

Silent Case of Pediatric Osteoarticular Tuberculosis: A Case Report and Review of the Literature

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Clinical Medicine Insights: Case Reports

Volume 17: 1–4

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DOI: 10.1177/11795476241263683



ABSTRACT

INTRODUCTION: Tuberculosis (TB) is one of the most prevalent infectious diseases globally, often presenting with nonspecific symptoms that can obscure diagnosis, especially when it manifests in uncommon sites such as osteoarticular tuberculosis (OA-TB).

CASE PRESENTATION: We report a rare case of a 9-year-old male diagnosed with right knee tuberculosis after enduring severe symptoms for several months. Despite multiple negative biopsies and aspirates during initial debridement surgeries, a biopsy taken 6 months later confirmed the presence of *Mycobacterium tuberculosis* (MTB). The patient was subsequently treated with debridement and anti-tubercular therapy.

CONCLUSION: This case underscores the critical need to consider tuberculosis in patients presenting with chronic bone pain to avoid misdiagnosis, particularly in the developing world. The atypical presentation of osteoarticular tuberculosis in this young patient emphasizes the need for healthcare professionals to recognize subtle symptoms. Advanced imaging studies like MRI and microbiological evaluations, including site biopsies, are essential for accurate diagnosis. Increased awareness and collaborative research are crucial to improving the understanding and management of pediatric osteoarticular tuberculosis and extrapulmonary tuberculosis.

KEYWORDS: Knee, tuberculosis, pediatric, osteoarticular tuberculosis, chronic pain

RECEIVED: February 5, 2024. **ACCEPTED:** June 6, 2024.

TYPE: Case Report

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Introduction

Extrapulmonary tuberculosis (EPTB) is defined as a *Mycobacterium tuberculosis* (MTB) infection affecting tissues and organs outside the lung parenchyma. EPTB cases account for 20% to 25% of all tuberculosis cases.¹ Osteoarticular infections (OAIs) account for 10% to 20% of extrapulmonary *Mycobacterium tuberculosis* complex infections in children, 5% to 6% of all pediatric extrapulmonary cases, and 1% to 2% of all pediatric tuberculosis infections.²⁻⁴

Pediatric patients are at higher risk than adults of progressing to tuberculosis disease and developing disseminated and extrapulmonary forms of the disease.⁵ Moreover, pediatric osteoarticular tuberculosis disease can affect any part of the knee joint, either the synovium, epiphysis, or metaphysis, with a preference for the epiphyseal region, which includes the proximal tibia and distal femur.³

Osteoarticular tuberculosis (OA-TB) symptoms are not specific; therefore, many differential diagnoses should be in mind before confirming the diagnosis, especially those with suppurative etiologies like pathological fractures, non-unions, dislocations, arthritis, ankylosis, instability, limb deformity, osteomyelitis, neurological deficits, avascular necrosis, and infections such as fungal, brucellosis, sarcoidosis, and leprosy.³ All of them can be mistaken for OA-TB because their clinical, radiological, and laboratory signs are often the same.

We present a rare case of a 9-year-old male patient presenting after falling down and experiencing pain in the same injured knee for months. Imaging studies revealed an osseous lesion at the distal metaphysis with growth plate and epiphyseal involvement. A review of the demographic, clinical, diagnostic, and therapeutic features of the case was described. Patient informed consent was obtained for this report.

Case Report

A 9-year-old boy, medically free, presented to the emergency department (ED), complaining of severe right knee pain for 1 day after falling down. The patient had a progressive onset of discomfort in the right knee over the course of many months, which was exacerbated after the fall. The pain was associated with episodes of fever reaching 38.5°Celsius and general weakness. The constitutional symptoms included weight loss, loss of appetite, night sweats, malaise, and fatigue. Notably, there was no documented history of prior pulmonary or extrapulmonary tuberculosis, and there was no family history of tuberculosis.

On physical examination, there was right knee swelling and tenderness without redness or hotness. The patient was able to bear his weight. There was no movement restriction and there was a full range of motion upon physical examination of the hip and knee joints.





Figure 1. (A) Anterior posterior and (B) lateral radiographs of the right knee joint at the initial visit showing osseous lesion at the distal metaphysis.

A knee X-ray was done, and showed an osseous lesion at the distal metaphysis (Figure 1). A full blood test was done when the patient was admitted. The results showed that the hemoglobin level was 12 g/dL, the white blood cell (WBC) level was 8500 μ L (neutrophils 57%), the erythrocyte sedimentation rate (ESR) was 60 mm/h, and the C-reactive protein (CRP) level was 17.2 mg/L. A chest X-ray was performed, and the results were normal. The patient was given analgesics for pain relief and admitted to the Jordan University Hospital (JUH) for magnetic resonance imaging (MRI) with contrast.

Right knee MRI with contrast was done on the next day and showed an osseous lesion at the distal metaphysis with growth plate and epiphyseal involvement along with cortical breach and fistula formation (Figure 2).

The patient underwent an incision and drainage procedure for the lesion located in the distal femur and the knee joint. In the operative setting, purulent material was observed and evacuated following the incision of the femoral canal and knee joint. Culture specimens were collected, and tissue samples were submitted for staining to detect acid-fast bacilli. Additionally, microscopy, culture, sensitivity testing, and tuberculosis polymerase chain reaction (TB PCR) analyses were requested. Fungal KOH smears were also performed and were negative. Following the procedure, the patient initiated a therapeutic regimen comprising ticoplanin and imipenem/cilastatin.

The histopathological reports from the surgically extricated tissue and pus showed signs of acute and chronic inflammation. The TB PCR was negative, and all cultures were negative for *Mycobacterium tuberculosis*. All tests, including those for Brucella titer, familial Mediterranean fever (FMF), rheumatic fever, and viral workup, came out negative. A new MRI was done, which showed residual infectious processes.

After 1 month of antibiotics, the patient was discharged home. CRP and ESR measurements at discharge were 3.7 mg/L and 42 mm/h, respectively.

After 5 months, the patient presented again to the outpatient clinic, complaining of the same knee pain and swelling.

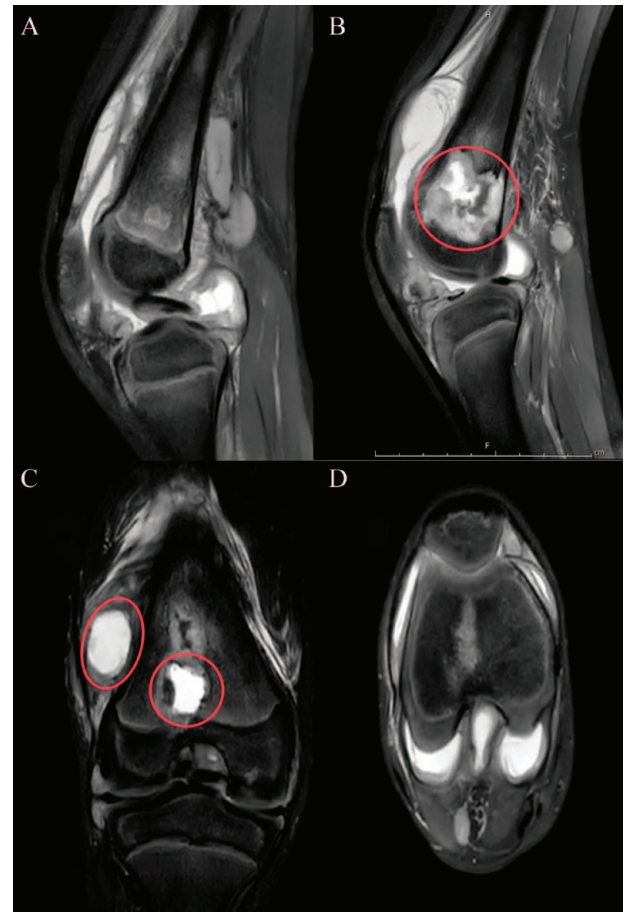


Figure 2. Right knee magnetic resonance imaging (MRI) with contrast showing an osseous lesion at the distal metaphysis with growth plate and epiphyseal involvement along with cortical breach and fistula formation. (A) Sagittal cut T2 magnetic resonance imaging (MRI) shows effusion in knee joint; (B) Sagittal cut T2 MRI shows lesion in metaphyseal area of distal femur lateral side; (C) Coronal cut lesion in distal femur metaphyseal area affecting the physis and localized collection in gutter; (D) Axial cut shows knee effusion.

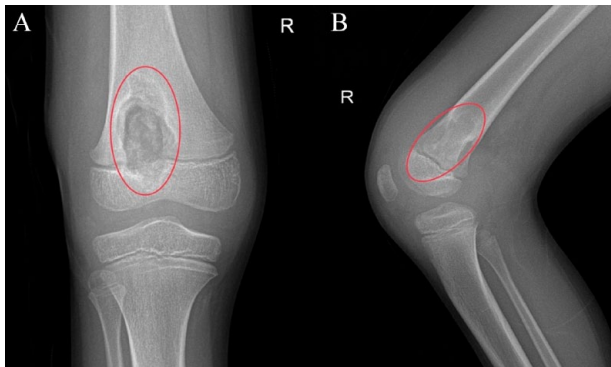
Blood tests were performed, and the results were as follows: CRP 2.5 mg/L, ESR 14 mm/h, and WBC 5000 μ L (lymphocytes 52%). Recurrent knee aspiration was done outside JUH and once in our department, with a large amount of synovial fluid cleared.

After 1 month, he came again to the outpatient clinic complaining of the same symptoms with restricted flexion about 90 degrees, limited extension on 10°, a CRP of 15.7 mg/L, an ESR of 68 mm/h, and a WBC of 10 000 μ L (lymphocytes 31% and neutrophils 60%), and he was admitted again. A new X-ray were done (Figures 3). Table 1 demonstrate a summary of the laboratory results since the initial visit.

He underwent incision and drainage again, and culture and tissues with a cheese-like appearance were sent for staining for acid-fast bacilli (Figure 4). The culture results showed that neither bacteria nor fungi could grow, but the Ziehl-Nelsen stain showed necrotizing granulomatous inflammatory tissue with strains of acid-fast bacilli. After that, the diagnosis of osteoarticular tuberculosis was confirmed, and the patient was started on multiple anti-tubercular therapies with isoniazid, rifampicin, pyrazinamide, and ethambutol, besides the conservative treatment.

Table 1. Laboratory investigation summary since the initial admission.

TEST NAME	ON INITIAL ADMISSION	ON DISCHARGE	AFTER 5 MONTHS	AFTER 1 MONTH
Hemoglobin, g/dL	12	—	—	—
White blood cell, per mm ³	8500 (neutrophils 57%)	—	5000 (lymphocytes 52%)	10 000 (neutrophils 60%)
Erythrocyte sedimentation rate, mm/h	60	42	14	68
C-reactive protein, mg/L	17.2	3.7	2.5	15.7

**Figure 3.** (A) Anterior posterior and (B) lateral radiographs of the right knee joint at the follow-up showing an increase in the size of the lesion and a well-defined lytic lesion on the metaphyseal area of the distal femur, crossing the physis toward the epiphysis.

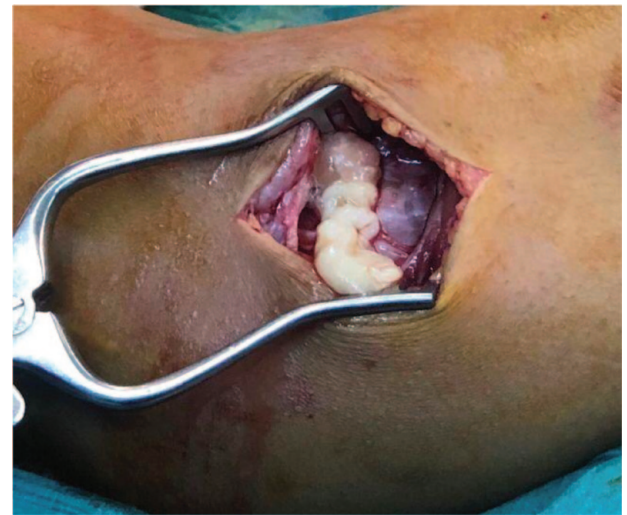
At his most recent appointment, which was 8 months after his previous one, the patient continued to complain of a minor ache that gets worse with strenuous activity, such as playing with friends or biking, but goes away with rest without the need for medication. Otherwise, he is doing well with no other symptoms or complications.

Discussion

The significance of our case is that it highlights the masked, atypical symptoms of pediatric osteoarticular tuberculosis as a minor chief complaint in a young patient who came to the ED complaining of severe pain after falling down. This emphasizes the importance of examining unusual chronic symptoms at a young age, such as intermittent episodes of fever, arthralgia, general fatigue and weakness, or joint swelling that is not caused by trauma or other known causes, as they may be indolent in the aftermath of a massive disaster.

Osteoarticular tuberculosis affects the pediatric age group more frequently than it does in adults; this can be related to the higher amount of bone marrow in immature bones.⁶ The diagnosis is often delayed because of the disease's nonspecific symptoms, like wasting of regional muscles, joint swelling, effusion, and tenderness. In addition to the non-characteristic imaging findings and lack of awareness of the condition in our scenario. In up to 25% of patients, delayed detection and treatment lead to a poor prognosis and death.⁷

The classical regional presentation of OA-TB in pediatrics includes the shoulder, which is less common in the pediatric age group.³ The elbow, which is more common and more

**Figure 4.** Postoperatively following a second incision and drainage.

advanced at the time of diagnosis.⁸ The wrist, hand, and hip joint, which is brought to attention by referred pain in the knee region.³ Besides the foot, ankle joints, and spine, the knee joint is considered the third most frequent location of osteoarticular tuberculosis, and patients often seek help early due to the superficial location of the joint.⁶ However, delayed diagnosis can lead to subluxation deformities in the knee joint, including flexion, internal rotation, and posterior subluxation.⁶

Early diagnosis and effective anti-tubercular treatment (ATT), which remains the gold standard treatment, are usually critical for full recovery and decrease morbidity and mortality rates. Although acid-fast bacilli culture takes a long time and has low sensitivity, it remains the gold standard for TB diagnosis; however, newer deoxyribonucleic acid (DNA)-based PCR and DNA detection methods have been shown to be more sensitive, specific, and faster.^{9,10} In Jordan, the high rates of antibiotic resistance, exacerbated by the widespread misuse and overuse of antibiotics, pose significant challenges in managing infections effectively. This issue necessitates the empirical use of high-order antibiotics to ensure adequate treatment coverage. A study on drug resistance in Jordan, highlights the prevalence of antibiotic resistance in the region, emphasizing the urgent need for optimizing the utilization of antibiotics and antimicrobial control programs.¹¹ Consequently, the empirical use of advanced antibiotics, such as ticoplanin and imipenem/cilastatin, was deemed necessary in this case to address potential resistant pathogens and ensure effective initial management.

Besides the OA-TB diagnosis being silent and ambiguous, the more challenging problem is our poor understanding when it comes to the management. The most important aspect of the treatment is choosing the correct course of anti-tubercular drugs due to the massive arising issue of multi-drug resistant tuberculosis, which is defined as MTB that is resistant to both isoniazid and rifampicin, regardless of other susceptibilities.^{12,13} One of the recommended treatment regimens for OA-TB is a minimum of 3 drugs, including isoniazid, rifampin, pyrazinamide, and streptomycin or ethambutol, to which MTB is susceptible, and at least one of these drugs must be bactericidal.¹³ Other studies recommend a therapy with 4 drugs, since the frequency of isoniazid resistance, for a duration of at least 9 months and longer in immunocompromised patients.¹⁴ According to the latest World Health Organization (WHO) guidelines, the recommended period of treatment for osteoarticular tuberculosis in children is 12 months, consisting of a 4-drug regimen using isoniazid, rifampin, pyrazinamide, and ethambutol for the first 2 months and followed by a 2-drug regimen using isoniazid, rifampin for the following 10 months.¹⁵ The optimal duration of therapy for OA-TB treatment is uncertain.

Approximately 90% to 95% of patients heal without sequelae if treated at an early stage, since the results of non-treatment or delays in treatment can be debilitating and contribute to an increase in the mortality rate.^{12,16-18} In addition to medical therapy, conservative treatment produces good results in the vast majority of cases. The role of surgery is mainly to collect tissue and reach the diagnosis.³ Moreover, surgery is reserved for select indications in around a quarter of the patients.⁴ These indications include decompressing bulky abscesses, patients not responding to medical therapy, and correcting limb deformities.^{3,18}

Conclusion

This case report highlights the significance of including tuberculosis in the differential diagnosis of chronic bone pain, particularly in pediatric patients. The presented case highlights the unusual manifestation of osteoarticular tuberculosis in a young individual and emphasizes the need of recognizing mild symptoms, such as intermittent fever and joint swelling, that may not be associated with injury.

Pediatric osteoarticular tuberculosis poses diagnostic challenges due to its nonspecific symptoms and delayed detection, often resulting in a poor prognosis. Early diagnosis and prompt initiation of anti-tubercular therapy are crucial for favorable outcomes. The case discussed here exhibited a delayed diagnosis, highlighting the need for increased awareness among healthcare practitioners. Hence, maintaining a high index of suspicion for tuberculosis in patients with persistent musculoskeletal symptoms is crucial, especially in regions with a higher prevalence of the disease. Collaborative efforts and research initiatives are necessary to improve our knowledge and clinical approach to pediatric osteoarticular tuberculosis and extrapulmonary tuberculosis in general.

Author Contributions

Mohammad Ali Alshrouf: supervision, data collection, literature review, manuscript preparation, revision, and editing.

Zuhdi O Elifranji: concept, image interpretation, supervision, and revision.

Sereen Halayqeh: literature review and manuscript preparation.

Munther Al-Saber: concept, image interpretation, and revision.

Abdulrahman M Karam: literature review, manuscript preparation, revision, and editing.

Availability of Data and Materials

This article has no new data were created in this study.

Ethics Approval and Consent to Participate

The study was performed in accordance with the Declaration of Helsinki. Written consent taken from the patient's legally authorized representative to publish data.

Consent for Publication

The study did not disclose any individual details, images, or videos.

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