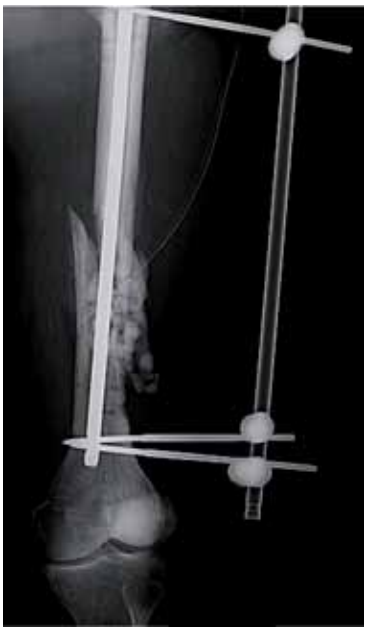


Figure 2. Anterior-posterior radiograph demonstrates a hybrid fixation of the pathological fracture with external fixation and intramedullary nail with antibiotic beads



imaging demonstrated discogenic changes at the L3 lumbar spine level and caudally. The patient was scheduled for an epidural injection on an ambulatory basis and was discharged with the diagnosis of radicular thigh pain. One month later, while treated with opiates, the patient suffered a few episodes of fever. One month later, he was readmitted with a 39° fever and septic shock, presumed to be caused by pneumonia. On clinical evaluation, thigh swelling was noted. A radiograph of the femur showed a lesion in the femur and involvement of the surrounding tissue [Figure 1]. A needle aspiration was performed, yielding brownish foul-smelling fluid, and Gram stain showed pus cells and Gram-positive cocci in chains.

The patient was treated with emergent surgical debridement, revealing frank pus draining from the femoral medullary canal. A diagnosis of femoral osteomyelitis was established. Bacterial cultures yielded *Streptococcus anginosus*. Blood cultures were negative. Intravenous antibiotics (piperacillin and metronidazole) were administered. The patient's hospitalization was characterized by nosocomial wound infection with *Pseudomonas aeroginosa* and Acinetobacter spp., which required several surgical debridements before control of his infection was achieved.

A month after the diagnosis of acute osteomyelitis, the patient sustained a pathological fracture through the infection site. The fracture was treated with an external fixator, augmented by antibiotic-impregnated cement in an intramedullery nail [Figure 2], and further intramedullary femoral nail exchange. At 17 months of follow-up the patient had no signs of infection but exhibited difficulty in walking and suffers from persistent pain.

CASE 2

A 47 year old woman, otherwise healthy, presented with a 2 week history of right thigh pain. The patient's medical history was unremarkable. Constitutional symptoms such as weight loss and night sweats were excluded. A few days earlier, nonsteroidal anti-inflammatory drugs were started as treatment for what appeared to be symptoms of sciatica.

On physical examination the vital signs were within normal limits, the patient could hardly bear weight on her right leg, and the thigh was tender to palpation in its middle third. A neurological examination was normal. The hip flexion-abduction-external rotation (FABER) test was negative and no nerve root irritation signs were present. Laboratory tests showed mild anemia with hemoglobin level of 9.4 mg/dl, normal white blood cell count and an elevated ESR (50 mm/1st hour). Radiographs of her lumbar spine, pelvis and femur revealed no pathology. A computed tomography scan of her thigh demonstrated a 1.5 x 1.5 mm hypodense lesion near the medial cortex. Magnetic resonance imaging demonstrated an 8 x 2 cm area of mixed hypointensity and hyperintensity near the periost at the diaphysis and distally. The patient underwent an open incisional biopsy and cultures were taken. Two weeks later she was readmitted because of intractable pain. Repeated blood test results were similar to those at presentation but radiographs demonstrated a hypodense "moth-eaten" like lesion. At that point, cultures taken during her biopsy came back positive for *Haemophilus aphrophilus*. She was then treated with intravenous ceftriaxone according to sensitivity. Eight weeks later she suffered a pathological fracture through the infection site [Figure 3] which was treated by an external fixation for a period of 4 months. At 1 year follow-up, the patient had regained full weight bearing, was limping but had no evidence of chronic infection.

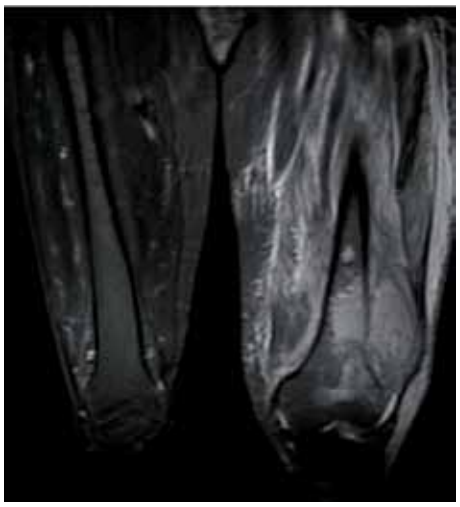
CASE 3

A 50 year old man was evaluated in the emergency room due following a 4 week period of left thigh and lateral knee pain. He had previously been discharged from the ER twice after radiography and Doppler ultrasound of his lateral thigh and knee were negative. The patient's medical history was remarkable for a splenectomy performed during peptic ulcer surgery 27 years prior to his current admission and a minor ipsilateral knee trauma 18 months before the admission. The

ESR = erythrocyte sedimentation rate
ER = emergency room

Figure 3. Anterior-posterior radiograph demonstrates a pathological fracture of the proximal femoral diaphysis through the infected site

Figure 4. Coronal T2 fat suppressed MRI image showing a well-defined area of increased signal density in the medullary space of the distal femur and soft tissue abscess on the lateral side



pain first appeared during a tennis game a few days before admission. Constitutional symptoms such as weight loss and night sweats were excluded.

The physical examination was unremarkable except for severe thigh and lateral knee pain with mild knee effusion. Laboratory blood analysis revealed elevated white blood cell count of 32,440 mm^3 with 81% neutrophils, and CRP 527 mg/L.

Radiography of his distal femur and knee revealed no pathology. Bone scan demonstrated increased uptake in the lateral femoral condyle, suggesting acute infection or tumor. MRI and CT were performed. MRI showed intramedullar involvement of the distal femur with cortical defect and edema in the surrounding soft tissue [Figure 4]. Aspiration of the fluid around the distal femur yielded frank pus.

The patient's hospitalization was characterized by nosocomial wound infection with *Enterococcus faecalis*, which required several surgical debridements and sensitivity-specific antibiotic treatment before his infection was controlled. At the last follow-up, 19 months after the first admission, blood analysis of inflammation markers were within normal limits, with full restoration of knee and hip range of motion.

DISCUSSION

We report three cases of femur hematogenous osteomyelitis in immune competent adults. The challenging diagnosis, the devastating clinical course and the residual morbidity are presented. Osteomyelitis is a well-described condition; in immune competent adults it may develop following extension of a soft tissue wound or open fracture. Hematogenous osteomyelitis is most commonly seen in metaphyses of long bones of children [6-10] or in immune suppressed patients. The pathogens involved in hematogenous osteomyelitis differ for each age group [11]. In neonates and infants the most common pathogen is *S. aureus*, followed by group B streptococci, coagulase-negative staphylococci, and other streptococci [11,12]. In adults, hematogenous osteomyelitis is usually monomicrobial, caused by *S. aureus* or Gram-negative bacteria and most often involves the appendicular skeleton: vertebrae, sternoclavicular or sacroiliac joints [10,13].

As hematogenous osteomyelitis of the femur in an immune competent adult is rare, diagnosis mandates a high index of suspicion. The patients in this series were initially diagnosed as having radicular or lateral thigh pain following an unspecific presentation of symptoms. Laboratory and imaging results, although exceeding the normal limits in some cases, were not indicative enough from the physician's point of view to establish the diagnosis as infection at that time and the patients were discharged with anti-inflammatory or analgesic treatment. Only unusual symptoms such as excessive pain or major illness presenting as sepsis prompted the physician to perform further evaluation in order to reach the right diagnosis.

Unfortunately, the clinical course of the infection was rapid and aggressive in all cases unrelated to the organism; surgery was performed in all cases with an average of five interventions per case. Pathological fractures were established in two of the three patients when they turned in bed, despite the fact that all of them were restrained from weight bearing. We could not find any report in the English literature of femur hematogenous osteomyelitis in an adult that was associated with pathological fracture, but we did find one in German

CRP = C-reactive protein

where a femoral fracture occurred through the infected site [14]. In that case an above-knee amputation was performed. In addition, we found a report of a pathological fracture due to hematogenous osteomyelitis of the humerus in an adult patient [15]. Since no other literature exists, we cannot recommend prophylactic fixation. We have presented only three cases of which only two had a fracture. Insertion of a foreign body into an infected site as prophylactic treatment may be associated with a higher prevalence of chronic infection. Again, we did not find any recommendation in the English literature.

In all three cases infection was caused by unusual or fastidious bacteria. In the first case wound cultures yielded *S. angiosus*, while in the third case *S. intermedius* was the primary pathogen. Both *S. angiosus* and *S. intermedius* belonging to the *S. angiosus* group are well described but are a rare cause of hematogenous osteomyelitis [16]. The most rare and unusual bacterium – *Haemophilus aphrophilus* – was found in the second case. *H. aphrophilus,* recently reclassified as *Aggregatibacter aphrophilus* [17], is a fastidious Gram-negative oral commensal considered to be a rare cause of human infections. The bacterium is a capnophilic, fermentative, slowly growing, non-motile Coccobacillus requiring X factor (hemin) but not factor V (nicotinaide adenine dinucleotide) for growth. *H. aphrophilus* was mainly described as a cause of endocarditis. Other infections related to *H. aphrophilus* include osteomyelitis, septic arthritis, brain abscesses, meningitis, sinusitis, otitis media, empyema, pneumonia, lymphadenitis, cellulitis, bacteremia and ophthalmic infections [18,19]. Only a few cases of appendicular skeletal hematogenus osteomyelitis with *Haemophilus aphrophilus* have been described in the literature [18,19], usually associated with dental procedures.

In conclusion, femoral hematogenous osteomyelitis may mimic other pathologies or present as non-specific leg pain. Although rare, this condition must be considered as a possible cause of pain. A high index of suspicion and thorough examination should be performed to avoid delay in diagnosis and associated complications. When an unusual manifestation or clinical examination in patients with radicular-like pain is present, we recommend that in addition to imaging, blood tests (complete blood count and inflammatory markers like ESR and CRP) be performed. We were able to culture the pathogen in all cases after performing a biopsy. Unfortunately, blood cultures were not sufficiently indicative as only one patient had a positive blood culture. We recommend performing biopsy whenever osteomyelitis is suspected to assure that the right antibiotic treatment is given. We also believe that awareness of hematogenous ostoemyelitis is the first step in establishing the right diagnosis.

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