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MINISYMPOSIUM: PEDIATRIC INFECTIOUS DISEASE IN LATIN AMERICA

Osteoarticular tuberculosis: imaging findings in pediatric patients

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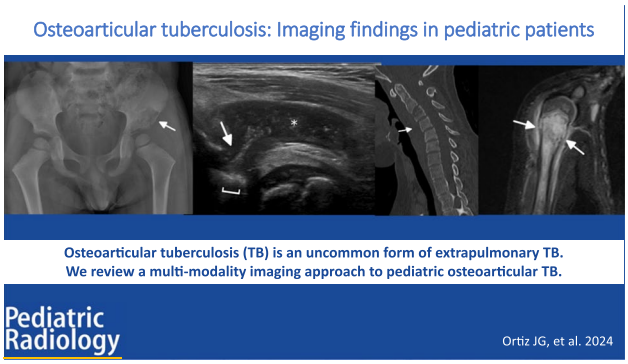
Abstract

Osteoarticular tuberculosis (TB) is an uncommon form of extrapulmonary TB that has the potential to damage joints and bones, generating long-term impairment. Mainly, the initial diagnosis of osteoarticular TB relies on clinical findings and imaging. When required, imaging can aim for less invasive tissue or fluid sampling for pathology, microbiology, and molecular biology analysis. Most TB diagnosis tests have variable and frequently poor sensitivities; however, bone biopsy samples have demonstrated a high percentage of culture positivity. Clinical and imaging findings of osteoarticular TB often mimic other processes, such as rheumatoid arthritis or chronic recurrent multifocal osteomyelitis. When the infection affects the growth plates, angular deformities and extremity length discrepancies can arise. Unfortunately, several osteoarticular TB cases are detected late due to the nonspecific nature of clinical symptoms and non-characteristic imaging findings. This article reviews the most common and atypical osteoarticular TB imaging presentations to increase awareness of osteoarticular TB.

Graphical Abstract



Keywords Bone · Children · Diagnostic imaging · Latin America · Tuberculosis

Introduction

Pediatric tuberculosis (TB) cases account for approximately 12% of all cases of TB infection worldwide. At the time of this publication, the proportion and number of pediatric cases remain increasing annually [1–3]. According to the 2023 World Health Organization (WHO) Global Tuberculosis Report, the incidence of TB in Latin America varies significantly between countries, with incidence ranging between 0.74 and 154 per 100,000 and most countries falling in the 10-100 per 100,000 range [3]. In children, TB infection is associated with higher mortality in comparison to adults due to delayed diagnosis and limited access to care [1]. This issue is further exacerbated in children below 3 years of age due to the high incidence of active disease after primary infection, up to 50% at 1 year and 25% at 2 years of age [4]. Most cases of active TB disease (80%) affect the lungs. About 4% of cases of active TB disease in pediatric patients affect the musculoskeletal system [5, 6]. Medical management approaches must prioritize improvements in prevention, diagnosis, and treatment [7]. Medical

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imaging plays a fundamental role in diagnosing and, when required, less invasive tissue and fluid sampling [1].

Pathogenesis

Tuberculosis is caused by the bacillus *Mycobacterium tuberculosis* [6, 8]. Once initial exposure and infection have occurred, these bacteria have evolved to thrive using the human immune system by surviving intracellularly within macrophages. Infected macrophages are isolated within the body by granulomas. Infection then can advance into primary infection with active disease or a variable length latent stage [6, 8, 9]. In a sizable number of cases, these granulomas prevent the bacteria from spreading systemically. However, in some cases, bacteria spread, generating multiple pulmonary and extrapulmonary clinical manifestations, including osteoarticular manifestation [10, 11].

Progression is due to an ineffective immune response. The main factors affecting the immune response are age and immune competence [11, 12]. Infants and preschool children are most susceptible to extrapulmonary spread. There is a second peak of active disease during adolescence, which happens particularly in areas of the world with high HIV coinfection rates [4, 13]. Children with rheumatologic diseases receiving immunosuppressant treatment are also more susceptible to TB infection. They also have a higher frequency of extrapulmonary presentation in comparison to the general population [14].

Specifically in the musculoskeletal system, bone and joint infections are most frequent due to hematogenous or lymphatic spread [15]. Direct extension from adjacent lymph nodes or by contiguous spread occurs less often [6, 8]. The infection can remain latent for months or years before the appearance of symptoms since the bacteria are much less active in osteoarticular lesions than in pulmonary lesions (paucibacillary) [6, 8]. Similar to bone infections caused by other bacteria, osteoarticular TB infection typically begins in the metaphysis of bones, causing necrosis either directly by the infection or by the pressure from granulation and caseating tissue [8]. Extension into the epiphysis and intra-articular space is considered a complication and is usually symptomatic [6, 8].

Clinical manifestations

Mycobacterium tuberculosis can infect almost any organ in the human body. Although respiratory symptoms and lymphadenopathy are the most common clinical manifestations [16], osteoarticular involvements, such as vertebral osteomyelitis, dactylitis, TB arthritis, and reactive arthritis (Poncet's disease), are other clinical manifestations that may appear in pediatric patients [8].

Skeletal lesions of TB tuberculosis are found in approximately 4% of children with active TB infection [4, 5]. According to most published literature, spinal TB and TB dactylitis tend to present in younger children, whereas involvement in large bones and joints tends to happen in the second decade of life [4, 5]. Nevertheless, there is a recently published paper by Drobish et al. describing spinal TB presentation in the second decade of life [17]. In comparison, in pyogenic osteomyelitis, about half of cases happen before 5 years of age [18]. The infection most frequently involves weight-bearing. In order of frequency, the most affected bones are the vertebrae, femur, tibia and fibula, and bones of the hands and feet. Bones such as the ribs, jaw, sternum, and other long bones are less frequently affected [6, 19]. In contrast, vertebral pyogenic osteomyelitis is rare in children, and about 75% of cases occur in the lower extremities [18]. Multifocal TB osteomyelitis involvement occurs more frequently in children in comparison to adults and is also more common in immunocompromised patients. About 5–15% of pediatric cases with osteoarticular TB will present with multifocal disease [20–24], often in patients with immunosuppression [24]. Accompanying non-specific systemic symptoms happen only in about one-third of patients and include low-grade fever, irritability, generalized weakness, weight loss, pain, and low-grade swelling at the site of infection [4, 25].

Approximately one-third to one-half of bone TB cases involve the spine [15]. The clinical presentation includes kyphosis, spinal rigidity, antalgic posture with avoidance of walking, and neurological symptoms such as decreased mobility and muscle spasms [19]. The presence of an epidural abscess, especially in the thoracic spine, is associated with cord compression and, in severe cases, paraplegia [15, 26]. Hyper-kyphosis can be associated with poor cardiopulmonary function [26, 27].

Joint involvement may present with a variable-sized effusion associated with marked stiffness and decreased range of motion [28]. A rare pediatric manifestation is tuberculosis-associated dactylitis [6]. TB tenosynovitis and bursitis are also uncommon osteoarticular presentations of TB infection [29].

Diagnosis

Although sputum smear microscopy is one of the most efficient markers of contagiousness [30], a negative test does not exclude the presence of TB infection. Not accounting for the low sensitivity of sputum smear in pediatric patients related to paucibacillary infection, pulmonary TB is seen concurrently in less than 50% of osteoarticular TB cases

[15]. Mainly, the initial diagnosis of osteoarticular TB relies on clinical findings and imaging. In osteoarticular TB, samples can be obtained for culture or staining by aspiration, drainage of abscesses, or biopsy of the affected site [8]. Despite cultures taking 4–6 weeks to return results, it is important to realize that bone biopsies have demonstrated in multiple prior studies high sensitivity for TB infection, ranging up to 94–100% [17]. This also aims to select an appropriate antibiotic treatment, given the ever-increasing rates of antibiotic resistance. Molecular biology has emerged in detecting microorganism genes and resistance genes to first-line drugs. This allows a faster diagnosis, considering that culture times last between 4 and 6 weeks [31].

Diagnostic imaging

Plain radiographs

Radiographs remain helpful in the initial evaluation. Radiological findings may vary and depend on the location of the infection and the affected structures. Although a chest radiograph is recommended as part of the initial imaging evaluation for patients with suspected or proven diagnosis [28] (Fig. 1), it is important to highlight that the lack of findings does not exclude the possibility of osteoarticular TB as half the cases will not have concomitant disease [5]. In osteoarticular infections, osteolytic lesions (Fig. 2), bone erosions (Fig. 3), and surrounding osteopenia (Fig. 4) can be observed. As destruction progresses, bone collapse, subluxation/dislocation, and joint deformity may be observed. Although non-specific, TB osteomyelitis tends to have less sclerosis, less sequestrum, and lower periosteal reaction than pyogenic osteomyelitis [5]. Injuries can destroy the physis, causing focal or diffuse physeal closure with subsequent angular deformities and/or extremity length discrepancy, which is seen as sequela in about 6% of children with osteoarticular TB [27]. In rare cases, transient physeal overgrowth may be observed due to hyperemia. However, radiographs have limitations in early detection and accurate characterization of lesions. Its primary deficiencies include underdiagnosing the extension of the lesions, decreased identification of multifocal lesions, and the inability to detect subdural abscesses in spinal involvement [32].

Technetium-99 m bone scan and PET imaging

Nuclear medicine studies are not indicated in the initial evaluation of patients with suspected osteoarticular TB due to the low specificity and high false positive rates of both techniques [24]. Nevertheless, osteoarticular TB should be considered in the differential diagnosis of a

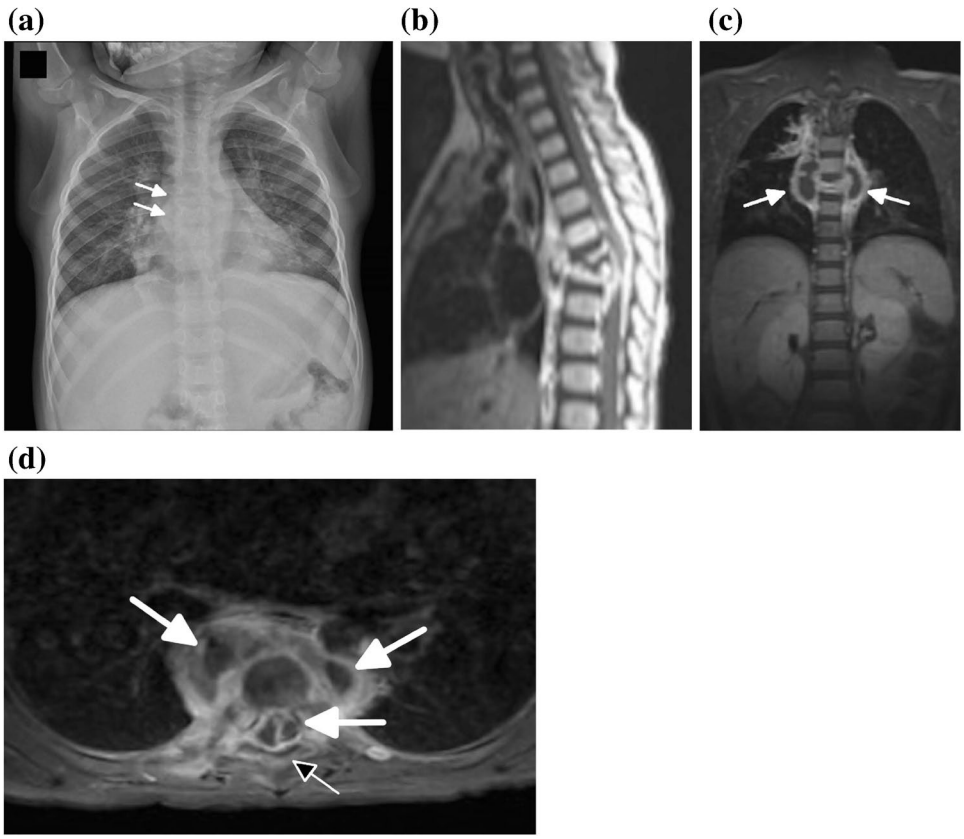

Fig. 1 A 5-year-old girl with AIDS presenting with back pain. A frontal chest radiograph (**a**) reveals multiple nodular opacities in the hilar regions with additional diffuse bilateral nodular opacities. Additionally, decreased vertebral body height involving the T6 and T7 vertebral bodies (*arrows*) and adjacent paravertebral soft tissue thickening is noted. A sagittal T1-weighted image (**b**) demonstrates osseous destruction and anterior predominant collapse of the T6 and T7 vertebral bodies with resultant gibbus deformity. There is also pre-vertebral and epidural soft tissue thickening. Coronal (**c**) and axial (**d**) post-contrast fat-suppressed T1-weighted images of the thoracic spine show paravertebral and epidural rim-enhancing fluid collections (*arrows*). There is mass effect with compression and posterior displacement of the spinal cord (*hollow arrow*). Imaging findings are suggestive of tuberculous spondylodiscitis

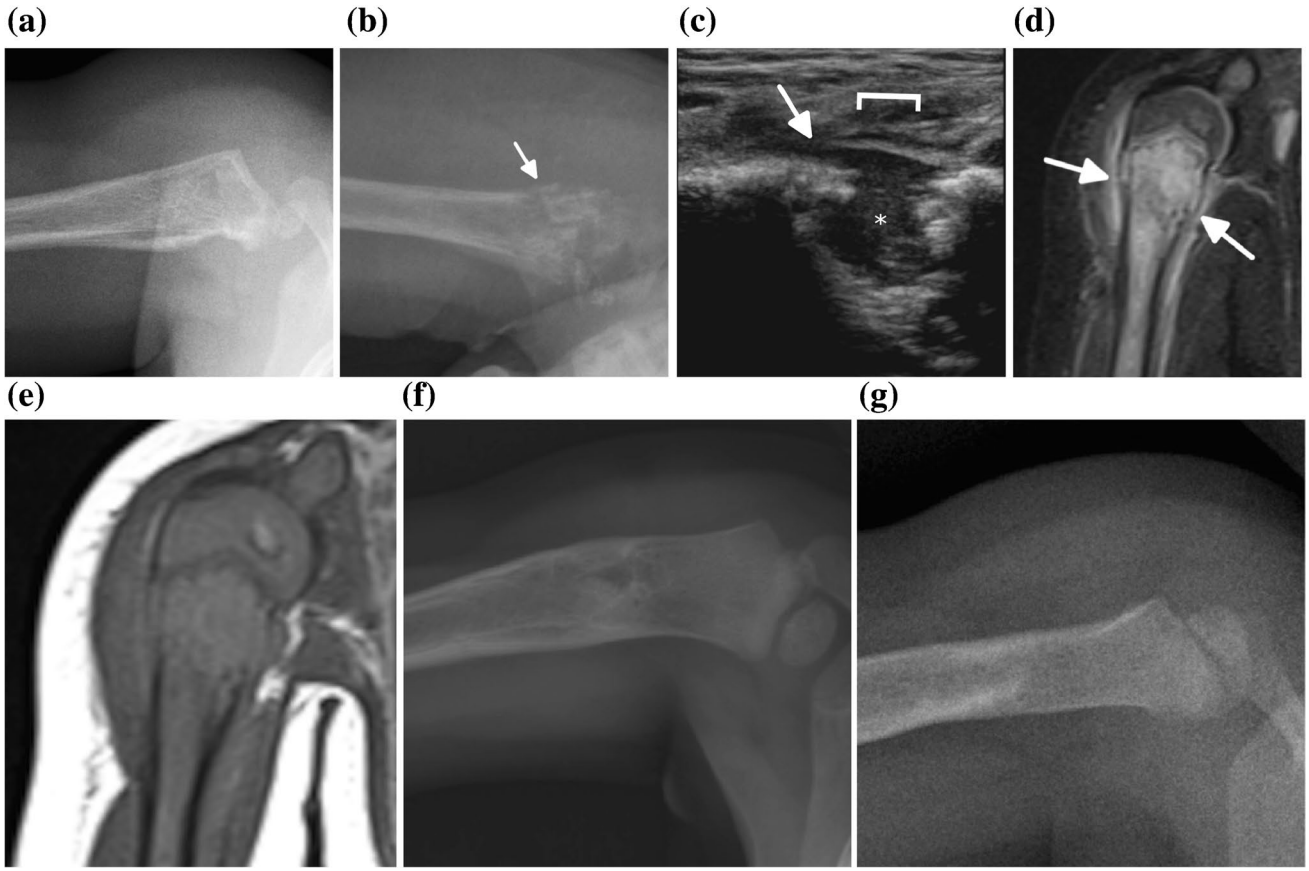

Fig. 2 A 3-month-old girl with proximal right arm swelling. A lateral radiograph of the right humerus obtained at presentation (**a**) and a short-term follow-up frontal radiograph of the same bone obtained 9 days after (**b**) demonstrate rapid progression of an osteolytic lesion in the proximal right humeral metaphysis with interval development of a pathologic fracture (*arrow*). Grayscale sagittal ultrasound image (**c**) of the proximal humerus shows a focal area of cortical destruction (*bracket*) with adjacent periosteal elevation (*arrows*) and hypoechoic fluid collection and/or inflammatory tissue (*asterisk*) extending into the intramedullary space and adjacent soft tissues. Coronal STIR (**d**) and coronal T1-weighted (**e**) MRI images of the right humerus demonstrate low T1-signal intensity and high T2-signal intensity within proximal humeral metaphysis in keeping with bone marrow replacement. Additional findings seen in the STIR image include periosteal elevation with subperiosteal fluid collection (*arrows*) and adjacent soft tissue regional inflammatory changes. After initiating antibiotic treatment, a frontal radiograph obtained at approximately 8 months (**f**) and a lateral radiograph obtained at approximately 11 months (**g**) after initial presentation demonstrate near-complete resolution of the osteolytic lesion and a healing fracture

patient from an endemic region. The primary utility of bone scintigraphy and PET lies in evaluating multifocal involvement [25].

Ultrasound

Ultrasound is a valuable ancillary technique to evaluate osteoarticular TB due to its availability and ease of completion in non-sedated patients. It can be useful to detect cortical erosions (Figs. 2 and 3), abscesses (Fig. 3), intra-articular fluid collections (Fig. 4), and inflammatory changes in the soft tissues (Figs. 2 and 3) [33, 34]. In addition, ultrasound can guide aspiration or biopsy of lesions for microbiological and pathology studies.

Computed tomography (CT)

CT provides better spatial resolution and sensitivity compared to plain radiography [28]. It allows evaluation of the disease extension, bone destruction, soft tissue involvement, and abscess presence [32]. Typical findings include osteolytic lesions with irregular margins, sclerotic areas, periosteal reaction, and focal bone erosions [28] (Fig. 5). Intravenous contrast administration improves lesion characterization, allowing visualization of enhancing joint effusions and better evaluation of soft tissue abscesses [32] (Fig. 6).

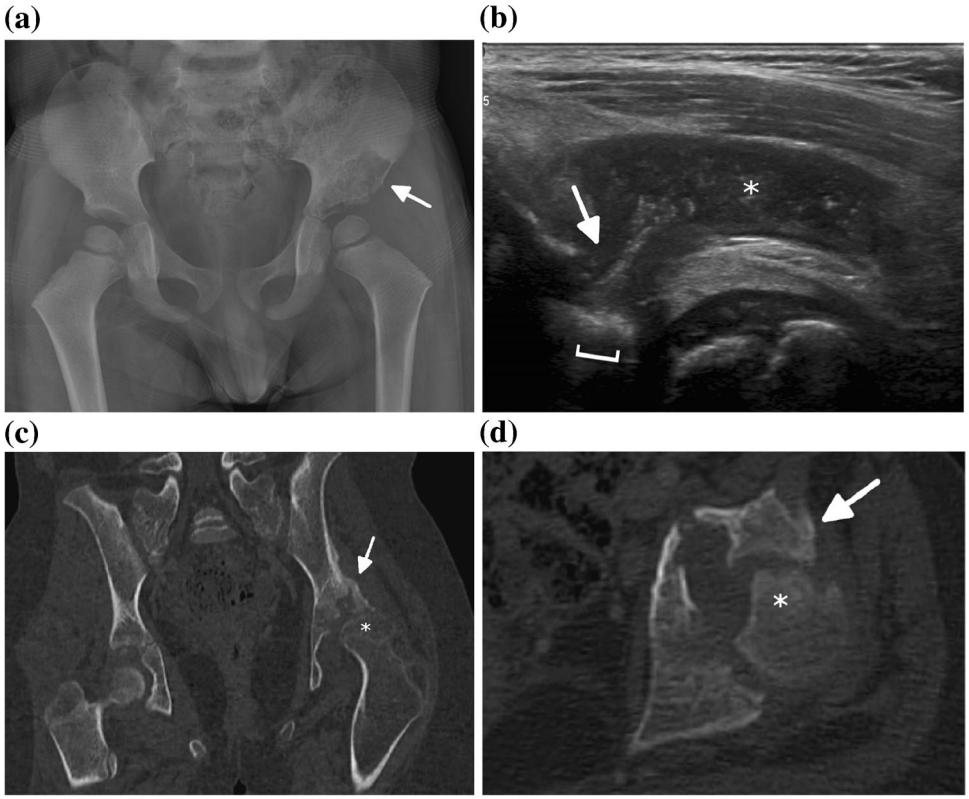

Fig. 3 A 2-year-old boy presenting with left hip pain. A frontal pelvic radiograph (**a**) reveals a lytic lesion with poorly circumscribed margins and an aggressive periosteal reaction involving the left iliac bone at the superior margin of the acetabulum (*arrow*). There is also adjacent soft tissue thickening, suggesting capsular involvement. The surrounding fat pad appears abnormal, with increased density and volume. A sagittal ultrasound image of the left hip (**b**) demonstrates a complex fluid collection centered within the left anterolateral hip soft tissues (*asterisk*). A deep, narrow tract extends into the superior acetabular rim with associated acetabular cartilage discontinuity (*arrow*), cortical irregularity, and hyper-echogenicity (*bracket*). Ultrasound images helped to understand the disease's full extent and plan appropriate interventions. Coronal (**c**) and axial (**d**) CT images of the pelvis reveal osseous destruction of the left acetabulum with capsular thickening and joint effusion. Left femoral head articular surface contour abnormality (*asterisk*) and osteopenia are noted when compared to the contralateral side. There is periosteal reaction on the lateral aspect of the acetabulum (*arrow*). Lateral subluxation of the left femoral head is also present. These images represent sequela of osteomyelitis and arthritis due to confirmed tuberculosis

Magnetic resonance imaging (MRI)

MRI is the most sensitive and specific technique for evaluating musculoskeletal manifestations of TB. It is particularly useful in detecting inflammatory changes before osteolytic changes. MRI is able to detect findings from spinal TB about 4–6 months before other modalities [35]. Findings include bone marrow replacement (Fig. 2), homogeneous or heterogeneous enhancement after contrast administration (Figs. 1 and 4), soft tissue edema, abscesses, and synovitis. It can also help to differentiate other diseases with similar clinical presentation [32].

Imaging modalities used for diagnosis and follow-up of osteoarticular TB must be chosen and analyzed on a case-by-case basis with the assistance of a multidisciplinary medical team. Variables that affect the decision-making process include patient factors such as the age and size of the patient, the need for sedation for cross-sectional imaging, the site of suspected infection, and the patient's immune status [28]. The diagnosis of osteoarticular TB can be incidental or related to latent infection in immunosuppressed children [36, 37]. Local environmental factors such as availability and expertise in the completion and interpretation of specific imaging modalities should also be included in the discussion.

Imaging findings

Spinal TB (Pott's disease) On radiographs, spinal TB often mimics conditions like pyogenic osteomyelitis or even primary tumors of the spine [36, 38]. Radiographic findings seen in spinal TB include vertebral collapse with anterior vertebral body predominance and the presence of paravertebral soft tissue thickening, indicating phlegmon and abscesses (Fig. 1). The most frequent location of spinal TB is the lower thoracic and the upper lumbar spine, between

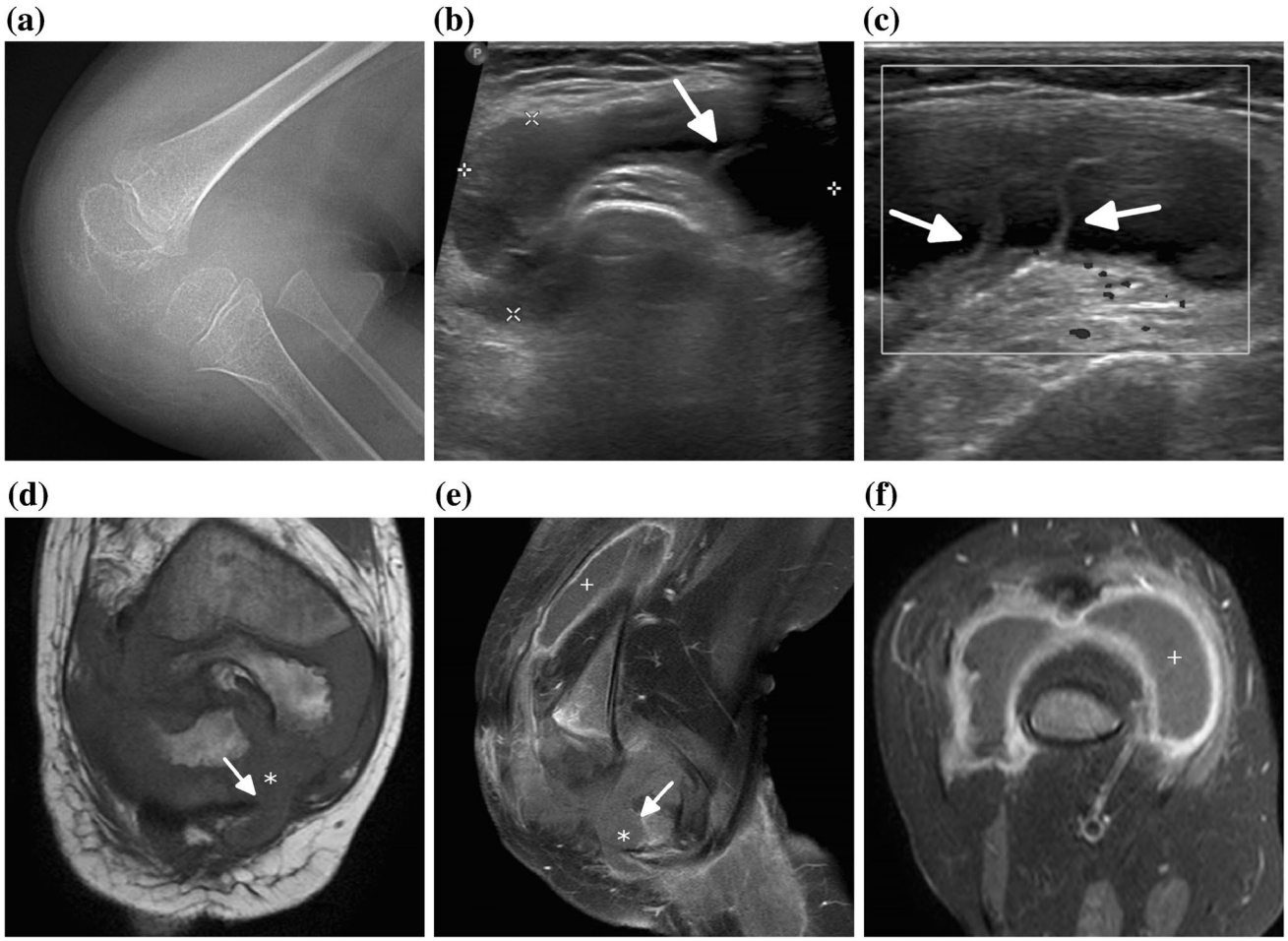

Fig. 4 A 6-year-old boy presents with knee swelling. A lateral knee radiograph (**a**) reveals marked articular surface irregularity with intra-articular calcification and juxta-articular osteopenia. The tibiofemoral joint space appears to be widened. The effacement of the fat pads further supports the presence of significant inflammation or fluid accumulation. Grayscale (**b**) and color Doppler (**c**) ultrasound images of the knee in a transverse plane demonstrate a large complex fluid joint effusion with multiple internal septations (*arrows*). There is also capsular thickening with hyperemia on color Doppler images (**c**), suggesting synovitis. These findings suggest an inflammatory or infectious joint effusion. Coronal T1-weighted image (**d**) and post-contrast T1-weighted images with fat-suppression in sagittal (**e**) and axial (**f**) planes demonstrate a rim-enhancing fluid collection centered at the proximal tibial metaphysis (*asterisk*). Note the trans-physeal extension into the proximal tibial epiphysis (*arrow*) and intra-articular extension into the knee joint capsule with associated joint effusion and enhancing synovitis (+). There is also a proximal tibial metaphyseal cortical defect with a soft tissue abscess in keeping with a cloaca. In the coronal T1-weighted image (**d**), there is a rim of intermediate to high T1 signal intensity surrounding the abscess in keeping with Brodie's abscess. Brodie's abscess is frequently seen in cases of tuberculous osteomyelitis due to the slow progression compared to pyogenic osteomyelitis. In further studies, the patient was proven to have tuberculous osteomyelitis and septic arthritis

the T8 and the L3 levels [26]. Involvement may be multisegmented and typically involves continuous segments but may also less frequently skip segments [6].

On cross-sectional imaging, anterior wedging with a degree of kyphosis is seen in up to 79% of cases [26, 39] (Fig. 7). If the infection spreads into the adjacent soft tissues, a rim-enhancing paraspinal and epidural abscess can be seen [13] (Fig. 8). An intact intervertebral disc space can help distinguish spinal TB from pyogenic spondylitis caused by other bacteria, as disc destruction happens late in spinal TB. In contrast, it occurs early in the disease in pyogenic spondylitis caused by different bacteria, most often caused by gram-positive bacteria such as *Staphylococcus aureus* [15, 38]. The presence of a gas-fluid level within a paraspinal or epidural abscess almost entirely excludes the diagnosis of spinal TB [15, 40].

Large- and medium-sized joint and bone TB This group includes infections in the large joints and bones, such as the knee, hip, shoulder, elbow, wrist, and adjacent bones. The appearance of TB osteomyelitis is similar to pyogenic osteomyelitis and also usually originates in the bone metaphyses. The presence of Brodie's abscess in TB

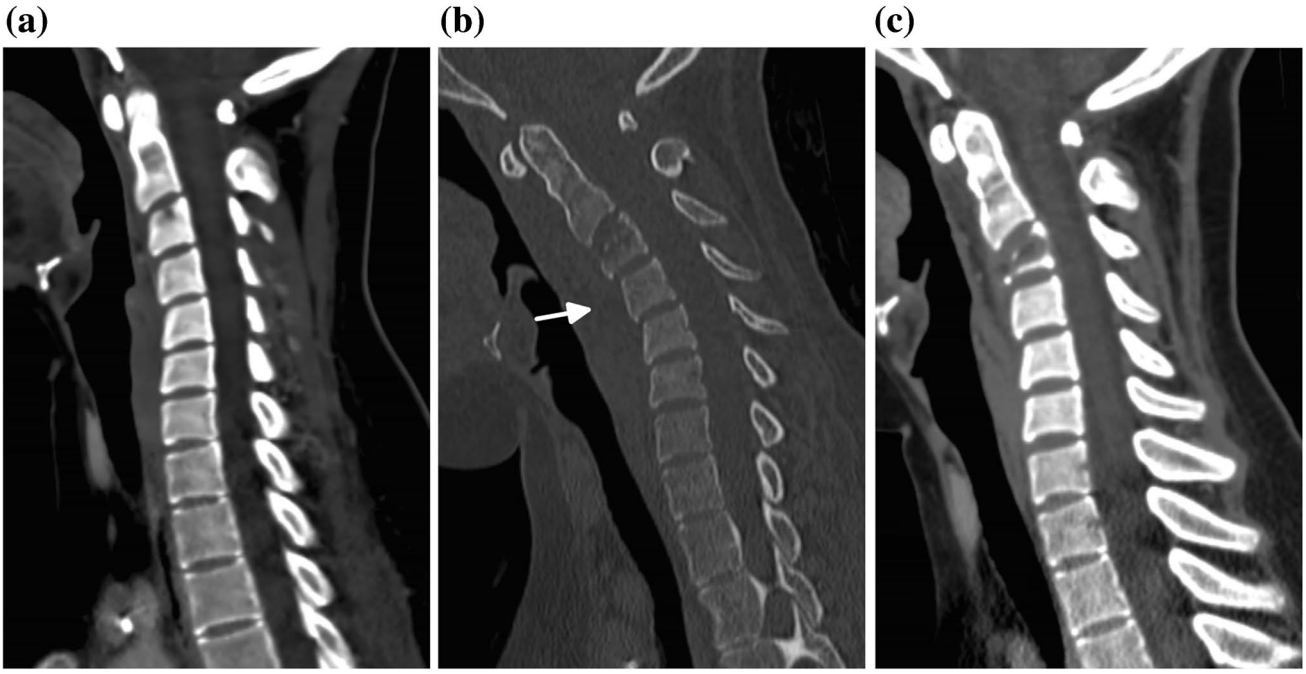

Fig. 5 A 14-year-old girl presenting with cervical pain. Sagittal CT images of the cervical spine at initial presentation (**a**), 13-day follow-up (**b**), and 31-day follow-up (**c**). There is progressive involvement of the C3 vertebral body with increasing anterior wedging. Pre-vertebral soft tissue thickening with pre-vertebral fat plane effacement (*arrows*) is also noted. This series highlights the evolving changes of the disease

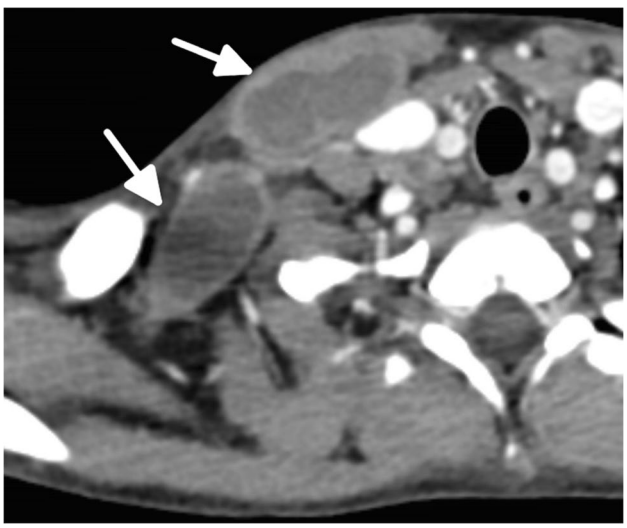

Fig. 6 A 7-year-old boy with right cervical swelling. Axial contrast-enhanced neck CT image reveals enlarged, necrotic, peripherally enhancing supraclavicular lymphadenopathy (*arrows*). This finding represents caseation necrosis and is characteristic of tuberculous lymphadenitis

osteomyelitis happens frequently to the slow progression of TB infection [41] (Fig. 4d). TB arthritis in these sites may present with joint effusion, soft tissue swelling, and bone erosion that may be visible on radiographs. These signs can mimic rheumatoid arthritis or septic arthritis. Usually, TB arthritis is associated with more profound osteopenia and more osseous erosions in comparison to septic arthritis caused by other organisms [29]. TB-related synovitis has been described as having low to intermediate T2 signal intensity due to the presence of caseating tissue and hemorrhage [29, 42]. In the wrist, TB may present with cystic bone lesions and periosteal reaction, which may resemble chronic osteomyelitis or neoplastic conditions like enchondroma or giant cell tumor.

Small joint and bone TB This group includes less frequent sites such as phalanges, metacarpals, and other small bones in the hands and feet. TB of smaller bones may present with nonspecific swelling and pain, often leading to misdiagnosing more common conditions like gout or sarcoidosis. Imaging plays a crucial role here; radiographs may show osteolytic lesions with a slow progression, while MRI can detect early marrow involvement and soft tissue abscesses. *Mycobacterium tuberculosis* quickly replaces the marrow space, substituting and enlarging it with granulation tissue. This leads to a spindle-shaped expansion of the affected bone with intramedullary cyst-like structures. These cyst-like structures are known as spina ventosa [29]. These imaging features help to distinguish tuberculous infections from other inflammatory or neoplastic conditions that might involve small bones [38].

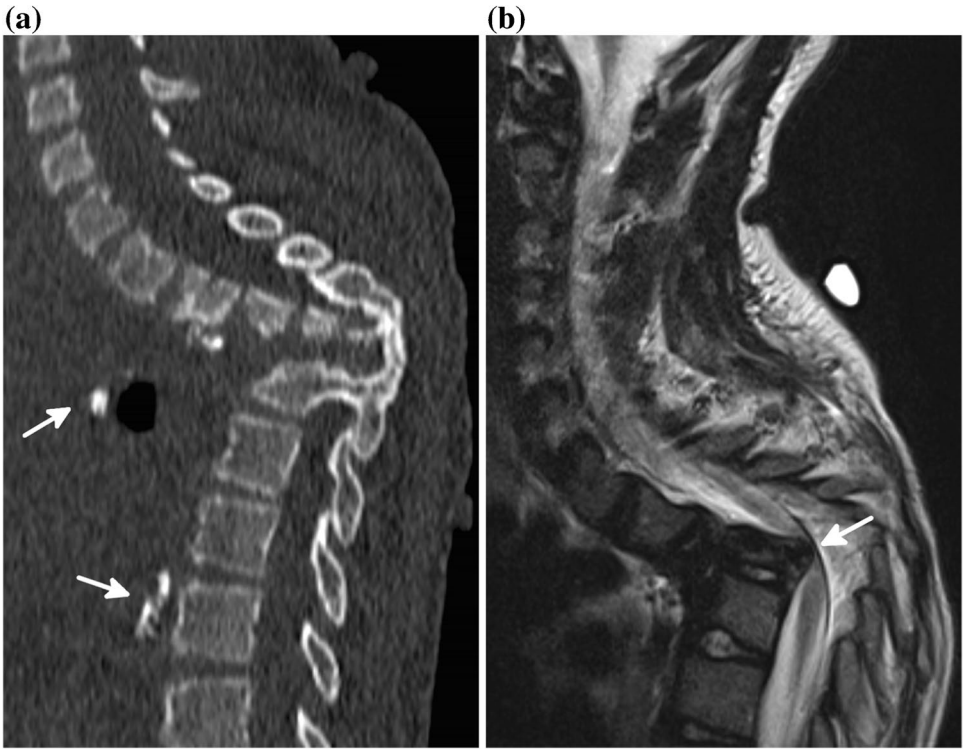

Fig. 7 A 10-year-old girl with history of treated spinal tuberculosis. **a** Sagittal CT image of the thoracic spine demonstrates anterior wedging and collapse of multiple mid-thoracic vertebral bodies as a sequela of prior infection. Calcified hilar and posterior mediastinal lymphadenopathies are also visualized (*arrows*). **b** Sagittal T2-weighted MR image demonstrates severe compression of the spinal cord at the level of hyper-kyphosis (*arrow*)

Differential diagnosis

Chronic recurrent multifocal osteomyelitis (CRMO) This rare pediatric disease, also known as chronic nonbacterial osteomyelitis (CNO), is an autoinflammatory disease characterized by bone involvement, recurrent flare-ups, and a lack of microbiological isolation. CRMO can mimic some radiological osteoarticular TB findings. Imaging findings seen in CRMO that can help in the differentiation from TB osteomyelitis include lack of abscess formation, fistulas or sequestra, presence of other autoimmune diseases such as inflammatory bowel disease or psoriasis, symmetric involvement or involvement of the clavicles, or sclerosis and hyperostosis at the affected area [43].

Poncet's disease, also identified as tuberculous rheumatism, is a reactive arthritis associated with tuberculosis infection, generally extrapulmonary [44]. This rare form of arthritis does not directly involve the joints but arises as a response to active tuberculosis elsewhere in the body [44]. Poncet's disease typically presents as a symmetrical polyarthritis, mainly affecting large joints, and spares the axial skeleton [45]. It is distinct from tuberculous arthritis, which tends to be a deforming, septic monoarthritis and can have *Mycobacterium tuberculosis* isolated from the joint [45]. Instead, Poncet's disease manifests with features of reactive arthritis without bacterial isolation within the joint fluid. The joint symptoms typically resolve with effective antituberculosis antibiotic therapy without sequelae [44].

The differential diagnosis for Poncet's disease includes other forms of arthritis like rheumatoid arthritis, which often shows specific antibodies, and septic arthritis, which involves direct microbial infection of the joints detectable in synovial fluid [45]. It is crucial to consider Poncet's disease in patients with polyarthritis and concurrent active tuberculosis, particularly in regions where TB is prevalent [44]. The diagnosis is supported by the absence of bacteria in joint samples and the rapid resolution of symptoms following the commencement of tuberculosis treatment [44].

Conclusion

Osteoarticular tuberculosis in pediatric patients tends to be severe due to a lack of awareness of the condition and because it is often confused with other diagnoses that have similar clinical presentation and laboratory and imaging findings. Cultures and other laboratory tests have variable and often low sensitivities. Cultures require up to 4–6 weeks to grow. Diagnostic imaging plays a central role in early disease detection; hence, it is essential to be familiar with the most common findings of osteoarticular TB to provide a prompt diagnosis and prevent complications.

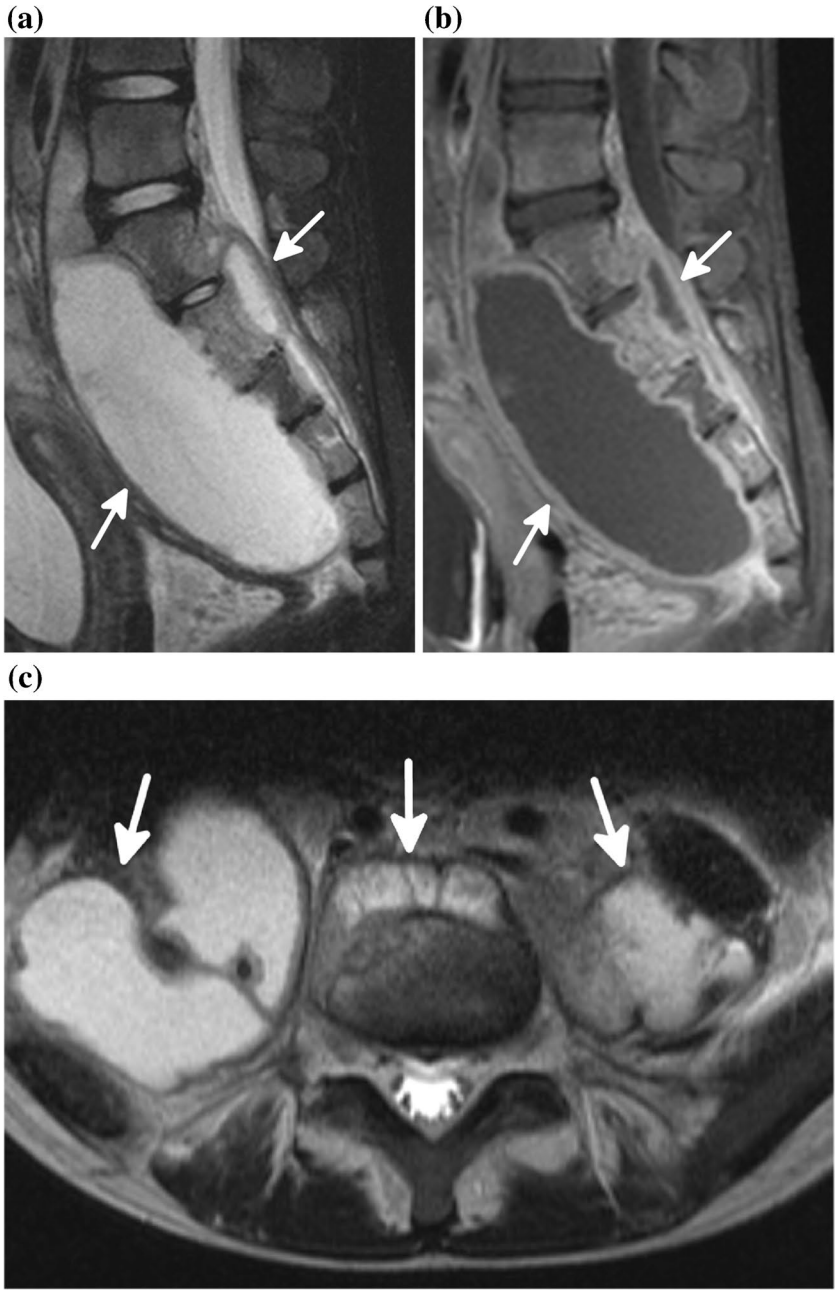

Fig. 8 A 10-year-old girl presenting with insidious lower back pain. Sagittal T2-weighted MR image (**a**) demonstrates heterogeneous bone marrow signal intensity and multifocal cortical discontinuity involving the L5-S4 vertebral bodies. Large presacral and epidural fluid collections (*arrows*) with rim enhancement on post-contrast fat-suppressed T1-weighted images (**b**) are present. Also, note the relative lack of disc destruction in relation to the extensive osseous involvement. **c** Axial T2-weighted MR image demonstrates cortical irregularity and bone marrow T2 hyperintensity along the anterior aspect of the L5 vertebral body. A pre-vertebral fluid collection and bilateral psoas fluid collections are present (*arrows*)

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Author contribution GO: wrote and collaborated with the contribution of the cases and their images, carried out a bibliographic search, and reviewed and approved the final submitted manuscript. JD: edited the manuscript, updated and improved the citations, verified the consistency of numerical data, contributed additional cases, edited the images, and reviewed and approved the final submitted manuscript. TR: wrote, carried out a bibliographic search, and critically reviewed and approved the final submitted manuscript. MG: wrote and collaborated with the contributions of the cases and their images and reviewed and approved the final submitted manuscript. NB: drafted, wrote, reviewed, and approved the final submitted manuscript. OP: wrote and collaborated with the contribution of the cases and their images and reviewed and approved the final submitted manuscript. GC: conceived the idea of the article, wrote, collaborated with the contribution of the cases and their images, and reviewed and approved the final submitted manuscript.

Declarations

Conflicts of interest None

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