

Isolated tuberculous arthritis of the ankle: a case report and review of the literature

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Abstract

Background: Isolated ankle joint tuberculous arthritis is extremely rare, comprising an incidence lower than 5 % of skeletal tuberculosis (TB).

Description of the case: We present an unusual case of isolated tubercular arthritis of the ankle in a 25-year-old male where the definitive diagnosis was difficult to be reached. The clinical examination revealed slight edema and a slight increase in local skin temperature. Based on magnetic resonance imaging performed, the diagnosis of septic arthritis was made. The arthroscopic appearance of the synovium and polymerase chain reaction analysis (PCR) of the synovial fluid revealed tuberculous arthritis.

Conclusion: TB should be included in the differential diagnosis of inflammatory arthritis in patients with persistent pain and swelling of the ankle. HIPPOKRATIA 2017, 21(2): 97-100.

Keywords: Ankle, infectious arthritis, arthroscopy, tuberculosis

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Introduction

Tuberculosis (TB) is an ancient disease described throughout history^{1,2}. Nowadays, TB still remains a huge health problem worldwide despite newer modalities for diagnosis and treatment of the disease^{3,4}. The most common form of the active disease is the pulmonary TB, which quickly invades other organs⁵. An incidence of 10-20 % of all extrapulmonary TB cases (2 % of all TB infections) represents the skeletal type of the disease⁶. Spinal TB (Pott's disease) accounts for 50 % of skeletal TB⁷, followed by extra-spinal locations in weight-bearing major joints (hip and knee joint), whereas the involvement of foot bones (calcaneus, talus, first metatarsal and navicular bones) is rare (less than 5 %)^{8,9}.

Early diagnosis of TB arthritis of the ankle is essential for the articular cartilage and joint space preservation. The diagnosis of TB arthritis is usually delayed due to lack of awareness, deficiency of typical early radiographic findings, lack of pulmonary involvement, and the potential to mimic other diseases^{10,11}. The presentation of the current case is a reminder that isolated cases of TB may occur in unusual sites of the skeleton; thus physicians should not forget to include the disease in the differential diagnosis of inflammatory arthritis.

Case report

A 25-year-old Caucasian male patient, in good gener-

al health, consulted a physician complaining of stiffness and pain of the right ankle lasting three months accompanied by limping. The pain was occurring during exercise, progressively increased in intensity and subsided only after the use of common analgesics. The patient had no history of fever, loss of appetite or weight loss, night sweats, dysphoric mood or fatigue. On further questioning, he reported a history of two sprains in the right ankle during the preceding three years. No trauma, pain or stiffness in other joints of the body was recorded. The patient has never received Bacille Calmette-Guerin (BCG) vaccination. During clinical examination, edema, loss of motor function and increased skin temperature were noted over the affected ankle joint, but no discoloration. The swelling was centered around the anterior surface of the ankle joint and on the malleoli. The joint was stiff, and movement was painful. No signs or symptoms from other systems or joints were recorded. The anteroposterior and lateral radiographic views of the right ankle joint did not demonstrate osteolytic lesion of the talus and his blood tests showed white blood cell (WBC) 8500/uL, erythrocyte sedimentation rate (ESR) 18 mm/h, C-reactive protein (CRP) 0.56 mg/l, uric acid 5.7 mg/dl, antinuclear antibody test (ANA) and Rheumatoid arthritis (RA)-test were negative, Anti-streptolysin O (ASO) was less than 200 units, Widal, Wright, and HIV tests were negative. The magnetic resonance imaging (MRI) of the right ankle

joint showed inflammation of talus and distal fibular and tibial epiphysis spreading to the metaphysis with synovial thickening and inflammation of the surrounding soft tissues and subcutaneous fat, findings consistent with septic arthritis (Figure 1). Arthroscopic synovial biopsy was carried out in which a sample from the synovial lesions was taken for histopathological examination along with synovial fluid analysis (Figure 2, Figure 3). Although the histopathology findings showed granulomatous arthritis (histiocytes and multinuclear Langerhans-type giant cells with surrounding lymphocytes), the interpretation of laboratory testing in the context of the clinical features gave us the suspicion of TB disease. The performed Mantoux tuberculin skin test was positive with an induration of 22 mm in diameter, 48 hours after the antigen injection. The

patient underwent a chest computed tomography scan (CT), a QuantiFERON-TB Gold In-Tube test (QFT-GIT) and a sputum culture of three specimens in consultation with a pulmonologist. The chest CT, QFT-GIT, and sputum culture were negative for any pulmonary diseases. Conversely, the QFT-GIT was strongly positive and traces of specific DNA sequences of *Mycobacterium tuberculosis* bacilli were found through polymerase chain reaction analysis (PCR) in the three synovial fluid specimens (Xpert MTB/RIF, Cepheid Inc, Sunnyvale, California, USA).

The patient received at the initial phase of his treatment a combination of four anti-TB drugs (300 mg isoniazid and rifampin, and 1.2 g ethambutol and pyrazinamide) given daily for three months, followed by a con-

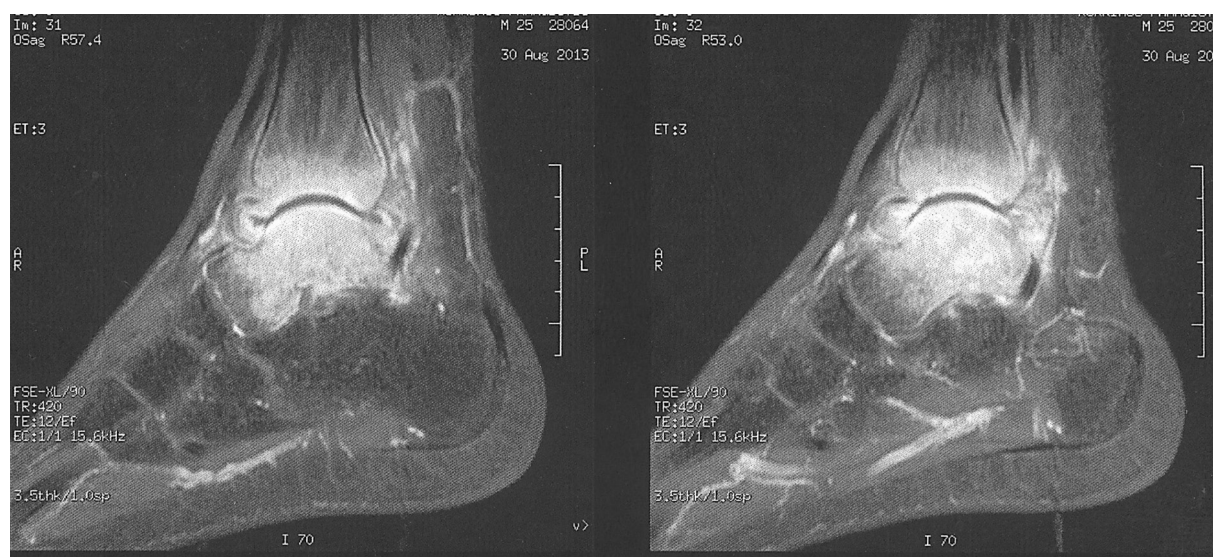


Figure 1: Sagittal view of the magnetic resonance imaging (PDWI) of the patient's ankle joint demonstrating inflammation (bone marrow edema) of the talus and distal tibia epiphysis spreading to metaphysis, synovial thickening, and enhancement as well as inflammation of the surrounding soft tissues and the subcutaneous fat.

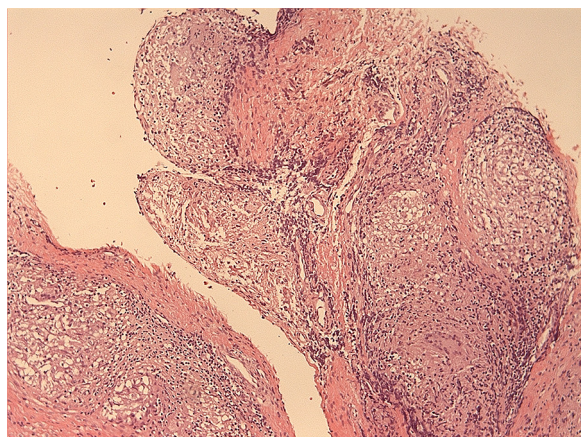


Figure 2: Histopathologic section of synovial membrane and joint capsule of the patient's ankle joint showing multiple granulomas (Hematoxylin & Eosin stain, x 10).

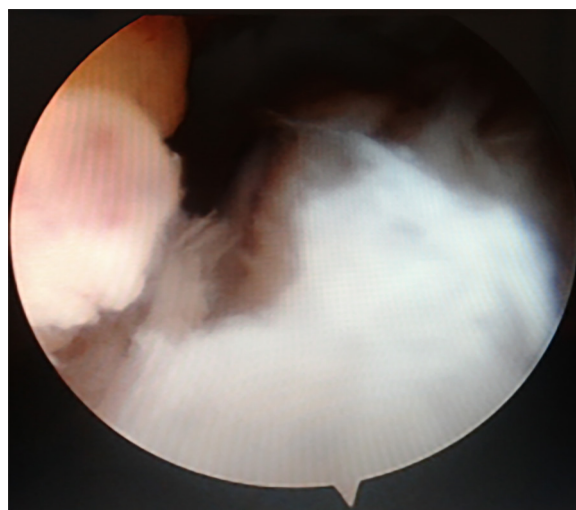


Figure 3: Arthroscopic view of the patient's ankle joint demonstrating synovium hyperemia indicative of inflammation - synovitis.

tinuation phase of isoniazid and rifampin for two months. Local inflammation gradually receded within two months from treatment commencement. Moreover, after a follow-up of two more months a paracentesis was undertaken by another clinician, aspirating excess synovial fluid and the result of this cytopathological examination was negative for *Mycobacterium tuberculosis* bacilli. However, the patient developed a fistula in the anteromedial surface of the foot that, under care by a general surgeon, healed in six weeks. A repeat MRI, eight months after the initial phase of his treatment, still displayed extensive edema of the bone marrow, of the articular surfaces of the tibiotalar joint, additional osteochondral lesions of the joint, joint effusion and joint space narrowing that appeared to have been significantly reduced compared to the previous MRI. These findings confirmed the diagnosis of post-infection arthritis and Sudeck's atrophy (acute bone atrophy due to inflammation). His drugs treatment was subsequently modified to a quadruple regimen of 500 mg levofloxacin in a daily dose and isoniazid, rifampin, and pyrazinamide in their previous doses for 12 additional months. His treatment was supplemented by physiotherapy for ten months to overcome muscle atrophy. Eighteen months after the treatment completion, he has lingering muscle atrophy in the right leg, especially in the gastrocnemius, and slight morning stiffness of the right ankle that recedes quickly.

Discussion

The ankle joint is an unusual location of TB arthritis. In the recent literature, only a few cases with isolated TB of the ankle and talus have been reported. Shams et al reported two patients with mild symptoms of swelling and pain in the ankle that were diagnosed with TB arthritis after synovial cultures and had been treated successfully with an anti-TB regimen¹². Dhillon et al studied 22 cases of TB of the foot, with eight of them being articular TB of the ankle¹³. Fattouh et al treated successfully four patients with articular TB of the ankle with no symptoms or clinical findings from the other systems¹⁴. Choi et al who studied cases from a radiological perspective, reported three cases of isolated TB of the ankle joint¹⁵.

The cause of isolated TB skeletal infections is still controversial, but some theories state that repetitive trauma encourages the local aggregation of macrophages that carry the bacilli that survived the primary infection¹⁶. Although TB infections of the ankle joint have rarely been reported, Gursu et al¹⁶ mention that TB of the foot and ankle may be seen at any age and the tibiotalar joint is the most commonly affected, followed by the talus and calcaneus. The typical symptoms are pain, swelling, and stiffness, while the most important signs of TB arthritis of the ankle include swelling with fullness around malleoli, tendoachilis insertion, and plantar flexion of the ankle joint. A non-healing ulcer with secondary infection may complicate the clinical manifestation of the disease. TB arthritis can be masked by a co-infection with other pathogens, leading to a delay in diagnosis and treatment

of the disease. Any previous trauma or surgery at the joint is a risk factor for TB arthritis¹⁷.

Clinical manifestations include a wide variety of non-specific signs, like stiffness, edema, and painful limitation of the range of motion that makes the early diagnosis of the disease extremely difficult. Skeletal TB may mimic other chronic and acute diseases like osteomyelitis, septic arthritis, actinomycosis, multiple myeloma, or secondary malignant deposits¹⁸. After reviewing cases of TB arthritis of the ankle, X-ray imaging shows non-specific findings, especially on the early stages of the disease¹⁹. Plain radiography of the affected area exhibits peripheral marginal erosion of the joint and space narrowing as the earliest change. The surrounding tissue may show synovitis, joint effusions, tenosynovitis, soft tissue collections or myositis¹⁸. The radiological features of TB arthritis may be similar to those of rheumatoid arthritis, neuropathic joints, sarcoidosis, and neoplasms. Also, the MRI appearance of the said joint bearing periarticular osteoporosis, marginal erosion, and joint space narrowing may be consistent with osteomyelitis, bony tumor, avascular necrosis, or a neuropathic joint¹⁹. Commonly many laboratory tests that detect inflammation are negative. In addition, the TB skin test (Mantoux) and Ziehl-Neelsen stain of synovial fluid may provide both false-negative and false-positive results²⁰. The high incidence of false negative results is due to bacteria- (paucity in the synovial fluid, highly fastidious growth or the impact of previous antibiotic therapy) and sampling-related factors²¹. The clinical history and radiologic findings are still of diagnostic importance when TB is suspected, and histopathologic evaluation provides the definitive confirmation of the diagnosis¹²⁻¹⁴, as in our case. Histopathology of the synovial biopsy is the standard diagnostic technique to identify the causative bacteria of TB arthritis¹³ because no specific clinical or radiologic findings exist¹⁴. In the same manner as in the reported case, the diagnosis may be confirmed with special staining techniques with higher sensitivity and higher predictive value, like PCR and QFT-GIT²².

One-third of the diagnosed osteoarticular TB also had active TB in the lungs²³. In all the cases pertaining osteoarticular TB as diagnosis, the respiratory system must be thoroughly investigated clinically, by utilizing imaging techniques, and by sputum examination with Ziehl-Neelsen stain and culture. As TB is a systemic disease, the differential diagnosis should also employ the use of PCR and QFT-GIT²⁴. In our case, the chest CT, QFT-GIT, and sputum culture were negative for pulmonary disease.

In most reported cases of TB of the foot and ankle, authors emphasized that the diagnostic delay makes surgical intervention necessary. This diagnostic delay is probably caused by the absence of pathognomonic findings specific for the osteoarticular TB and its potential of mimicking other acute and chronic diseases, like a malignant bone or soft tissue tumor, a pyogenic infection, an inflammatory arthritis, an osteochondrosis, and a Charcot arthropathy²⁵.

Conservative treatment with anti-TB drugs includes

isoniazid, rifampicin, pyrazinamide, and ethambutol for two months followed by isoniazid and rifampicin for 16 months. All patients must receive Pyridoxine to prevent neuropathy. Prolonged treatment in osteoarticular TB is justified only in cases of resistance²⁶.

Surgical intervention is justified after failure of the conservative therapy and spread of the disease. In cases of severe joint destruction, debridement of the joint and curettage, resection of destroyed bone, synovectomy, and arthrodesis should be performed^{11,12,27}. In the reported case, during arthroscopy of the ankle joint, a partial synovectomy was undertaken. Follow up with a plain X-ray of the foot and blood tests (liver function) every three months throughout treatment is necessary. Physicians should always be alerted, as TB is not yet eradicated and may affect multiple systems and therefore display a variety of symptoms.

Conclusion

The isolated ankle TB is a diagnostic challenge, due to its rare appearance. Diagnosis is delayed due to lack of specific clinical and radiological signs and non-confirmatory biopsy reports. Delay in diagnosis may further complicate the condition of the disease. Osteoarticular TB of the ankle may be suspected in cases with persistent joint pain and swelling. As the synovial fluid aspiration is doubtful to lead to a definitive diagnosis, a bone biopsy should preferably be taken for histopathological examination. A high index of suspicion and inclusion of TB in the differential diagnosis of inflammatory arthritis is needed to achieve early diagnosis of the disease and appropriate treatment.

Conflict of interest

Authors declare no conflicts of interest.

Acknowledgment

The patient gave written informed consent to present in this case report all the details from his history, clinical examination, test results and images.

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