



Osteoarticular tuberculosis in infancy and its clinical outcome: A case series

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An estimated 1.25 million children and young adolescents developed tuberculosis (TB) in 2022, of whom 47% were children aged < 5 years.^[1] This pediatric burden accounted for approximately 12% of the global TB incidence (10.8 million cases).^[2] Tuberculous osteoarticular infection (OAI) is a rare manifestation in children, accounting for only 10 to 20% of extrapulmonary cases and 1 to 2% of all pediatric TB infections.^[3-5] Malaysia, an endemic country for TB, reported a total of 771 TB cases among children under 15 years old in 2022, with an incidence rate of 9.9 per 100,000 population.^[6]

Received: January 14, 2026

Accepted: April 02, 2026

Published online: October 18, 2026

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DOI: 10.52312/jdrs.2026.2828

Citation: Pancharatnam D, Soo YZ, Hii XXF, Voon YW, Rashid MLA, Aik S, et al. Osteoarticular tuberculosis in infancy and its clinical outcome: A case series. Jt Dis Relat Surg 2027;38(x):1-11. doi: 10.52312/jdrs.2027.2828.

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ABSTRACT

Osteoarticular tuberculosis (TB) in infancy is rare, often presenting with non-specific clinical features that delay diagnosis and treatment. In this article, we present a case series of seven infants diagnosed with osteoarticular TB at a tertiary center. The patients (6 girls, 1 boy; aged 9 to 12 months) presented with painless, progressive limb swelling involving the femur, tibia, and ankle. Only one had intermittent low-grade fever. *Mycobacterium tuberculosis complex* was detected by polymerase chain reaction (PCR) in six cases, and three cases were culture-positive for *Mycobacterium bovis* (Bacille Calmette-Guérin [BCG] strain). All compliant patients received standard anti-tuberculosis therapy (2HRZE/10HR) and were followed for at least three years. One child developed pyrazinamide-induced hepatotoxicity, which was managed successfully with monitored reintroduction of therapy. Five patients showed complete radiological and functional recovery with normal gait and no limb-length discrepancy at a minimum three-year follow-up. Two patients were lost to follow-up. In conclusion, early suspicion, combined with histopathological evaluation and nucleic acid amplification testing, is crucial for prompt diagnosis. Despite its rarity, osteoarticular TB should be considered in infants with unexplained limb swelling, even in the absence of systemic features. Timely surgical intervention and adherence to therapy result in excellent clinical outcomes.

Keywords: Bacille Calmette-Guérin osteomyelitis, infancy, Mycobacterium tuberculosis, osteoarticular, polymerase chain reaction.

The diagnosis of osteoarticular TB is frequently delayed.^[7] In this article, we present a case series of seven rare pediatric osteoarticular TB outlining the clinical features, treatment, and outcomes to highlight the importance of early diagnosis through detailed history, histopathological and nucleic acid

amplification test (NAAT) for confirmation and speedy initiation of targeted treatment.

CASE REPORT

Ethical approval for this case series was obtained from the University Malaya Medical Centre Medical Research Ethics Committee (Date: March 26, 2026, No. 2026215-16344). A written informed consent was obtained from the parents and/or legal guardians of all patients for publication of the case details and accompanying images.

Case 1—A one-year-old male infant presented with progressive swelling at the right proximal thigh for five days. His parents reported reduced activity and appetite, although the child remained fully mobile and did not complain of pain. There was no history of known TB contact, recent travel, or exposure

to contaminated environments. Plain radiograph revealed osteolytic lesion confined to right proximal femur with increased soft tissue shadow (Figure 1). Magnetic resonance imaging (MRI) demonstrated hyperintense signal involving the right proximal thigh with extension to the hip joint (Figure 1). Ultrasound (US)-guided aspiration and tissue biopsy were performed, with TB polymerase chain reaction (PCR) test confirming *Mycobacterium tuberculosis complex* (*M. tuberculosis complex*) and histopathology showing granulomatous inflammation. The TB culture test result was negative. Baseline blood investigations demonstrated mildly elevated white blood cell (WBC) count and C-reactive protein (CRP), with a normal erythrocyte sedimentation rate (ESR).

Surgical debridement was performed to evacuate the collection. Subsequent history

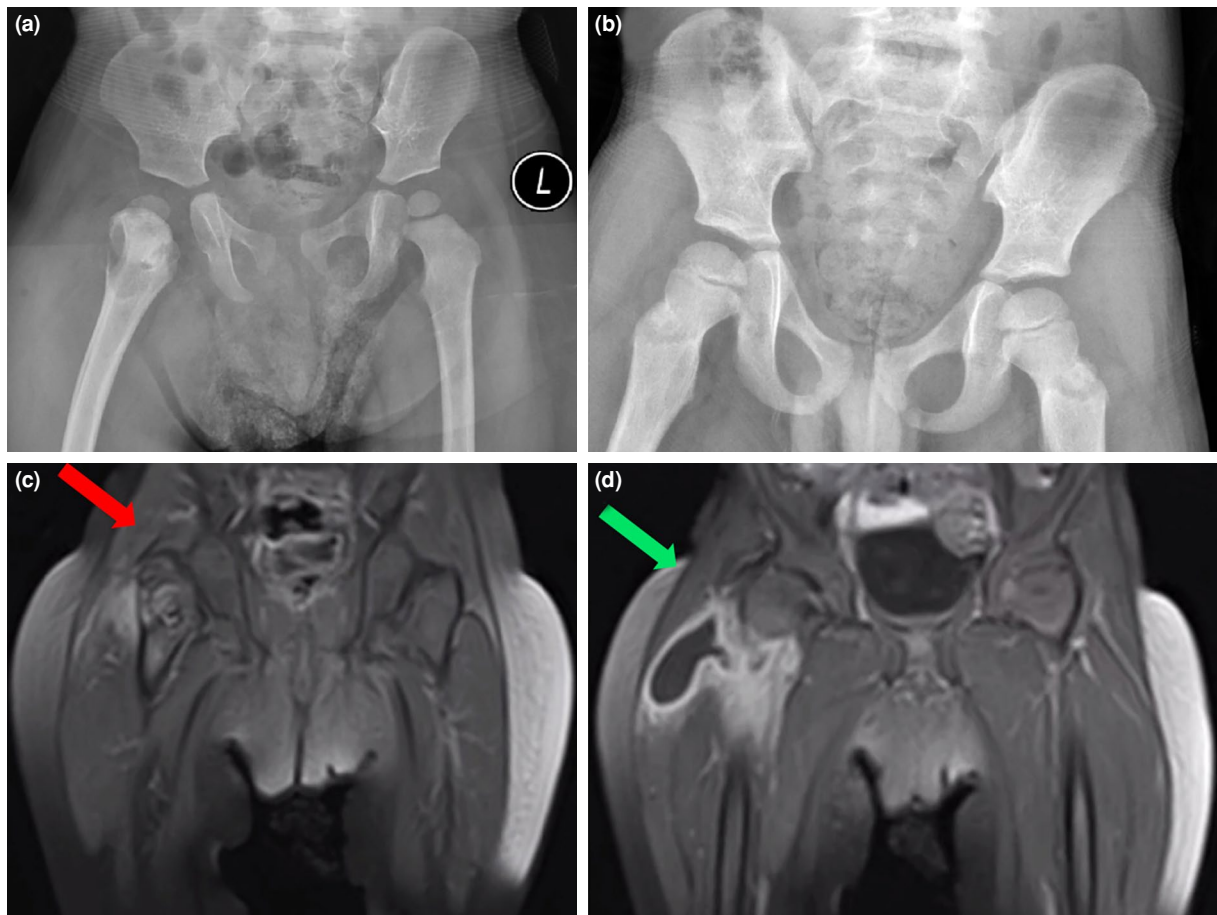


FIGURE 1. (a) Plain radiograph showing osteolytic lesion confined to right proximal femur. (b) Follow-up imaging at 4 years after diagnosis showing complete reconstitution of bone at proximal femur (c, d) Contrast-enhanced MRI showing metaphyseal osteomyelitis at proximal femur (red arrow) with well-defined, rim-enhanced collection at proximal thigh (green arrow) which extends into hip joint.

MRI, magnetic resonance imaging.

revealed contact with the babysitter's sibling, who completed pulmonary TB treatment. The patient completed a total of one year of anti-TB therapy (ATT) consisting of 2HRZE/10HR with pyridoxine supplementation. The treatment was well tolerated

without complications. At three years of follow-up after ATT treatment, the child was active, with equal limb lengths and full, pain-free hip motion.

Case 2– A nine-month-old male infant presented with recurrent swelling at proximal right leg for



FIGURE 2. Ultrasound finding at point of diagnosis and serial plain radiographs demonstrating interval healing. (a) Ultrasound showing an intramuscular hypoechoic lesion measuring $0.7 \times 3.2 \times 3.2$ cm (AP $\times$ W $\times$ CC) (red arrow), with internal calcifications. No peripheral or internal vascularity is observed. The underlying bony cortex appears intact, with no intra-articular or local bony extension. (b) Taken during diagnosis showing a well-defined lytic lesion at the proximal tibia. (c) Taken three months into treatment (d) Taken six months into treatment (e) Taken 1 year, at completion of anti-tuberculous treatment (f) Taken at 3 years post-anti tuberculosis therapy.

10 days. He remained mobile and could stand, although his parents observed avoidance of the affected leg when placed in a walker. A similar self-limiting episode occurred two months earlier, resolving spontaneously within a week. Radiographs demonstrated a well-defined lytic lesion at the proximal tibia with associated soft-tissue swelling, initially interpreted as Brodie's abscess with cellulitis (Figure 2). Surgical drainage yielded 5 mL of frank pus with thick debris. The periosteum was breached, though the underlying bone was intact. Curettage of friable tissue was performed via a bone window created by drilling.

Tuberculosis PCR confirmed *M. tuberculosis complex*, and tissue culture grew *M. bovis* (Bacille Calmette-Guérin [BCG] strain), sensitive to isoniazid, rifampicin, and ethambutol. Baseline blood investigations showed mild leukocytosis ($23.3 \times 10^9/L$) and mildly elevated CRP (10.0 mg/L), with a normal ESR (3 mm/h). The patient completed one year of ATT (2HRZE/10HR), with good clinical

response. At four-years of follow-up after ATT treatment, the child was active, with equal limb lengths and full, pain-free knee motion.

Case 3– A one-year-old female infant presented with progressive enlarging swelling at right leg over three months. Despite the swelling, her activity and mobility remained normal. She denied fever, cough, TB contact, or trauma, and all immediate family members tested negative for TB. On physical examination, the swelling below the right knee was soft, non-fluctuant, and non-tender. Radiographs revealed a lucent bone lesion at the proximal tibia extending across the growth plate (Figure 3), while US scan showed well-defined heterogenous echogenic lesion with peripheral vascularity and specks of calcification anterior to right proximal tibia, interpreted as an organizing hematoma or collection.

Surgical exploration yielded 2 mL of thick, caseous pus extruding from the anterolateral proximal tibia into the soft tissue. The anteromedial



FIGURE 3. Serial plain radiographs demonstrating interval healing with bone healing. (a) Taken at diagnosis showing lucent bone lesion at the proximal tibia. Follow-up radiographs (b) taken three months into treatment, radiographs, (c) taken six months into treatment (d) taken at completion of ATT, and (e) taken 3 years post-completion of ATT.

ATT, anti-tuberculosis therapy.



FIGURE 4. Ultrasound finding at point of diagnosis and serial plain radiographs demonstrating interval healing. **(a)** Ultrasound images of the right ankle showing a heterogeneous collection (red arrow) with moving internal debris at the medial malleolus, measuring approximately $1.0 \times 2.3 \times 3.4$ cm, with partial liquefaction. The collection is in continuity with the distal tibial defect, suggestive of intraosseous-soft tissue fistulous communication. **(b)** Taken during diagnosis showing a solitary lytic lesion at the distal tibial metaphysis with surrounding sclerosis and adjacent increased soft tissue shadow. **(c)** Taken six months into treatment **(d)** Taken nine months into treatment **(e)** Taken 1 year, at completion of anti-tuberculosis therapy, show resolution of the previously described distal tibial lytic lesion, with interval bone remodeling and cortical reconstitution **(f)** Taken at 3 years post-TB treatment.

TB, tuberculosis.

cortex and periosteum were intact, and the physal plate and knee joint were not involved. The TB culture test result was negative; however, TB PCR detected low levels of *M. tuberculosis complex*. Baseline blood investigations were unremarkable, with a normal WBC, CRP and ESR. Further history revealed past contact with her maid with chronic

cough, who cared for the patient in infancy. The patient was treated with standard ATT (2HRZE/10HR) and showed a favorable clinical response at three years post-treatment completion with normal gait and equal limb length.

Case 4– A one-year-old female infant presented with progressive swelling over the right ankle.

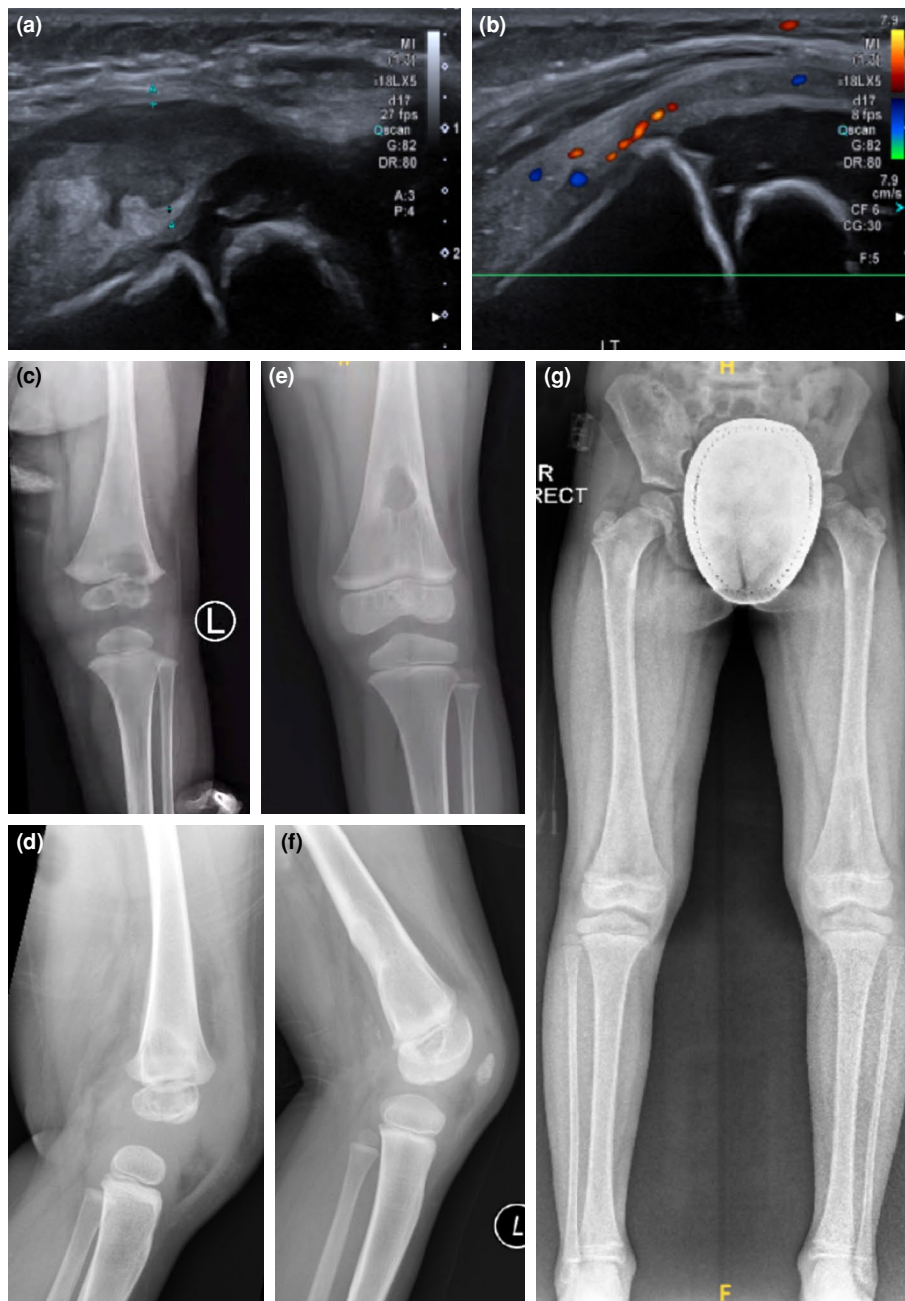


FIGURE 5. (a, b) USG taken during 1 month post initiation of anti-tuberculosis therapy showing synovial thickening at the suprapatellar bursa space with increased vascularity. (c, d) Radiograph taken during diagnosis (e, f) taken one year post completion of anti-tuberculosis therapy (g) taken three years post-TB treatment with full recovery. USG, Ultrasonography; TB, tuberculosis.

The swelling, initially coin-sized, was associated with intermittent low-grade fever, subsided transiently, then recurred medially with induration and discharging sinuses. There was no history of trauma, insect bite, or known TB contact. Examination revealed a firm, fluctuant swelling over the distal tibia with two draining sinuses. She was otherwise active, afebrile, and systemically well. Radiographs showed lytic changes in the distal tibia (Figure 4), while core biopsy demonstrated necrotizing granulomatous inflammation. The TB PCR confirmed *M. tuberculosis complex*. Baseline blood investigations were unremarkable, with normal WBC, CRP and ESR.

She was started on standard ATT, but developed hepatotoxicity within two weeks, likely pyrazinamide-induced, presenting with orange urine and deranged liver enzymes. Therapy was withheld and subsequently reintroduced stepwise under pediatric infectious disease supervision. The intensive phase was resumed with isoniazid, rifampicin, ethambutol, pyrazinamide and pyridoxine, with close monitoring of liver function. Surgical incision, drainage, and curettage of the distal tibia yielded slimy necrotic material without frank pus. She ultimately tolerated treatment and completed a 12-month course with good functional recovery at three years after treatment.

Case 5– A 10-month-old female infant presented with a 10-day history of intermittent fever and progressive reduction in mobility of the left knee, accompanied by swelling. Radiographs revealed lytic lesions involving the distal femoral metaphysis extending into the epiphysis (Figure 5). She was

initially treated for septic arthritis and arthrotomy washout was performed. Synovial fluid culture grew *M. bovis* (BCG strain) two weeks later. Baseline blood investigations demonstrated an elevated CRP (49 mg/L).

Following culture confirmation, her antibiotic regimen was switched to ATT. Midway through treatment, the patient achieved full, pain-free range of motion of the left knee. Compliance with medication was excellent, and no significant drug-related adverse effects were observed. She completed one month of HRZE, after which pyrazinamide was discontinued in the second month of the intensive phase as the culture showed resistance. She subsequently completed 10 months of isoniazid and rifampicin. Follow-up imaging at three years after therapy demonstrated complete bony remodeling with preserved joint space.

Case 6– A one-year-old female infant presented with one-month history of right thigh swelling. Although the infant was able to move independently, she was unable to fully flex her right knee. Otherwise, the patient denied reduced weight or appetite, fever, shortness of breath, and TB contact.

Physical examination revealed a firm swelling of the proximal thigh. Mantoux testing showed 14-mm induration with non-necrotic blisters. Radiographic findings showed lytic lesion at right femur (Figure 6). The MRI demonstrated cortical erosion posteriorly with extraosseous soft tissue enhancement encasing the posterolateral circumference of the distal femur. Surgical debridement was performed and caseous material was drained. Right femur tissue histopathological

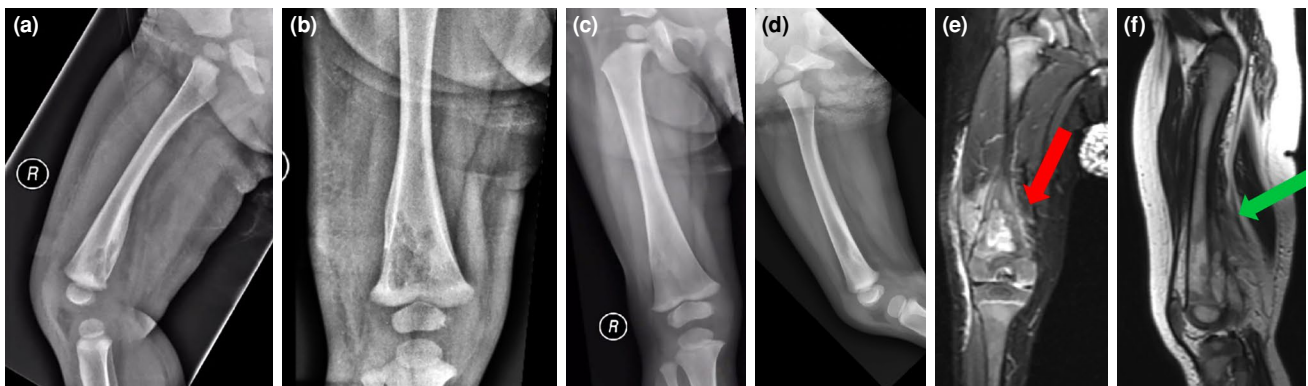
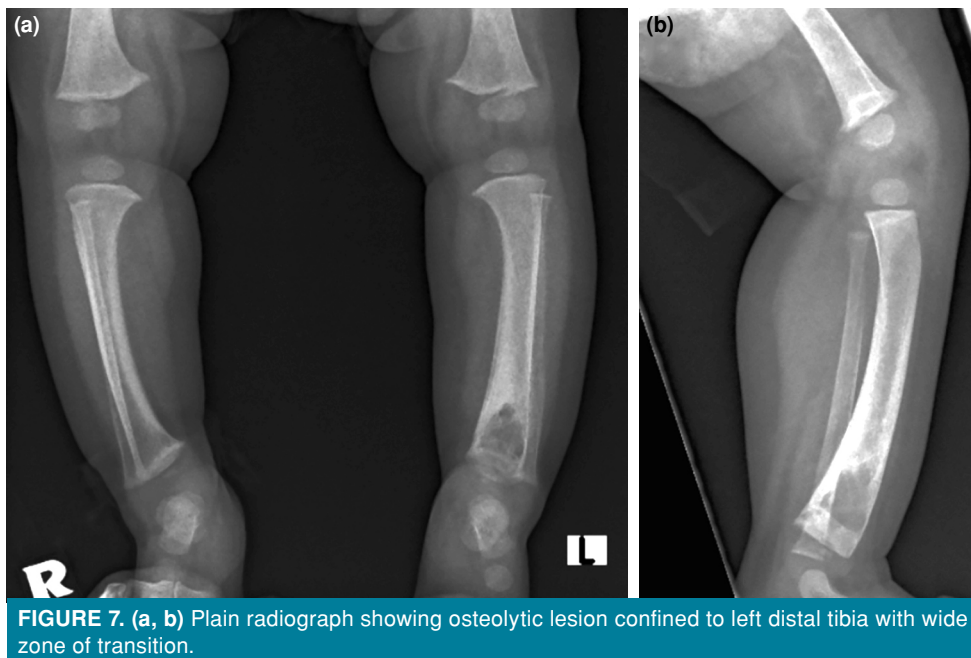


FIGURE 6. (a, b) Plain radiograph showing osteolytic lesion confined to right distal femur. (c, d) Follow-up imaging at six months after diagnosis showing near complete reconstitution of bone at distal femur (e, f) Contrast-enhanced MRI showing cortical erosion posteriorly (green arrow) with physeal plate involvement and extraosseous soft tissue enhancement (red arrow) encasing the circumference of the distal femur.

MRI, magnetic resonance imaging.



examination showed granulomatous inflammation. The TB PCR confirmed *M. tuberculosis complex*, and tissue culture grew *M. bovis* (BCG strain), sensitive to isoniazid, rifampicin, and ethambutol and streptomycin. Baseline blood investigations demonstrated mildly elevated WBC, including the ESR, and a normal CRP.

However, the parents refused the initiation of ATT and defaulted further follow-up. Four years after the initial diagnosis, her mother reported that the child had no deformity or limb shortening, was able to walk normally, and never received ATT.

Case 7– A nine-month-old girl with up-to-date immunization presented with a one-month history of a bony hard swelling measuring 3 × 3 cm over the anterolateral aspect of the left lower leg, associated with skin depigmentation at the posterior ankle. The swelling was non-tender. She achieved normal developmental milestones, fed well, and was able to crawl, stand, and jump without pain. There were no constitutional symptoms such as fever, weight loss, or night sweats.

On physical examination, she was afebrile and active, with stable vital signs, warm peripheries, intact distal pulses, and full, painless movement of the lower limb. Radiographs revealed a distal tibial lytic lesion with a wide zone of transition, a washed-out appearance, and periosteal elevation (Figure 7). Core needle biopsy yielded slime-like

material, and TB PCR confirmed the presence of *M. tuberculosis complex*; however, tissue culture was negative. Baseline blood investigations demonstrated mild leukocytosis with normal CRP and ESR. She subsequently defaulted all further follow-up and was not traceable.

DISCUSSION

Tuberculous OAI is a rare form of extrapulmonary TB and poses significant diagnostic challenges due to its non-specific clinical presentation.^[8] It may mimic pyogenic osteomyelitis or subacute forms such as Brodie's abscess, leading to delayed recognition and treatment.^[9] Constitutional symptoms were uncommon.^[10] Prakash et al.^[11] reported a toddler with TB osteomyelitis whose swelling and imaging findings closely resembled Brodie's abscess, illustrating the subtlety of this disease. Consistent with previous reports, our patients exhibited painless, progressive limb swellings without systemic symptoms, making early diagnosis challenging, unless a high index of clinical suspicion was maintained. These findings suggest that infants with TB OAI can recover without sequelae when diagnosed early and treated appropriately.

Routine inflammatory markers were largely unremarkable in this cohort, despite radiologically and microbiologically confirmed osteoarticular

TB.^[5] Total WBCs were within normal limits in all patients. Three patients demonstrated elevated CRP at the time of diagnosis, while ESR were normal in all patients. This contrasts with pyogenic osteomyelitis, in which inflammatory markers are typically markedly elevated.^[12] The relative absence of systemic inflammatory response in infantile osteoarticular TB may contribute to diagnostic delay and misclassification as subacute or benign conditions.^[5,13] Where inflammatory markers were elevated, assessment of serial trends rather than isolated values proved more informative.^[14] In patients with raised CRP at the time of presentation, levels declined following surgical debridement and initiation of ATT, correlating with clinical and radiological improvement.^[14] This supports the use of inflammatory marker trends as an adjunctive tool for monitoring treatment response, rather than as a primary diagnostic discriminator in osteoarticular TB.^[15]

The diagnosis of TB OAI for the infants described in this study was made through a combination of clinical features, histopathologic and microbiologic data, and NAAT testing, although gold standard for diagnosis is a positive tissue mycobacterial culture.^[16] However, confirmation of TB infection by positive culture often takes up to six weeks,^[17] with reported poor culture yield at 10 to 30% in osteoarticular TB.^[14,18] High percentage of TB samples were likely culture-negative due to low bacillary load, prior empirical therapy, or sampling issues.^[13] The NAAT, such as the Xpert MTB/RIF assay, represents a major advancement in TB diagnosis, allowing rapid detection of *M. tuberculosis* DNA and, in some assays, rifampicin resistance, with results available within approximately 2 h.^[19] A meta-analysis investigating osteoarticular TB reported that X-pert MTB/RIF had a pooled sensitivity and specificity of 96% (95% confidence interval [CI]: 90-98%) and 85% (95% CI: 57-96%) compared to culture, respectively.^[20]

In our case series, all affected children received age-appropriate immunizations, including BCG vaccination given at birth, in accordance with the Malaysian national immunization program. The BCG, as a live attenuated bacterial vaccine, offers strong protection against disseminated TB in young children,^[21] providing up to 90% protection against severe or disseminated disease during the first year of life.^[22] While BCG vaccination in neonates and infants confers substantial protection against the most severe forms of TB (e.g., meningeal

and disseminated TB) in early life,^[21,22] its efficacy is incomplete, particularly for extrapulmonary forms,^[23] and protection wanes over time.^[22] In this article, we reported three confirmed case of infant BCG osteomyelitis by tissue culture identification. Of note, BCG osteomyelitis in infancy is rare systemic adverse reaction following BCG vaccination,^[24] with reported incidence of 2.0 and 3.68 cases per million vaccinations in Japan and Taiwan respectively.^[25,26] Most patients recovered well without sequelae.^[26] Two reported infant cases of BCG osteomyelitis were successfully treated with surgical curettage, and two ATT (rifampicin and isoniazid) for 12 months, showed epiphyseal regeneration and mild leg-length discrepancy of < 1 cm due to overgrowth.^[27]

Timely initiation and adherence to appropriate ATT remain critical determinants of outcome.^[2] In this series, all patients who completed standard therapy demonstrated excellent functional recovery, normal gait, and radiographic bone remodeling at long-term follow-up. On the other hand, patients who defaulted treatment or follow-up could not be adequately assessed for late sequelae. These findings reinforce that, even in the absence of systemic illness or markedly abnormal laboratory parameters, prompt treatment is essential to prevent growth plate damage, deformity, and chronic morbidity.^[5,8]

The World Health Organization (WHO) consolidated guidelines on TB recommends a four-drug regimen (HRZE) for two months, followed by HR for 10 months (total 12 months) for children with suspected or confirmed osteoarticular TB.^[28] One case demonstrated hepatotoxicity attributed to pyrazinamide, which has the highest potential for liver toxicity among first-line agents.^[29] Hepatotoxicity typically occurs within the first two to eight weeks of intensive therapy, with younger age being a recognized risk factor.^[29] Immediate management involves withdrawal of ATT, followed by stepwise reintroduction at incremental doses with periodic monitoring of liver function.^[29]

In conclusion, infantile osteoarticular TB is a rare condition which may present with significant musculoskeletal involvement. In this case series of seven infants, patients who completed a minimum of three years of follow-up demonstrated favorable functional and radiographic outcomes, including normal gait, no significant limb-length discrepancy, and radiographic evidence of bony regeneration without apparent physeal abnormalities. These findings suggest that, despite the potential for

substantial skeletal involvement in infancy, satisfactory long-term functional and structural outcomes may be achieved with appropriate management and prolonged follow-up. Given the rarity of this condition, further studies with larger cohorts and longer follow-up are warranted to better characterize growth-related outcomes and potential late sequelae.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: D.P., K.W.L.: Conceptualization; K.W.L., D.P., A.M.: Managed patient care; Y.Z.S., X.X.F.H., Y.W.V.: Data collection, writing draft; M.L.A.R., A.M., S.A., D.P., K.W.L.: Review & editing.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

AI Disclosure: The authors declare that artificial intelligence (AI) tools were not used, or were used solely for language editing, and had no role in data analysis, interpretation, or the formulation of conclusions. All scientific content, data interpretation, and conclusions are the sole responsibility of the authors. The authors further confirm that AI tools were not used to generate, fabricate, or ‘hallucinate’ references, and that all references have been carefully verified for accuracy.

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