

Case Report

Primary diaphyseal tuberculosis of the tibia, presenting as a pathological fracture – A case report

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ABSTRACT

Background: Isolated involvement of the shaft of a long bone is a rare presentation of skeletal tuberculosis (TB). To our knowledge, primary skeletal TB of the tibia manifesting as a pathological fracture has not been widely reported. We report a case of primary TB of the right tibia in an immunocompetent 85-year-old woman.

Case presentation: An immunocompetent 85-year-old woman with tuberculosis osteomyelitis of her right tibia and fibula, presenting as pathological fracture. Fibular osteotomy was performed followed by application of a bioabsorbable bone substitute and an Ilizarov external fixator. The patient was pain-free and ambulating with a walking frame one year post-operatively.

Conclusions: Tuberculosis osteomyelitis is challenging to diagnose due to the absence of distinctive clinical and radiographic features. This case highlights the potential of a bioabsorbable bone substitute in achieving osteoconduction and providing sustained local antimicrobial release in tuberculous osteomyelitis.

Introduction

Tuberculosis (TB) affecting bone and joints account for 2.2 to 4.7 % of all TB cases, most commonly affecting the axial skeleton [1]. Isolated involvement of the shaft of a long bone is a rare presentation of skeletal TB, only described in dotted case reports [2–5]. We report a case of primary TB of the right tibia in an immunocompetent 85-year-old woman. This case is particularly rare in view of the first presentation as a pathological fracture of the tibial shaft, and in an immunocompetent patient.

Case presentation

An 85-year-old woman with unremarkable past health was admitted to the Department of Orthopaedics & Traumatology ward with a fractured right tibia and fibula with an overlying wound. Prior to presentation, she was able to walk unaided. It was reported that there was a grape size swelling with an unhealing overlying wound for more than a year. She sought medical attention from her local general practitioner and was given antibiotics. However, improvement was minimal. She eventually decided to seek help from the emergency department as family noted deformity of her right leg. The patient and her family denied any significant trauma history of

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the right lower limb.

Upon admission, she was cooperative, haemodynamically stable but febrile. The lower 1/3 of her right leg showed obvious varus deformity, with a 3×3 cm wound over the shin with surrounding erythema and slight discharge (Fig. 1). Examination of her left lower limb was unremarkable, and examination of other systems were normal.

Routine laboratory investigations revealed grossly normal blood workup besides mild normocytic normochromic anaemia. Liver and renal function tests were within normal limits. Radiograph of the chest was unremarkable.

Radiograph of the right lower limb revealed an obvious fracture across the tibia and fibula 5 cm above the ankle syndesmosis, with underlying osteomyelitic changes, varus angulation and displacement (Fig. 2). Mild swelling of the overlying soft tissue was also noted. She was hence immediately put on intravenous Augmentin and a long leg slab.

With the working diagnosis of pyogenic infection or neoplastic condition with pathologic fracture of the right tibia, an urgent contrast CT of the right leg was performed. Pertinent findings include a complete transverse fracture of distal tibia and fibula with angulation and callus formation. An irregular rim-enhancing collection was seen that tracks to a dermal indentation, which could be the draining sinus, suspicious of abscess formation (Fig. 3).

The patient then underwent surgery with copious irrigation and debridement, followed by an oblique fibular osteotomy for compression of the fracture site and soft tissue coverage. With the working diagnosis of pyogenic osteomyelitis, a bioabsorbable bone substitute (Stimulan®, Biocomposites, Keele, UK) was mixed with Vancomycin 1 g, Gentamicin 240 mg, and applied locally in an attempt to control infection and achieve osteoconduction. An Ilizarov external fixator was applied for stabilization and compression of the fracture site. It also provides an option for lengthening at a more proximal tibia osteotomy site when the bone lost is significant with large leg length discrepancy. However, lengthening was not necessary in our case (Fig. 4). Intraoperative tibial bone biopsy and granulation tissue were sent for section, routine culture, fungal and acid fast bacilli (AFB) culture. Post-operative alignment was well and patient was started on gradual walking exercises. Intra-operative bone specimens show negative AFB culture and Ziehl-Neelsen (ZN) stain, but routine section showed necrotizing granulomatous inflammation, and the specimen was tested positive for tuberculosis polymerase chain reaction (PCR). Anti-tuberculous therapy was started immediately after consulting the microbiologists. The final diagnosis was a pathological fracture of the tibia and fibula caused by diaphyseal tuberculous osteomyelitis (TB OM) of the right tibia. The patient was started on a 9 month, four drug anti-tuberculous regimen comprising of daily Rifampicin 450 mg (R), Isoniazid 300 mg (H), Pyrazinamide 1000 mg (Z) and Ethambutol 400 mg (E). Detailed history was taken with extensive efforts made to exhaust environmental factors and contact leading to TB infection. An HRCT thorax was later booked to rule out possible past history of



Fig. 1. Initial presentation with a 3×3 cm wound over the medial right shin.



Fig. 2. X-ray on presentation with fracture distal right tibia and fibula, with underlying osteomyelitic changes and varus angulation and displacement.

pulmonary TB, and it showed no sign of past infection (Fig. 5). 1 year after the removal of the Ilizarov external fixator, the wounds have healed (Fig. 6), with radiograph showing good union of the pathological fracture at the tibia (Fig. 7). Patient was pain-free at the injury site, and was able to ambulate independently with a walking frame.

Discussion and conclusion

Mycobacterium tuberculosis (MTB) is an obligate aerobe, and is the leading cause of death from a single infectious agent, infecting >10 million people in 2019 out of which 1.5 million succumbed from its complications [6]. Most cases were found in South-East Asia, which contributed to 44 % of total cases [7]. Due to the high amount of lipids present in the cell wall, it renders the bacteria relatively impermeable to Gram staining [8]. Instead, acid-fast staining such as ZN stains is commonly used to identify MTB by microscopy. The bacteria is also unique by the fact that it has a very slow growth rate compared to other pyogenic bacteria – it only divides every 18–24 h [9]. MTB is often known as the “great mimicker” [10] as it can virtually attack any part of the body and has exceptionally non-specific symptoms.

Tuberculosis (TB) affecting bone and joints account for 2.2 to 4.7 % of all TB cases, most commonly affecting the axial skeleton [1]. Primary diaphyseal involvement is rare, and is postulated to be caused by a TB embolus that remains lodged in the nutrient vessel that fails to spread to other areas [11]. In literature, only one third of patients with skeletal TB are reported to have pulmonary TB [12]. Two types of involvement have been identified, namely the caseous exudative type and the granular type. The caseous exudative type is

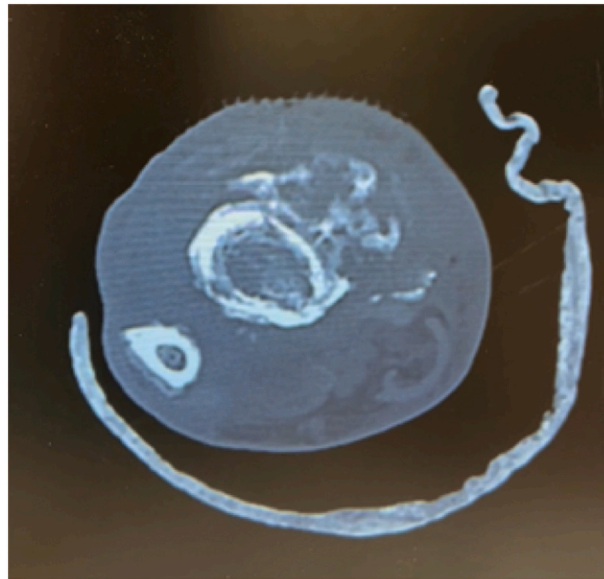


Fig. 3. CT showing complete transverse fracture of right distal tibia and fibula with an irregular rim-enhancing collection that tracks to a dermal indentation.

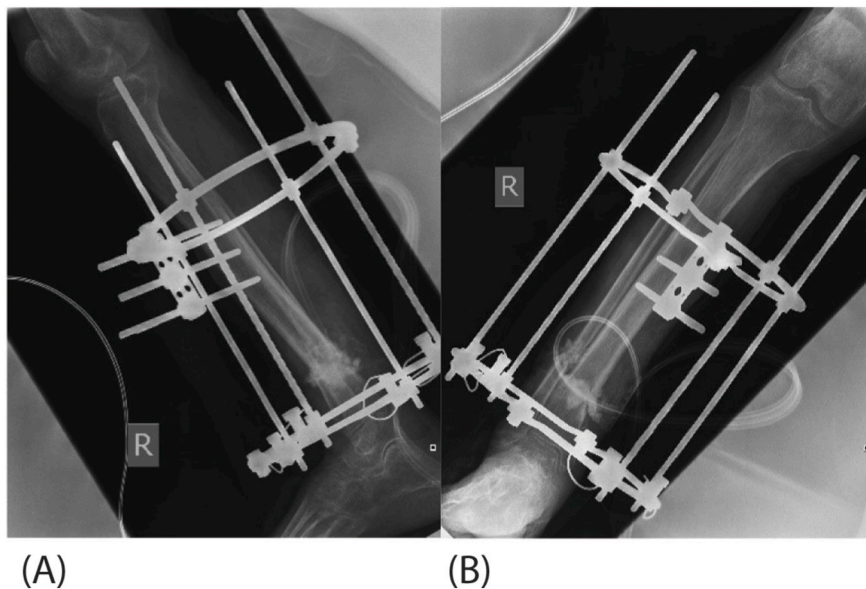


Fig. 4. (A) Lateral radiograph post operation: fibular osteotomy with antibiotic loaded bone substitute, application of Ilizarov external fixator. (B) Anterior Posterior radiograph post operation: fibular osteotomy with antibiotic loaded bone substitute, application of Ilizarov external fixator.

characterized with bone destruction, local swelling, abscess formation, sinus formation, and constitutional symptoms. For the granular type, it is more insidious and less destructive than the caseous exudative type, and abscess formation is relatively less common. However, it should be noted that a mixed pattern is often found, as the host-parasite interaction in TB is very polymorphic, and management will typically be very similar.

In literature, tuberculosis infection of the tibia is not widely reported. Examples include a previous case report with very similar clinical presentations was published in Singapore regarding a 28-year-old immunocompetent Indian man [4], and another case report on a 65-year-old man with chronic kidney disease presented with pain and swelling in the left leg [2]. Akin to our case, Ziehl-Nielsen, Gram staining and culture were performed on the samples taken, but no pathogens were detected. Diagnosis was only made when MTB-specific deoxyribonucleic acid (DNA) was detected by PCR.

Our case and previous case reports have exemplified difficulties in the accurate diagnosis of such rare pathology. A study showed

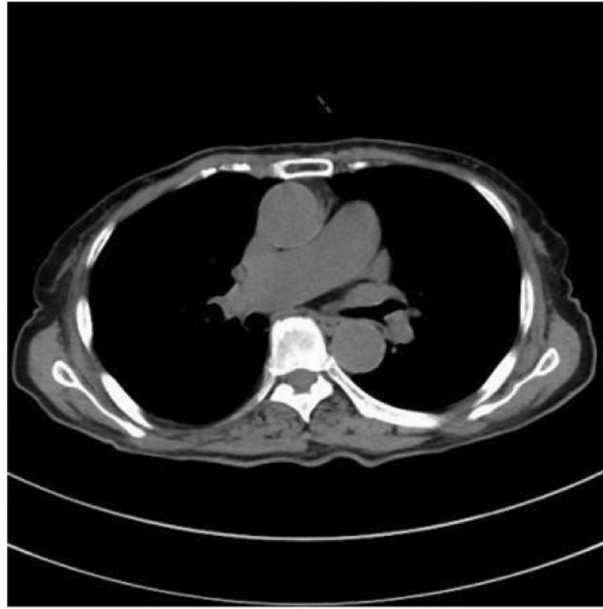


Fig. 5. HRCT thorax showing no sign of previous TB infection.

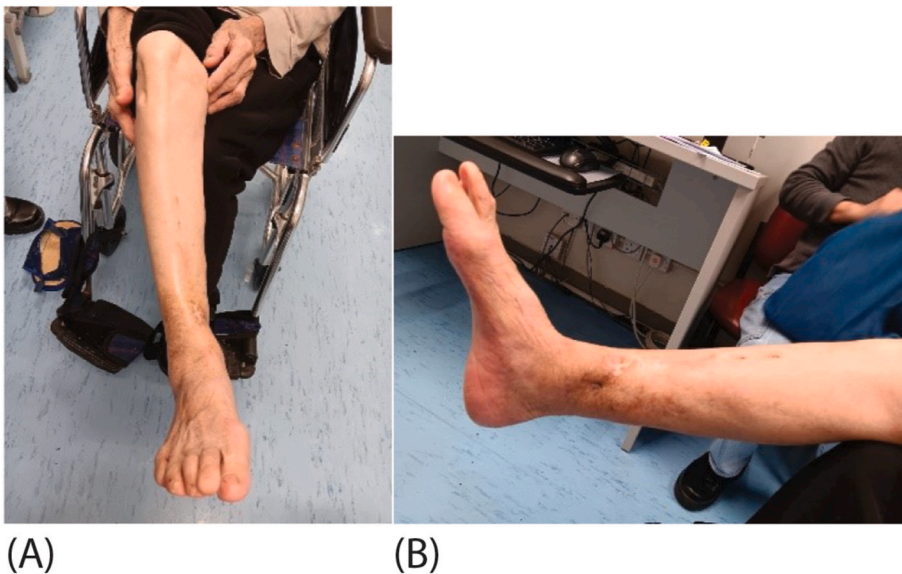


Fig. 6. (A) Clinical photo of right leg from anterior aspect. 1 year post removal of Ilizarov external fixator. (B) Clinical photo of right leg from lateral aspect. 1 year post removal of Ilizarov external fixator.

that diagnosis of TB OM is delayed 6.6 months on average partly because of such mild local symptoms and low index of suspicion, and partly because routine culture results are positive in only 10–30 % of TB OM cases [13]. Additionally, although microscopy with ZN staining is the most commonly used and accessible procedure to diagnose TB globally, the specimen must contain at least 10^4 colony forming units (CFU)/mL to yield a positive result [14]. The sensitivity of AFB smear is poor, especially with extra-pulmonary manifestations, ranging from 22 to 78 % [6], owing to a low bacilli yield with extrapulmonary specimens. As expected, such poor sensitivity has contributed to many incidences of false negatives in TB OM cases. There are many other established methods in diagnosis of Tuberculous infection, for example acid-fast staining by microscopy, increase in adenosine deaminase level, detection of urine lip-oarabinomannan (LAM) antigen, Tuberculin skin test, in-vitro interferon- γ release assay (IGRA) etc. Each has displayed a modest range in sensitivity and specificity, but in the recent decade the role of nucleic acid amplification has been gaining momentum as an alternative reliable diagnostic tool [15]. It has several important advantages, for instance a specificity of >95 %, a relatively fast

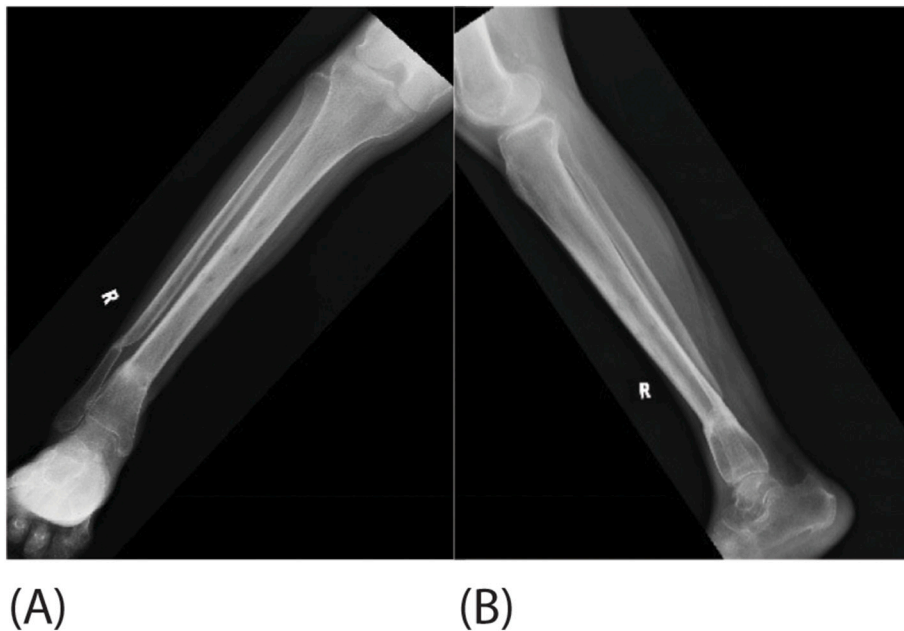


Fig. 7. (A) Anterior Posterior Radiograph of right leg 1 year post removal of Ilizarov external fixator. (B) Lateral Radiograph of right leg 1 year post removal of Ilizarov external fixator.

turnaround time compared to culture, and the ability to identify the specific species of *Mycobacterium*. However it also has a few limitations, as PCR is very expensive, and it does not provide any information regarding drug susceptibility or resistance. But approximating our case and the case report from Turkey where the only diagnostic finding was a positive PCR test, this proves that PCR maintains an importance and reliability in the diagnosis of extrapulmonary TB.

Furthermore, the most common presentation of extraspinal TB OM clinically is a cold abscess with mild swelling, pain and erythema, with a solitary lesion in the diaphysis of long bones radiographically [1]. Top differentials that are likely first entertained would be chronic pyogenic OM, Brodie's abscess, cystic lesions, tumours (e.g.: osteoid osteoma) etc. Consequently, in the absence of specific clinical features and radiographical signs, awareness of diaphyseal TB and a high index of suspicion in adults with unexplained pain and swelling of the bone is the only way to establish a diagnosis.

With regards to treatment of skeletal TB, the general approach comprises mainly of antimicrobial therapy and surgical intervention only if indicated. The choice of antibiotics is by and large the same as that for pulmonary TB, although the optimal duration of therapy remains unclear due to the concern with poor drug penetration into osseous tissues. A large prospective cohort study was done in Hong Kong back in 1986 that demonstrated 6 months of anti-TB therapy combined with surgery was comparable in efficacy with 9 to 18 months of anti-TB therapy alone [16].

The management of fracture related infections (FRI) is known to be a challenging topic. Recent systematic reviews showed that the condition can be even more challenging when infection occurs in osteoporotic bone [17], and there is a lack of literature covering infections involving multiple, drug resistant, or atypical organisms [18]. To manage cases of FRI, traditional surgical debridement followed by systemic antibiotic treatment is often insufficient as it was suggested that small amounts of debris remain in the wound site after debridement, which includes small biofilm fragments and a organisms that are usually unresponsive to antimicrobial agents in the concentration achieved with systemic routes [19]. To tackle this uprising threat, efforts have been made to summarise existing novel strategies to tackle FRI, including implant coating materials [20] and local antibiotic delivering vehicles for sustained local antibiotic administration [21]. Novel antibiotic delivering strategies like hydrogel mixed with an antibiotic and a biofilm dispersing agent have also shown promising effects on the management of FRI [22].

Our case demonstrated a successful attempt in managing TB OM with Stimulan®, a calcium matrix bone substitute that was mixed with the antibiotic of choice. Compared with traditional surgical debridement and systemic antibiotic treatment, the advantages of this approach include sustained local release of antibiotics to achieve and higher local concentration, and dead space management after debridement [19]. Although the antibiotic applied in our case, vancomycin and gentamycin may have limited effect in the eradication of TB OM, the osteoconductive effect of Stimulan® may have contributed to bone healing. The application of Stimulan® has been documented in multiple studies involving osteomyelitis [23]. However, to our knowledge, our case is the first case report on successful treatment of TB OM with Stimulan®. Given the rarity of TB OM, robust clinical trials on the effect of antibiotic loaded bone substitute on TB OM may be difficult. However, our case provides a piece of evidence that such an approach may be considered in future cases of TB OM.

In summary, we acknowledged the difficulty in the diagnosis of extrapulmonary TB osteomyelitis, especially when the osseous and joint involvement turned out to be atypical. The current case merits unique attention because our patient is a rare documented case of

an isolated diaphyseal tuberculous osteomyelitis presenting with a pathological fracture. With absence of distinctive clinical and radiographic signs in TB OM, as suggested by previous literature, “culturing for every tumour and biopsy for every infection” [24] should always be kept in mind to achieve timely diagnosis. To manage challenging cases of fracture related infection, our case also demonstrated a successful attempt by using Stimulan® (Biocomposites, Keele, UK) a calcium matrix mixed with antibiotics to achieve osteoconduction and sustained local release of antimicrobial agents.

Written consent for publication

The written informed consent for publication of this case report and any accompanying images has been obtained from the patient.

CRedit authorship contribution statement

Cheuk Kin Kwan: Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Formal analysis, Conceptualization. **Stephanie Wing Sum Tso:** Writing – review & editing, Validation, Methodology, Investigation, Formal analysis, Conceptualization. **Wing Hong Liu:** Writing – review & editing. **Chi Yin Tso:** Writing – review & editing. **Wing Hoi Cheung:** Writing – review & editing. **Ronald Man Yeung Wong:** Writing – review & editing, Supervision. **Ning Tang:** Writing – review & editing, Supervision.

Ethics approval

The study was approved by the Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee (CRE Ref No.: 2023.477).

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Declaration of competing interest

The authors declare that they have no competing interests.

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Data availability

Not applicable (this manuscript does not report data generation or analysis).

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