Salmonella osteomyelitis: A rare differential diagnosis in osteolytic lesions around the knee

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Summary  Salmonella osteomyelitis in immunocompetent adults is uncommon. It usually has a diaphyseal location or present as spondylitis. Metaphyseal affection is extremely rare. A 51-year-old male presented with refractory knee pain. Plain X-rays showed a rounded osteolytic lesion in the proximal tibia without marginal sclerosis. A minimal C-reactive protein elevation and a normal leucocytic count were present. Further imaging raised suspicion of malignancy so that a biopsy was done. After fenestering the lesion, 15-ml turbid fluid was evacuated. Microbiological examination showed Salmonella enteritidis. Repeated debridements were done and antibiotic therapy with ciprofloxacin was initiated. The cavity was then filled with synthetic bone graft leading to progressive healing. Although rare, Salmonella bone infection usually lacks the typical periosteal reaction and the laboratory evidence of infection of pyogenic osteomyelitis. It should therefore be considered in the differential diagnosis of osteolytic neoplastic lesions.

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Introduction

Salmonella infection of bones and joints is rare, accounting for only 0.8% of all Salmonella infections and 0.45% of all types of osteomyelitis [1,2]. It may affect infants or adults with sickle cell anaemia or immune compromise due to general or local causes or who are chronic Salmonella carriers [2—5]. Only few case reports about infection in otherwise healthy persons are available [6—16]. Some uncommon human pathogens like Salmonella panama, virchow or arizonae and rare modes of infections like direct or indirect contact with reptiles or ingestion of snake-based products like meat and traditional medical preparations were here described [6—8,17—21].

This report presents a case of chronic infection of the proximal tibia caused by Salmonella enterica in an immunocompetent adult patient that raised suspicion of a malignant lesion because of its osteolytic nature, metaphyseal location and activity in the imaging studies. To the best of my knowledge,
there is no similar case report with such a constellation in the literature.

The aim of the current report is to provide a clear description of the diagnosis and management of this case, to look through the available literature and highlight the consideration of atypical bone infection with unusual non-pyogenic organisms in the differential diagnosis of osteolytic lesions around the knee joint.

Case report

A 51-year-old male patient has been suffering from persistent deeply seated dull-aching pain in his left knee. There was no history of trauma, recent foreign travel or a preceding diarrheal or pyogenic infection and no knee injections or operations have been done in the past. The conservative management by his family doctor using analgesics and physiotherapeutic measures over several weeks brought no improvement. Upon presentation in the hospital, plain X-rays were done and revealed a central rounded osteolytic lesion in the proximal tibial metaphysis without cortical expansion, marginal sclerosis, new bone formation or articular encroachment (Fig. 1). The laboratory studies showed a minimal C-reactive protein (CRP) elevation (8 mg/l, normal value <5 mg/l) and a normal total leucocytic count. The examination for tumour markers was negative and the Hb%, blood electrolytes, renal and liver function tests showed no abnormalities. In order to identify the nature of the lesion, a PET-CT was done. This raised suspicion of malignancy by showing a hot osteolytic metaphyseal lesion with reactive margins and enlarged hypermetabolic inguinal lymph nodes so that we decided to do an open biopsy. After having an informed consent, the patient was operated upon without delay.

As the lesion was fenastered, 15-ml turbid fluid was evacuated leaving a bone cavity with a fine necrotic margin behind. Surgical debridement was done, the cavity was irrigated and the wall was curetted up to healthy bleeding bone. The microbiological examination of the fluid and tissue specimens showed infection with Salmonella enteritidis. Retrospectively, the immune-competent patient reported that he suffered gastrointestinal Salmonellosis 7 years ago. Repeated debridements of the abscess cavity were done and antibiotic-impregnated PMMA beads (Septopal®, Biomet, Berlin, Germany) were inserted. Systemic antibiotic therapy with intravenous then oral ciprofloxacin according to culture and sensitivity was initiated.

After normalisation of the CRP, the Septopal® beads were removed and the cavity was filled with Actifuse® (Baxter, Unterschleißheim, Germany), a synthetic bone graft material (silicate substituted calcium phosphate), approximately four weeks after the first operative debridement. The patient was discharged on oral ciprofloxacin and mobilised on crutches with a partial weight bearing to avoid fractures for 6 weeks. Free mobilisation and full weight bearing without local pain were achieved after 2 months. Progressive healing of the lesion and integration of the synthetic bone graft was shown in the follow-up radiographs.

Discussion

Osteolytic lesions of long bones occur most frequently in the metaphyseal region, specially around the knee. A neoplastic origin in form of a primary bone tumour or bone destroying metastasis should
always be excluded [1,22–24]. Nevertheless, rare aetiologies like atypical osteomyelitis with non-pyogenic organisms or in immune suppressed patients may mimic an osteolytic neoplastic lesion as it lacks a clear laboratory evidence of infection and is not associated with the usual systemic inflammatory and local periosteal reactions of pyogenic bone infections [1,24].

*Salmonella bacilli* are gram-negative non-sporo-forming rods belonging to the *Enterobacteriaceae* family [2,5,9]. Salmonellosis can be divided into five separate or overlapping syndromes: enterocolitis (food poisoning), enteric (typhoid) fever, bacteraemia/septicaemia without localisation, local infection and a chronic carrier state [7,10,13]. The mechanism of infection is usually through ingestion of contaminated water or food like eggs, poultry, non-pasteurised milk, snake meat and snake-based traditional medications or through skin contact with amphibians and cold-blood reptiles like snakes, lizards and turtles [2,7,9,15–21]. There is no healthy carrier of *Salmonella* infection in humans. On the other hand, 90% of reptiles are reservoir carriers of one or more potentially pathogenic *Salmonella* species [9,21]. There is an increasing prevalence of non-typhic zoonotic reptile-related *Salmonella* infections in the United States due to the growing number of exotic pet reptile owners and the use of snake-based traditional medications in Spanish–American communities [9]. A case of infection through snake bite has also been reported [20].

Bone and joint infection with *Salmonella* species is shown to be rare in humans [1,2]. Infants and adults suffering from sickle cell anaemia or other haemoglobinopathies, systemic lupus erythematosus or immune deficiency may be victims of such a seldom infection [2–5]. Osteoarticular *Salmonella* infection in immunocompetent persons is very unusual with just few cases reported in the literature [6–16]. It has mostly a haematogenous way of spread [3,10]. Non-typhi serotypes are frequent causative agents [6,7,10]. Whereas primary bone tumours usually have a metaphyseal preference, *Salmonella* osteomyelitis typically involves the diaphyses of long bones as well as the vertebrae [5,9,11,12]. This can be attributed to the increased bone marrow activity and blood degradation products [4,5]. The most common long bones involved are the femur and the humerus [13]. The knee is the most common joint affected by articular infection [9]. Not all patients present with a history of a diarrheal illness or have positive stool cultures [7]. The bacilli may remain quiescent in the reticuloendothelial system or the bowel to be activated later by lowering of the immune response [7,10].

Furthermore, it may take months or years afterwards for the cases to become symptomatic. Lang et al. reported a case in which 2 separate events of osteomyelitis caused by *Salmonella paratyphi C* that occurred at 2 different anatomical sites of the lower limb (left distal tibia and right proximal tibia), 17 years apart [14]. Banky et al. presented a case of *Salmonella virchow* causing a relapsing bone infection at the same site 12 years apart in an otherwise healthy patient [15]. The duration of symptoms can range from a few months to several years. *Salmonella* osteomyelitis tends to be chronic, relapsing and difficult to eradicate [5,14,15].

To my knowledge this is the first report on *Salmonella* metaphyseal tibial affection in an immunocompetent adult resembling an osteolytic bone neoplasm. Only few authors reported other tumour-like presentations of *Salmonella* osteomyelitis. Charosky and Marcove presented a case of S. *paratyphi* osteomyelitis simulating a giant cell tumour [22]. Sanchez et al. reported on a case of *Salmonella* osteomyelitis of the proximal tibial diaphysis presenting as a monoostotic fibrous dysplasia [1]. Bettin et al. described a rare case of *Salmonella* osteomyelitis in the humerus as a differential diagnosis to a malignant bone tumour [23]. Schulze et al. described a case presenting as a primary lymphoma of the whole distal femur in an immunocompromised patient [24].

A successful treatment of osteoarticular *Salmonella* infection usually requires extensive and sometimes multiple debridements in addition to prolonged antibiotic therapy [1,9,23]. The antibiotic treatment should ideally start after obtaining sufficient bacteriological samples. Ampicillin, chloramphenicol, Azithromycin third-generation cephalosporins like ceftriaxone and fluoroquinolones like ciprofloxacin have all been used successfully in these cases [1,9,15]. Fluoroquinolones offer a potent activity against *Salmonella* and a good bone penetration; however, these drugs are to be avoided in children [23]. The use of antibiotic combinations can reduce potential antibiotic resistance [9,25]. Hyperbaric oxygen therapy has also been used as an adjunct [15].

In conclusion, metaphyseal bone infections with non-pyogenic organisms may mimic osteolytic bone tumours as they usually lack laboratory evidence of infection and are not accompanied by the typical periosteal reaction of chronic pyogenic osteomyelitis. These cases, although seldom, should therefore be considered in the differential diagnosis of osteolytic metaphyseal lesions. The clinical diagnosis should be suggested on the basis of infection symptoms in patients who had previous
Salmonellosis, contact with reptiles, ingested snake by-products or weakened immune response.

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