

## Book Chapter

# Tuberculosis Monoarthritis of the Knee: A Pediatric Case Report

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## Abstract

**Introduction:** The overall incidence of acute septic arthritis is estimated to be 4–10 per 100,000 children in well-resourced countries. *Staphylococcus aureus* and respiratory pathogens are the most common causative agents. Only 3% of global tuberculosis (TB) cases were identified in the European region and 3% in the region of Americas. Bone and joint infection represent just 9% of extrapulmonary TB affection and, overall, for almost 2% of all cases. **Case Report:** We present a case of a 15-year-old boy, born in Guinea Bissau, living in Portugal for nine months, who presented to the Emergency Department, with clinical and laboratory signs of acute knee arthritis. After proper surgical arthroscopic intervention and antibiotic therapy, he was discharged, asymptomatic. One week later, he was readmitted with a relapsed knee arthritis, without other positive clinical findings. At day 7 after intervention, there were imagiological signs of femoral osteomyelitis and although proper surgical and pharmacological intervention, there was no favorable evolution of clinical inflammatory signs. It was decided to perform an arthrotomy and curettage, demanding broader culture test with atypical microorganism studies and mycobacterium TB screening. Despite negative microbiological identification of mycobacterium, there was a positive Interferon Gamma Release Assay test, which forced us to test for intra-articular mycobacterium TB DNA through polymerase chain reaction

(PCR), which was positive, and made it possible to apply an anti-TB regimen with four agents. Conclusion: Although rare in developed countries, monoarthritis TB is difficult to diagnose and treat, demanding a high clinical index of suspicion, crucial to timely and accurately diagnose and treat this condition.

## Keywords

Knee Arthritis; Mycobacterium Tuberculosis; Pediatric

## Introduction

The overall incidence of acute septic arthritis is estimated to be 4–10 per 100,000 children in well-resourced countries. The most commonly affected joints are in the lower extremities: knees, hips, and ankles account for up to 80% of the cases [1]. *Staphylococcus aureus* and respiratory pathogens are the most common causative agents [2].

Approximately 10.0 million people (range, 9.0–11.1 million) developed TB disease in 2017 (5.8 million men, 3.2 million women, and 1.0 million children). Only 6% of global cases were identified in the WHO European Region (3%) and WHO Region of the Americas (3%) [3]. The increased incidence of bone and joint TB in some European countries might be related to migration of certain groups from Africa with a high incidence of TB [4].

Bone and joint infection may account for approximately 9% of cases of extrapulmonary TB and, overall, for almost 2% of all cases of TB. Musculoskeletal TB involves the spine in approximately one-half of patients. Sites more frequently affected are peripheral joints, followed by extra spinal TB osteomyelitis [5].

There is a general lack of publications about tuberculous arthritis especially in developed countries and a substantial part of them are case reports [5,6].

Given the difficulty in diagnosis and adverse outcomes of delayed diagnosis, we present a case of a 15-YEAR-OLD boy, who was diagnosed and treated for monoarticular septic arthritic due to mycobacterium TB.

## Case Report

We present a case of a 15-YEAR-OLD boy, born in Guinea Bissau, living in Portugal for nine months (in a social care institution). Prior medical history of refractory epilepsy and intellectual disability followed by pediatric neurology.

The patient came to the Emergency Department with an uncharacteristic two weeks history of pain and swelling in his left knee, associated with axillary temperature of 37.5°C. No history of trauma or other symptoms found.

At physical examination swelling and increased temperature of the left knee were present, which were painful at passive and active mobilization, with a limited range of motion of 100°–20° (extension–flexion). The remaining joints were assessed and signs of inflammation were excluded. General condition maintained. Meningeal signs and cutaneous lesions were absent. There were no signs or symptoms of respiratory distress or other positive findings.

Plain radiographs of his left knee revealed a moderate knee effusion but were unremarkable for any bony erosion or joint space narrowing (Figures 1 and 2). Laboratory findings included an elevated erythrocyte sedimentation rate 34 mm/h, C-reactive protein 17.6 mg/dL, and platelet count  $227 \times 10^3/\text{mm}^3$ . The complete blood count was normal without evidence of leukocytosis. Given the elevated inflammatory laboratory findings and knee effusion, a knee aspirate was performed in clinic. Synovial fluid aspirated from the joint was turbid and yellow, contained 49,200 total nucleated cells/mm<sup>3</sup>, with 90% neutrophils, lactate dehydrogenase (LDH) 446U/L. The decision was made to perform a knee arthroscopic lavage/debridement and multiple soft tissue samples were obtained for microbial culture as well as histologic examination. Tissue samples taken

intraoperatively were positive for *S. aureus* (methicillin sensitive). He completed a total of 30 day of antibiotic therapy with flucloxacillin [both intravenous (IV) and per os] with clinical and analytic resolution.

One week after being discharged from the pediatric ward he presented in the Emergency Department with complains similar to the first episode, compatible with a relapse knee pyogenic arthritis. A second knee arthroscopy was performed and multiple samples for the most common pathogens were tested as well as histologic examination. Empiric antibiotic therapy was introduced based on anterior antibiogram.

All intraoperatory sample cultures were negative and histologic findings were unspecific compatible with chronic inflammation. At day 7 there was no improvement in clinical status, with increase of inflammatory signs. Plain radiographs were repeated and it was possible to determine a round radiolucent image in the external femoral condyle involving the cortical (Figures 3 and 4). An urgent magnetic resonance exam was performed and it described a lesion located posteriorly and superiorly to the external femoral condyle with bone contact and cortical destruction of undetermined etiology (Figures 5 and 6).

It was performed an open arthrotomy for articular lavage and debridement and X-ray-guided curettage of the admitted osteomyelitis condylar lesion (Figure 7). Bone and synovial samples were tested for atypical pathogens including mycobacterium. Further laboratory tests were performed including human immunodeficiency virus (HIV), hemoglobinopathies, tuberculin, and Interferon- Gamma Release Assays (IGRAs) test. Intra-articular gram stain, aerobic cultures, anaerobic cultures, and acid-fast bacilli culture were negative. Human immunodeficiency virus and tuberculin skin tests were negative. Based on positive IGRAs test, bone samples were tested by PCR, resulting positive for mycobacterium TB. After a positive mycobacterium TB PCR in the bone sample and a positive IGRA test, he began an anti-TB regimen with four agents: Isoniazid (300 mg/day), Rifampicin

(600 mg/day), Pyrazinamide (1000 mg/day), and Ethambutol (600 mg/day).



**Figure 1:** Initial anteroposterior view plain radiograph of left knee, interpreted as without relevant findings.



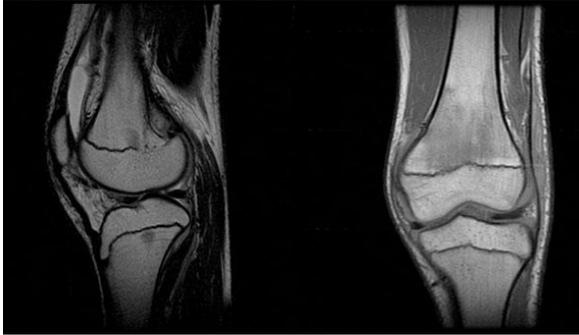
**Figure 2:** Initial lateral view plain radiograph of left knee, interpreted as without relevant findings.



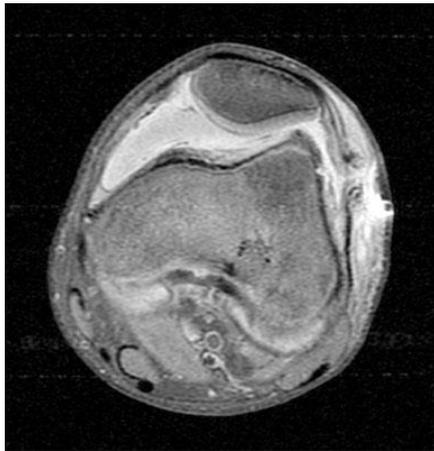
**Figure 3:** Anteroposterior view plain radiograph of left knee, one week after being discharged from hospital—identifiable radiolucent round image in the lateral metaphysis of distal femur.



**Figure 4:** Lateral view plain radiograph of left knee, one week after being discharged from hospital—interpreted as without relevant findings.



**Figure 5:** Magnetic resonance, T2 sagittal and coronal reconstruction. Possible to identify in coronal reconstruction lesion of lateral condyle proximal to physis plate with cortical bone contact and destruction.



**Figure 6:** Magnetic resonance, T2 axial T1 reconstruction. Same lesion of lateral condyle proximal to physis plate with clear cortical bone contact and destruction.



**Figure 7:** Intraoperative X-ray-guided curettage of the admitted osteomyelitis condylar lesion.

After an initial period of two weeks immobilized with an orthotics, he began a daily specific physiotherapy protocol focused in regaining articular range of motion and quadriceps's contractile power.

Both complete spine X-rays, thoracic X-rays, direct examination of mycobacteria in gastric secretions, and cultures for Koch's bacillus in gastric secretions were negative, without any signs of pulmonary or extrapulmonary TB.

The patient was under therapy for 12 months, 2 of them under quadruple therapy with Isoniazide, Rifampin, Pirazinamide, and Ethambutol and 10 months of Isoniazid and Rifampicin, without adverse effects with excellent compliance, with complete resolution of knee inflammatory signs.

Unfortunately, at the last clinical evaluation (two years postoperative) there was no recover of complete range of motion, with painless walking and no periarticular destruction on imagiological controls.

## Discussion

Tuberculosis monoarthritis is a rare form, accounting for just 1–2% of all US TB cases [7, 8]. Mycobacterium TB infection is especially rare in children in the absence of associated pulmonary disease. Disseminated TB that presents as isolated monoarticular arthritis is a rare form, with an estimated incidence of 1–2% within the United States [9].

Synovial fluid analysis is highly unspecific, although very low glucose levels favor the diagnosis of TB. Synovial fluid smear for acid-fat bacilli is positive in only 20–40% of cases [10], remaining the gold standard for laboratory confirmation of TB disease, a positive culture [11]. Even after careful revision, we believe our failure in histological and microbiologic isolation might be related with the residual number of TB cases diagnosed in our center, reflected in unexperienced evaluators.

Different from other causes of septic arthritis, monoarticular TB is characterized by transepiphyseal spread of osteomyelitis, given the ability to cross the epiphysis into the joint space.

Being critical for diagnosis of septic arthritis, isolation of bacteria from synovial fluid should be free from any contamination, since it may provoke unnecessary surgical interventions and antibiotic treatment. Unfortunately, no firm criteria for differentiating contamination from true infection have been identified so far. Recent data suggest an incidence of as high as 5.2% of contaminated synovial fluids [12].

According to some pharmacological studies [13], there is a high and substantiated antituberculin action of some antibiotics, mainly for the beta-lactam antibiotics class, as flucloxacillin. Contrary for believing our patient suffered an initial *S. aureus* arthritis we strongly believe our patient suffered, since the first episode, from a misdiagnosed knee TB, which had a partial and temporary response to beta-lactam antibiotic administration.

In 1924, D.B. Phemister described three the radiographic findings of mycobacteria septic arthritis— Phemister’s triad: (1) periarticular osteoporosis; (2) erosion of subchondral bone; and (3) joint space narrowing representing the destruction of articular cartilage.

Based on radiographic evaluation Martini developed a classification system (Kerri and Martini classification, Table 1) that placed patients into one of the four stages, our patient would be classified into stage I. Radiographic stage at the time of presentation is predictive of overall functional outcome of the affected knee [2,14].

Most cases of monoarthritis TB result of reactivation of latent disease marked by a latency period of 1–3 years. Recurrence of infection does occur in patients treated with medical and surgical management, with rates estimated to be as high as 29% in adult population in endemic countries [14]

**Table 1:** Kerri and Martini radiological classification.

<b>Stage</b>	<b>Radiographic findings</b>
I	Localized osteopenia, no bone lesions, ± soft tissue swelling
II	One or more areas of osseous erosion, without narrowing of the joint space
III	Narrowing of the joint space without gross anatomical disorganization
IV	Narrowing of the joint space with gross anatomical disorganization

## Conclusion

Although rare, monoarthritis TB is difficult to diagnose and treat, which makes a high clinical index of suspicion, a proper clinical history, a correct physical examination, and diagnostic workup so important, in order to timely and accurately diagnose and treat this condition. Consistent follow-up with both orthopedic and infectious disease specialists during a prolonged period of

therapy is essential to guarantee therapy efficacy and to recognize as early as possible treatment failures or complications.

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