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TIBIAL OSTEITIS CAUSED BY MYCOBACTERIUM TUBERCULOSIS A CASE
REPORT

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--Manuscript Draft--

CONFIDENTIAL

TIBIAL OSTEITIS CAUSED BY MYCOBACTERIUM TUBERCULOSIS:

A CASE REPORT

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1119

Keywords: tuberculosis, tibia, PCR

ABSTRACT

Tuberculosis is a major scourge, posing a serious public health problem in countries where it is endemic. Osteoarticular involvement accounts for 3 to 5% of all tuberculosis cases and 10 to 15% of extrapulmonary tuberculosis cases. We report a case of tibial osteitis caused by *Mycobacterium tuberculosis* in a 52-year-old female patient who presented to the trauma department at the Mohammed V Military Teaching Hospital with a painful swelling of the lower part of her left leg. Standard X-rays and computed tomography (CT) scans revealed bone involvement, specifically in the tibia. In an endemic context, any persistent and atypical bone lesion should raise suspicion of osteoarticular tuberculosis to enable rapid diagnosis and appropriate therapeutic management. In the absence of other suggestive pulmonary or extrapulmonary lesions, the diagnosis also relies on the exclusion of other pathologies, such as malignant tumors, which may present with similar clinical and radiological features.

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26 ¹
DATA SUMMARY

27 No data were reused or generated in this study.

28 **INTRODUCTION**

29 Tuberculosis is a significant public health issue, particularly in countries where it is
30 endemic. Although pulmonary tuberculosis is the most well-known form, osteoarticular
31 tuberculosis represents a considerable portion of the disease. It is a relatively common form,
32 accounting for approximately 3 to 5% of all tuberculosis cases and 35 to 50% of extrapulmonary
33 tuberculosis cases worldwide (1). It is characterized by an infection that may affect various
34 bones, joints, the synovium, and the spine. This is a serious condition that can lead to bone
35 destruction. The presentation is often atypical, sometimes mimicking severe conditions such as
36 malignant tumors (2).

37 Tibial tuberculous osteitis is a specific infection of the tibia caused by the Koch bacillus
38 (*Mycobacterium tuberculosis*), which is characterized by persistent pain in the tibia, often
39 insidious and progressive, localized swelling, and systemic symptoms such as fever, weight
40 loss, and fatigue, although these may be absent in chronic cases. Medical imaging reveals
41 characteristic bone lesions, such as cavities or bone sequestra, and bone biopsy confirms the
42 diagnosis by identifying, through molecular biology techniques, the presence of tuberculous
43 bacilli in the bone tissue (3).

44 ¹⁵
We report here the case of a 52-year-old woman with tuberculosis of the lower part of
45 her left leg, presenting as a bone tumor, an atypical manifestation rarely seen in the literature.

46 **CASE REPORT**

47 ¹⁰
This case involves a 52-year-old woman with no significant medical history and no
48 known tuberculosis contact, admitted due to the presence of a mass on her left leg that had been
49 progressing for a year, with no history of trauma. The initial symptoms included a tingling pain,
50 worsening at night and exacerbated by movement of the affected leg. The pain was initially

51 relieved by analgesics, leading her to consult a rheumatologist, where she received treatment
52 without success. Due to the persistence of symptoms, ¹⁷ the patient was referred to the trauma
53 department for further management.

54 On questioning, the patient appeared to be in good general condition. She reported no
55 general symptoms of infection and no specific ² signs of tuberculosis such as fatigue, fever, or
56 night sweats.

57 During clinical examination, the patient was afebrile, with normocolored conjunctivae,
58 and no signs of systemic infection were noted. A hard, painful swelling was noted on the distal
59 part of the left leg, localized over the tibia, along with swelling of the ankle without
60 inflammatory signs. Given the presentation, the differential diagnoses included neoplastic
61 pathology and other non-specific infections. However, the absence of typical malignant features
62 on imaging and the identification of characteristic lesions helped narrow the diagnosis to
63 osteoarticular tuberculosis.

64 Respiratory examination revealed clear pleuropulmonary sounds, with an oxygen
65 saturation of 94%. ¹ There were no signs of respiratory distress or paradoxical breathing.

66 Cardiovascular examination showed that ² the patient was hemodynamically stable
67 (120/50 mmHg) ¹ with no signs of hypoperfusion, a regular and strong pulse, and a heart rate of
68 74 bpm. Cardiac auscultation revealed normal heart sounds (B1 and B2).

69 ¹ Neurologically, the patient was conscious (Glasgow Coma Score ¹ 15/15), well-oriented
70 ¹ in time and space, and exhibited no sensory or motor deficits. Pupils were equal and reactive.

71 Blood tests showed no abnormalities. Activated partial thromboplastin time (aPTT) was
72 normal at 1.0, and the prothrombin rate (PT) was 63% (normal range: 70-100%). Kidney
73 function tests were normal, with a urea level of 0.17 g/L (normal: 0.15-0.38 g/L), and creatinine
74 was slightly low at 5 mg/L, equivalent to 44.25 μmol/L (normal: 53-115 μmol/L). ⁴ The elevated
75 C-reactive protein (CRP) level of 24.2 mg/L suggests an inflammatory process, consistent with

76 the clinical and radiological findings. There were no electrolyte imbalances on ¹ the blood
77 chemistry panel, and liver function was normal with aspartate aminotransferase (AST) at 34
78 IU/L and alanine aminotransferase (ALT) at 17 IU/L. Serological tests for HBV, HCV, and HIV
79 were negative. Rheumatoid factor and antinuclear antibodies were also negative.

80 Radiologically, standard X-rays of the left leg (anteroposterior and lateral views)
81 revealed an osteolytic or osteosclerotic lesion in the lower diaphyseal-metaphyseal-epiphyseal
82 region of the tibia, with associated periosteal reaction in a “flame” pattern, and minor
83 osteosclerosis of the distal phalanx of the great toe, without cortical bone rupture (Figure 1).

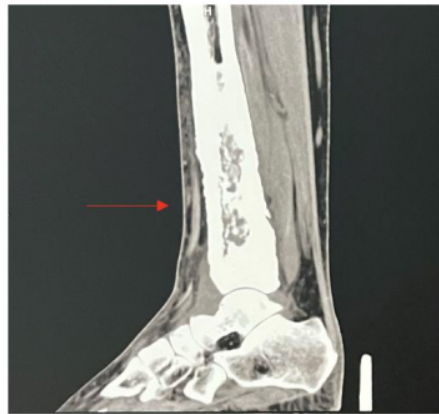


84 *Figure 1: Standard X-ray of the left leg, frontal (a) and lateral (b) views showing a marked*
85 *osteosclerosis (indicated by the red arrow) in the distal tibial region.*

86 Computed tomography (CT) and magnetic resonance imaging (MRI) of the left leg
87 revealed an effusion in the talocrural joint with diffuse synovial thickening enhanced by contrast
88 injection (Figure 2) (Figure 3).



89 *Figure 2: Volumetric reconstruction on CT scan of the left leg showing the synovial*
90 *thickening (red arrows))*



91
92 *Figure 3: Volumetric reconstructions on CT scan of the left leg with synovial thickening (red*
93 *arrow).*

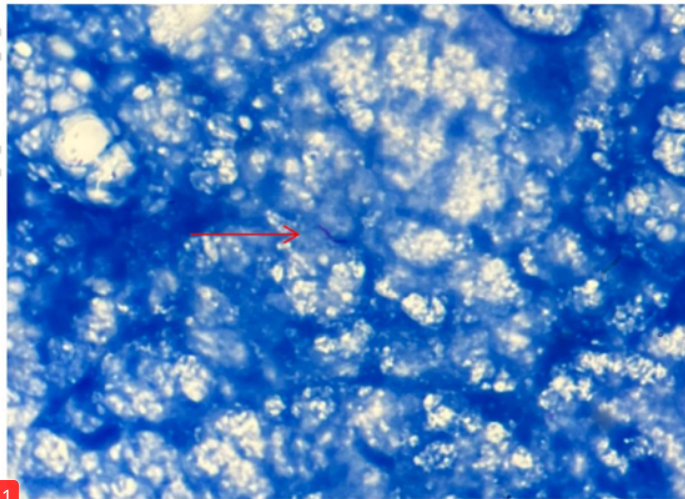
94 A frontal chest X-ray showed a consolidation focus in the upper third of the right lung
95 field.

96 A thoracoabdominal-pelvic CT scan was also performed to investigate the primary
97 lesion and revealed a superinfected bronchiectasis focus and splenic lesions suggestive of
98 secondary involvement.

99 A biopsy was performed by the trauma department to obtain a tissue sample. This
100 procedure aimed to allow histological and microbiological analysis to confirm the diagnosis,
101 determine the nature of the lesion, and identify the presence of bacteria such as Mycobacterium
102 tuberculosis. The biopsy results will guide appropriate treatment and help assess the severity of
103 the condition.

104 **RESULTS**

105 Bacteriological examination of the bone biopsy revealed acid-fast bacilli (AFB) on
106 direct Ziehl-Neelsen staining (1 to 10 AFB per 100 fields), confirming the presence of
107 Mycobacterium tuberculosis (Figure 4). The culture on Löwenstein-Jensen solid medium and
108 in liquid MGIT medium became positive on days 21 and 14, respectively, further supporting
109 the diagnosis. Real-time PCR (GeneXpert MTB/RIF®, Cepheid) detected the Mycobacterium
110 tuberculosis complex at a low level. Importantly, the test did not detect rifampicin resistance,
111 providing crucial information for treatment planning.



112 **1** Figure 4: Acid-fast bacilli detected on direct examination using Ziehl-Neelsen staining (red
113 arrow).

114 Histopathological examination revealed caseating granulomas, which are characteristic
115 of Mycobacterium tuberculosis infection. These granulomas were surrounded by a

116 granulomatous inflammatory reaction with prominent lymphocytic and macrophagic infiltrates,
117 indicating a strong immune response consistent with a tuberculous infection.

118 The diagnosis of tibial tuberculous osteitis was established based on clinical,
119 radiological, microbiological, and histopathological findings, ruling out other causes of osteitis
120 and bone infection.

121 After the detection of the Mycobacterium tuberculosis complex, the patient was started
122 on a therapeutic regimen similar to that used for pulmonary tuberculosis, but adapted with an
123 extended duration due to bone involvement. For the first two months, a daily four-drug regimen
124 was administered, including Isoniazid (INH) at 5 mg/kg/day, Rifampicin (RIF) at 10 mg/kg/day,
125 Pyrazinamide (PZA) at 25 mg/kg/day, and Ethambutol (EMB) at 15-25 mg/kg/day. After this
126 initial phase, the treatment continued with a two-drug regimen of Isoniazid and Rifampicin for
127 an additional 7 months, bringing the total treatment duration to 9 months. This extended
128 duration is necessary to ensure the complete eradication of the bone infection. The diagnosis of
129 tibial tuberculous osteitis was confirmed based on the integration of clinical, radiological,
130 microbiological, and histopathological findings. With the confirmation of Mycobacterium
131 tuberculosis, the patient was promptly initiated on a tailored treatment regimen, ensuring
132 comprehensive management of the bone infection.

133 **DISCUSSION**

134 Tuberculosis remains a major public health issue, particularly in developing countries
135 where it is endemic, such as Morocco (4)(5). Among the extrapulmonary forms, tuberculous
136 osteitis is a relatively common manifestation, often complicating other forms of tuberculosis
137 such as Pott's disease or tuberculous arthritis (3). It is usually chronic, with a long diagnostic
138 delay, and manifests as slowly worsening pain and/or swelling (6).

139 Tuberculous osteitis is often diagnosed late due to its slow progression and nonspecific
140 symptoms, which can resemble other conditions. In countries with high TB endemicity, such as
141 ours, the lack of awareness of bone tuberculosis may contribute to delays in diagnosis (7).

142 Standard radiography may be normal in the early stages or reveal nonspecific images
143 such as osteolysis, periosteal reaction, soft tissue opacity, or pathological fracture (8). In 1920,
144 Jungling described a finely rimmed lacunar image of osteocondensation, referring to it as
145 pseudocystic multiple tuberculous osteitis (9). The presence of bone sequestra, forming a
146 "rattle" image, may cause diagnostic confusion with bone tumors (3).

147 Computed tomography (CT) is an excellent tool for delineating bone involvement and
148 soft tissue abscess extension. MRI is likely more sensitive for detecting early bone marrow
149 edema and soft tissue involvement.

150 Polymerase chain reaction (PCR) offers 100% specificity for detecting mycobacterial
151 DNA, making it an invaluable tool for rapid diagnosis. However, direct Ziehl-Neelsen staining
152 can often yield negative results due to the paucibacillary nature of the lesions, which makes
153 PCR even more crucial for confirming the diagnosis (10). In our case, direct examination after
154 Ziehl-Neelsen staining revealed positive results.

155 Diagnosing tuberculous osteitis is challenging in the absence of suggestive pulmonary
156 or extrapulmonary lesions, particularly since other diseases, such as malignant tumors, can
157 present with similar clinical and radiological features (11). Therefore, a bone biopsy is generally
158 indicated to establish a histological diagnosis by identifying ⁴ epithelioid giant-cell granulomas
159 with caseous necrosis.

160 The treatment ⁵ for tuberculous osteitis involves a combined medical and surgical
161 approach. The standard regimen consists of rifampicin, isoniazid, pyrazinamide, and
162 ethambutol for the first two months, followed by a maintenance regimen with rifampicin and
163 isoniazid for an additional seven months. This extended treatment is critical to eradicate the

164 infection completely, particularly in bone lesions, which require prolonged therapy for effective
165 healing. Surgical intervention is generally conservative and reserved for complications such as
166 soft tissue abscesses, fistula tracts, or the need for bone debridement in cases of extensive
167 infection. Orthopedic management, such as immobilization, is used to manage pain and prevent
168 deformities (12). With appropriate treatment, the prognosis for tuberculous osteitis is generally
169 favorable. However, ¹⁸ early diagnosis and prompt initiation of therapy are crucial to prevent bone
170 destruction and long-term complications, ensuring better outcomes for patients (13).

171 **CONCLUSION**

172 In conclusion, osteoarticular tuberculosis presents significant diagnostic and therapeutic
173 challenges, particularly in developing countries like Morocco, where it remains endemic. The
174 often nonspecific presentation of this disease necessitates increased vigilance and a rigorous
175 diagnostic approach, including radiological, bacteriological, and histopathological
176 examinations. Early and accurate diagnosis, combined with appropriate management, which
177 includes both medical treatment and selective surgical interventions, is crucial for improving
178 clinical outcomes. Multidisciplinary coordination, particularly among microbiologists,
179 radiologists, and clinicians, is essential for the timely and effective management of this complex
180 pathology.

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183 **Author contributions**

184 M.B. contributed to the initial drafting of the manuscript, while B.E. and B.Y. revised it
185 critically for important intellectual content. M.C. ¹ provided final approval for the version to be
186 published.

187 **Conflicts of interest**

188 The authors declare no competing interests.

189 **Consent to publish**

190 Written informed consent was obtained from the patient to publish this report in accordance
191 with the journal's patient consent policy. The patient agreed to the publication of her personal
192 and medical details, including her name and other identifying information, in this article.

193 **Institutional Review Board Statement**

194 The study was conducted in accordance with the Declaration of Helsinki and was
195 approved by the Ethics Committee of Mohammed V Military Teaching Hospital/Faculty of
196 Medicine and Pharmacy (protocol code 3596; approval date: 24 June 2024)

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