Tuberculosis osteomyelitis of the tibia mimicking Brodie abscess: A case report and review of the literature

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Abstract
Background: Tuberculosis osteomyelitis is rarely seen in the diaphyseal bones. It may be confused with Brodie’s abscess due to similar clinical, radiological and laboratory findings. Late diagnosis of the disease causes bone destruction. Tuberculosis osteomyelitis of the bone is a rare condition caused by the Mycobacterium tuberculosis. Its incidence has increased in Western countries in recent years due to HIV infection, increasing elderly population and emerging resistant strains. The slow progress of tuberculous osteomyelitis, due to lack of significant elevations in the laboratory values and changes in the radiographic appearance, often leads to confusion with the subtypes of subacute osteomyelitis, defined as Brodie’s abscess. These two low-virulence clinical cases often lead to delays in diagnosis and progressive bone destruction.

Case presentation: We report a 65-year-old male patient who presented to our clinic with pain, swelling and sensitivity in the left leg. Diagnosed with infection in the tibia, the patient had undergone antibiotherapy. However, the patient’s symptoms were not resolved and we performed bone curettage and cementation. M. tuberculosis-specific DNA was detected by real-time polymerase chain reaction and the M. tuberculosis complex was produced from the perioperative samples.

Conclusion: In conclusion, histopathological examination and polymerase chain reaction are essential before surgery of subacute and chronic osteomyelitis with atypical clinical, laboratory and radiological findings for early diagnosis and accurate treatment.

Keywords
Brodie’s abscess, real-time polymerase chain reaction, tibial diaphyseal osteomyelitis, tuberculous osteomyelitis

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Background
Tuberculosis osteomyelitis of the bone is a rare condition caused by the Mycobacterium tuberculosis. Although relatively it is seen more frequently in Asian countries, in recent years, its incidence has increased in Western countries due to HIV infection, increasing elderly population and emerging resistant strains. According to the 2017 World Health Organization report, 6.3 million new tuberculosis cases and 1.6 million deaths due to tuberculosis have been reported in 2016.

In 75% of tuberculous osteomyelitis cases, causative pathogen in the lungs is spread via hematogenous ways. Lung lesions on radiographs are seen in only 47% of the patients with skeletal involvement, and in only 27% of the patients with active tuberculosis. Although the skeletal system involvement is often seen in the joints, soft tissues, vertebrae, pelvis, phalanges, metacarpals, the long bones, ribs, the sternum, the skull and the patella, carpal and tarsal bone involvement may also be seen. In general, in order to support the hematogenous spread, as in osteomyelitis, tuberculosis involvement in children is usually seen in the metaphyseal region of the long bones compared to the diaphyseal region. The femur and the tibia are the most affected long bones.
the adult population, however, involvement of the axial bones and the pelvis is more frequent.\(^5\)

The slow progress of tuberculous osteomyelitis, due to lack of significant elevations in the laboratory values and changes in the radiographic appearance, may be confused with the subtypes of subacute osteomyelitis, defined as Brodie’s abscess.\(^1,6\) These two low-virulence clinical cases often lead to delays in diagnosis and progressive bone destruction.\(^1,2,4\)

In this study, we present a case of tuberculosis osteomyelitis in the tibia mimicking Brodie’s abscess and draw attention to the difficulties in diagnosis.

**Case presentation**

A 65-year-old male patient presented to our clinic with pain, swelling and sensitivity in the left leg. The patient had experienced a trauma to the same leg 12 years ago, but did not develop any impairments in the integrity of the skin. A year after the trauma, he experienced pain, swelling and sinus leakage. Diagnosed with bone infection, the patient had undergone antibiotherapy. Complaints of the patient have increased in the last 6 months with occasionally increasing pain. Chronic sinus orifice, pain, edema and minimal temperature increase were observed in the medial leg at the diaphyseal-metaphyseal junctional region of the tibia during physical examination. No fever was detected.

The patient was a laborer in the low–middle range income level. He was a smoker and had chronic kidney problems. He had received Bacillus Calmette–Guérin (BCG) injections, and his family had no history of tuberculosis. Appearance of sequelae lesion in the lung radiographs and calcification and pleural thickness in the thorax on the computed tomography (CT) images were observed. Erythrocyte sedimentation rate, C-Reactive protein (CRP) and leukocyte values were 36 mm/h, 7.15 mg/dL and 10.05 \(\times 10^3\) µL, respectively. The purified protein derivative (PPD) test result was negative.

Intramedullary sclerosis accompanied by cortical thickness and multifocal radiolucent areas were observed in the direct roentgenograms, starting from the tibia, below the diaphyseal region, and extending to the metaphyseal region (Figure 1).

The maximum intensity projection (MIP) method was employed in the examination of the leg with the Multidetector Computed Tomography (MDCT; Aquilion 64; Toshiba Inc., Tokyo, Japan). In the metaphyseal-diaphyseal region, a significant cortex thickness with an irregular contour and an accompanying periosteal reaction were observed. In the intramedullary region, areas surrounded with a sclerotic halo and a high fluid density were detected (Figure 2).

Magnetic resonance imaging (MRI) was performed using the Signa 1.5T HDxt MR system (GE Healthcare, Chicago, IL, USA). On T1-weighted coronal images, a hypointense serpiginous appearance, which is typical for Brodie’s abscess, in the metaphyseal-diaphyseal region of the tibia was seen (Figure 3).

On T2-weighted images, a hyperintense intramedullary cavitary lesion, which can be considered as a demonstrative sign for Brodie’s abscess, was detected (Figure 4). On contrast-enhanced fat-suppressed images, pre-contrast imaging revealed multifocal hypointense lesions, as post-contrast images showed diffuse peripheral contrast enhancement reminiscent of abscess. The heterogeneous contrast enhancement in the soft tissue was thought to be due to inflammation and edema (Figure 5).

Ziehl-Neelsen staining and Gram staining were performed on the samples taken with injection; however, no pathogen was detected. In addition, no pathogen was isolated from the culture samples. Broad-spectrum antibiotics were started considering pyogenic osteomyelitis. The patient’s complaints did not resolve with medical treatment; biopsy was performed followed with curettage and antibiotic cement (Vancomycin; 4 grams added to 40 grams cement package) application.

On histopathological examination, caseating granulomas with Langhans giant cells and a mixed inflammatory cell infiltration were seen. Dead bone fragments (sequestra) were present within the inflamed granulation tissue (Figure 6). Acid-fast bacillus (AFB) staining did not reveal any bacilli. However, \(M.\) tuberculosis-specific DNA was detected by

![Figure 1. An expansile lesion with intramedullary sclerosis in the metaphyseal-diaphyseal region on plain (a) AP and (b) lateral radiographs.](image-url)
real-time polymerase chain reaction (Real-Time PCR; Anyplex™ MTB/NTM Real-time Detection Kit, CFX96™ Real-Time PCR System; Seegene, Inc., Seoul, South Korea) performed on formalin-fixed paraffin-embedded (FFPE) tissue block (Figure 7). The *M. tuberculosis* complex was produced from the perioperative samples in the Löwenstein–Jensen

**Figure 2.** (a) Significantly irregular cortical thickening and periosteal reaction is observed medially (large arrow) and the area with high fluid density and a thin sclerotic halo (small arrows) especially in the metaphyseal intramedullary region can be observed on the coronal MDCT image. (b) Hypodense areas accompanied by irregular thickening of the cortex (arrow) and common irregular periosteal reaction is observed in the intramedullary region on the axial MDCT image. (c) Periosteal reaction (arrow) accompanied by a thickening of the cortex on the sagittal MDCT MIP image.

**Figure 3.** Hypointense and serpiginous appearance in the metaphyseal-diaphyseal intramedullary region which is typical for Brodie abscess. The thickness of the cortical bone and the accompanying periosteal reaction (arrow) is noteworthy on the coronal T1-weighted FSE image.

**Figure 4.** A hyperintense cavitary lesion (thick arrow) which indicates Brodie abscess in the metaphyseal-diaphyseal intramedullary region and edema in the tibiotalar articular region can be observed on this sagittal T2-weighted TSE fat-suppressed image.
medium after 5 weeks. The patient was treated with anti-
tuberculosis treatment (Isoniazid $1 \times 300$ mg, Rifocin
(Rifamycin) $1 \times 600$ mg, Ethambutol $1 \times 1500$ mg and
Pyrazinamide $1 \times 1500$ mg for 3 months and then Isoniazid
$1 \times 300$ mg and Rifocin $1 \times 600$ mg for 3 months). At the
first year follow-up, the clinical, radiological and laboratory
findings were normal.

Discussion

Tuberculosis osteomyelitis can mimic many diseases clini-
cally and radiologically.\textsuperscript{6} The course, laboratory findings and
radiological appearance of the disease makes it necessary to
be considered in the differential diagnosis of pyogenic
infections, Brodie’s abscess, osteoid osteoma, chondroblas-
toma, osteogenic sarcoma, eosinophilic granuloma, Ewing’s
sarcoma, giant cell tumor of the bone, aneurysmal bone
cyst, nonossifying fibroma, intracortical hemangioma,
plasmacytoma and benign and primary malignant bone
pathologies.\textsuperscript{7,8}

In his study, Rasool\textsuperscript{9} classified the Brodie’s abscess as Type
1b based on the radiological assessment and considered it in
the differential diagnosis of the Type 2, Type 5 and Type 6
tuberculosis osteomyelitis which exhibit a similar radiological

Figure 5. (a)–(f) T1-weighted pre- and post-contrast images on the axial, coronal and sagittal planes. Multiple hypointense lesions causing an expansion in the intramedullary region are observed (arrows). Peripheral enhancement like abscess lesions is noteworthy in postcontrast series (arrows). (c) and (d) The heterogeneous contrast in the soft tissue was considered as inflammation and edema (stars).
appearance. Current classification systems cannot evaluate the osteomyelitis cases as a whole; instead, the duration and course of the disease, host resistance, anatomical location, soft tissue involvement, the type and amount of damage to the bones and radiographic appearance is evaluated separately in classification. Therefore, a new, comprehensive classification system is necessary as a guidance for treatment. Basically, Brodie’s abscess is defined as a low-virulence pathology that has mutual balance between the pathogen and host. Its slow clinical course is similar to the course of patients with

Figure 6. Granulomatous osteomyelitis. (a) Caseating granulomas with Langhans giant cells (black arrows) (H&E, ×100). (b) Caseous necrosis (H&E, ×200). (c) Langhans giant cell within a granuloma (black arrow) and necrosis near the granuloma surrounded by mixed inflammatory cells (H&E, ×200). (d) Sequestrum (black arrow head) and granulomas (white arrow head) dispersed in inflamed granulation tissue (H&E, ×40).

Figure 7. Real-time polymerase chain reaction (Real-Time PCR) results and amplification curves for the *M. tuberculosis* (MTB) DNA. Blue curve represents the MTB, pink curve represents the non-tuberculosis mycobacteria (NTM) and dark red curve at the bottom represents the internal control. MTB curve is the first curve that passes the cycle threshold, indicating an MTB DNA positivity.
tuberculosis, thus, they are often mixed. Vohra et al.\textsuperscript{11} reported about a case series of 28 patients with tuberculosis osteomyelitis and mentioned of six cases who had pyogenic osteomyelitis and exhibited clinical and radiological findings similar to Brodie’s abscess. In another study, Akgul et al.\textsuperscript{1} noted that clinical, radiological and laboratory findings of their tuberculous osteomyelitis case showed close similarity with subacute osteomyelitis. Brodie’s abscess is known as a solitary lesion in the metaphyseal region and is characterized by the new bone formation around it. The lesion may sometimes exhibit a different radiological appearance. Contrary to the common knowledge, diaphyseal involvement is more frequent in publications of African origin. This may be due to the fact that metaphyseal involvement is usually seen among children while diaphyseal involvement is seen among adults, and the series of African origin may involve adult cases mostly.\textsuperscript{12} Siddiqui et al.\textsuperscript{13} reported that the MRI findings seen in cases with Brodie’s abscess may also be encountered in patients with tuberculous osteomyelitis. Tobacco use still negatively affects the course of the disease. According to Olasinde et al.\textsuperscript{12} and Khoshhal et al.,\textsuperscript{4} trauma to any area causes hypoxia in that region so the host resistance weakens and the risk of infection increases. Our patient was advanced aged, a smoker and had a trauma history to the anteromedial aspect of the tibia, which is more sensitive to hypoxia and infection.\textsuperscript{9}

Host resistance, which was introduced in osteomyelitis classification systems first by Cierny et al.,\textsuperscript{14} plays an important role in the course of the disease. Treatment of the autoimmune kidney disease in our case caused the immunosuppression. It is believed that this condition increases the sensitivity to specific agents such as \textit{M. tuberculosis} rather than the more frequent \textit{Staphylococcus} and \textit{Streptococcus}.\textsuperscript{8}

Vohra et al. showed that the resistance of sinus tract like in our case may cause incorrect microbiological studies and misdiagnosed pyogenic infections. Often, the tumor can be mixed with cases of infection. In order to achieve rapid diagnosis and treatment, “culturing for every tumor and biopsy for every infection” should always be kept in mind.\textsuperscript{11}

According to Akgul et al.,\textsuperscript{1} diagnosis of tuberculosis osteomyelitis may be delayed up to 6.6–10 months. Culture results are positive in only 29%–61% of subacute osteomyelitis cases.\textsuperscript{9} This rate decreases to 10%–30% in tuberculosis cases.\textsuperscript{15} In case series where biopsy is performed, the rate of histological diagnosis of tuberculosis osteomyelitis varies between 72% and 97%; in some series it may even rise up to 100%.\textsuperscript{15} PCR assay and histopathology is the gold standard in the diagnosis of tuberculous osteomyelitis.\textsuperscript{15}

**Conclusion**

In conclusion, histopathological examination and PCR is essential before surgery in subacute and chronic osteomyelitis cases with atypical clinical, laboratory and radiological findings for early diagnosis and accurate treatment. We believe that tuberculous osteomyelitis should be kept in mind in cases where MRI findings are reported as Brodie’s abscess.

**Ethical approval**

Our institution does not require ethical approval for reporting individual cases or case series.

**Declaration of conflicting interests**

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**Informed consent**

The patient described herein had given consent to the use of de-identified patient data for use in research and education.

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