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# Multifocal Skeletal Tuberculosis Mimicking Langerhans Cell Histiocytosis in a Child: a Case Report With a Long-Term Follow-Up

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**Abstract**

**Introduction:** Multifocal skeletal tuberculosis is a rare condition that may masquerade as Langerhans cell histiocytosis, especially in children.

**Case Presentation:** We report a case of multifocal osseous tuberculosis in a 5-year-old female patient admitted to our hospital with a complaint of low back pain but no history of respiratory symptoms or malaise. Radiological findings included vertebra plana and multiple lytic lesions in both the frontal and pelvic bones. An initial diagnosis of Langerhans cell histiocytosis was made based on imaging findings; however, the patient underwent further evaluation for *Mycobacterium tuberculosis,* and histopathologic findings confirmed the diagnosis of tuberculosis. The patient showed a nearly complete response after receiving a course of anti-tuberculosis drugs.

**Conclusions:** A high index of suspicion is required for the early diagnosis and prompt treatment of patients with osseous tuberculosis. Given the high prevalence of tuberculosis in developing countries, tuberculosis should be considered in the differential diagnosis of multifocal lytic lesions and vertebra plana, especially in children.

*Keywords:* Tuberculosis, Bone and Bones, Spine

## 1. Introduction

Tuberculosis is a universal concern with a vast spectrum of clinical and radiological features. Musculoskeletal tuberculosis constitutes 1% - 3% of all tuberculosis cases, with multifocal bone involvement accounting for approximately 10% patients with skeletal tuberculosis (1). Moreover, the involvement of multiple flat bones in an immunocompetent patient is exceedingly rare. The clinical and radiological manifestations of osseous tuberculosis may mimic other destructive bony lesions. Thus, a high index of clinical suspicion and familiarity with the unusual imaging features of tuberculosis are mandatory for the prompt diagnosis and appropriate therapeutic management. Herein, we describe the radiological findings of a case of multifocal osseous tuberculosis, initially misdiagnosed as Langerhans cell histiocytosis.

## 2. Case Presentation

A 5-year-old female patient presented with a 2-year history of lower thoracic pain for evaluation of progressively worsening symptoms in 1997. She had been living in Robat-Karim, a rural area of Tehran, Iran. She had also been experiencing difficulty in walking and intermittent low-grade fever for 8 months. In the meantime, the patient had shown poor clinical response to analgesic drugs. Despite the lack of any reliable history of prior contact with tuberculosis, her grandfather had died from an undetermined lung disease with a clinical history of chronic productive cough.

On physical examination, the patient was febrile with a hunched posture, and her back pain aggravated with any applied movement. There was also a warm, soft-tissue swelling on her frontal scalp measuring about 2 cm in diameter with no accompanying erythema. The growth indices and neurologic evaluation were normal. The laboratory tests revealed leukocytosis (white blood cell count, 11,000/cm$^3$) with a predominance of lymphocytes (55%). Erythrocyte sedimentation rate was elevated (122 mm/h). Other laboratory test results were negative, including thyroid-function, Wright, Coomb's Wright, and 2-mercaptoethanol tests.

On lateral thoracic and lumbar radiographs, near-complete anterior wedging of the T7 vertebral body was evident along with partial collapse of the L2 vertebral body (Figure 1).

Thoracolumbar magnetic resonance imaging (MRI) showed complete anterior wedging of the T7 vertebral body. Prevertebral soft tissue and epidural changes extended from T5 to T8 levels. MR images also showed partial loss of height in the L2 vertebral body.

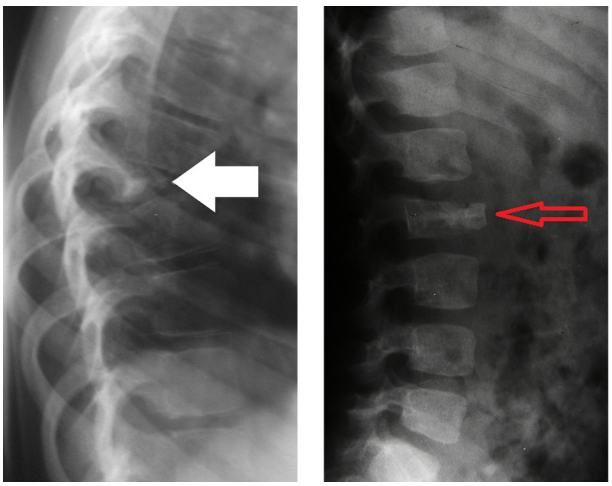
Bone radiographs showed small, scattered lytic lesions with an indistinct margin in the frontal bone, right scapula, left iliac, and pubic bones of both the right and left sides (Figure 2). On brain computed tomography (CT), there were multiple lytic lesions on the frontal bone with a distinctive margin. The brain parenchyma was intact.

On the chest CT scan, the lung parenchyma and mediastinum appeared normal. Whole-body bone scintigraphy revealed increased tracer uptake in the skull, right scapula, mid-thoracic vertebrae, and left hemipelvic and right pubic bones.

With respect to the clinical and radiological features, the patient was initially diagnosed as having Langerhans cell histiocytosis, but histopathologic examination of the scalp and skull lesions revealed multiple granulomas of varying sizes containing caseous necrosis along with epithelioid and giant Langerhans cells. The findings were indicative of chronic granulomatous inflammation and compatible with tuberculosis (Figure 3). The definite diagnosis of tuberculosis was confirmed with a polymerase chain reaction of the specimen by detecting the *Mycobacterium tuberculosis* genome.

The patient underwent 8 months of anti-tuberculous treatment, including isoniazid, pyrazinamide, and rifampin. An excellent outcome was obtained in a short period with a mild kyphotic deformity that was persistent at the long course of follow-up (as long as 15 years) (Figure 4).

**Figure 1.** On a Lateral Lumbosacral Radiograph, Complete Collapse and Vertebra Plana Appearance of the L2 Vertebral Body are Noted (White Solid Arrow)



A lateral thoracic radiograph shows anterior destruction of the T7 vertebral body (red open arrow).

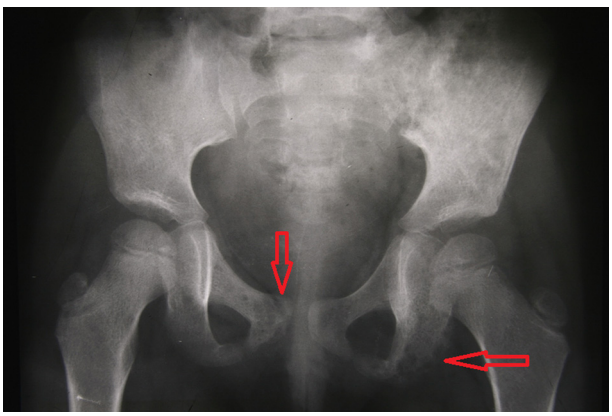


**Figure 2.** A Pelvic Radiograph Shows Multiple Ill-Defined Lytic Lesions (Arrows) in the Right Side of the Symphysis Pubis and Inferior Ramus of the Left Pubic Bone

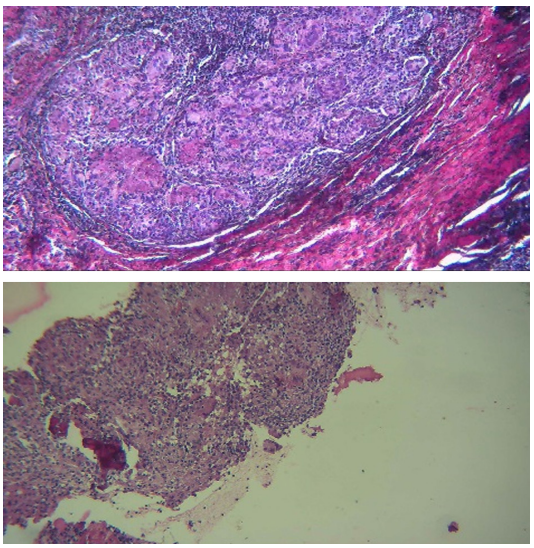


**Figure 3.** Histopathology sections show features of chronic granulomatous inflammation (hematoxylin and eosin staining at 40× and 100× magnification).

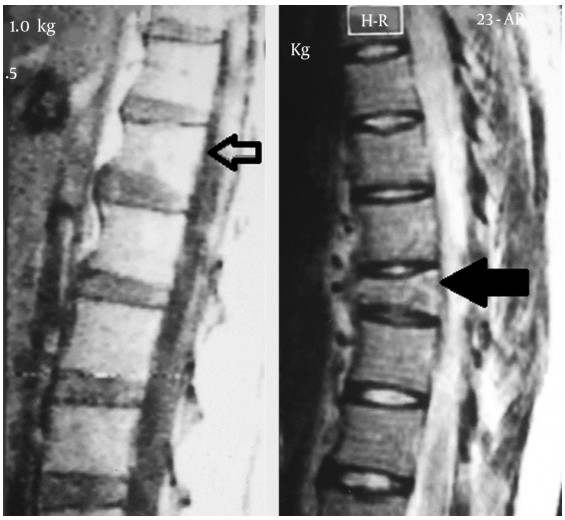



**Figure 4.** After Treatment, MR Images Reveal Only a Mild Loss of Heights of L2 (Open Arrow) and T7 (Solid Arrow) Vertebral Bodies in the Left- And Right-Sided Images, Respectively.

## 3. Discussion

Tuberculosis is a common infectious disease, particularly in developing countries, and might be a cause of morbidity or mortality if left untreated. Skeletal tuberculosis usually results from lymphohematogenous dissemination of visceral tuberculosis, and the most common site of tuberculous osteomyelitis is the thoracolumbar spine, followed by any other flat or long bones. Multifocal skeletal tuberculosis is an extremely rare condition, especially in immunocompetent patients even in endemic areas, accounting for 1% - 3% of all tuberculosis cases. The average prevalence of osteoarticular tuberculosis was reported to be 5% - 15% of all extrapulmonary tuberculosis cases among children, and the initial erroneous diagnosis of different forms of skeletal tuberculosis has commonly appeared in the literature (2).

Two distinct patterns of vertebral tuberculosis are described. The first is spondylitis without disc involvement, which is exceedingly more common. Multilevel vertebral body involvement could occur in this form as skip lesions. However, disc space may be involved in tuberculous spondylitis among children with pyogenic spondylitis that is because of differences in vertebral microcirculation between children and adults. The second pattern is destruction of 2 or more contiguous vertebrae associated with late-onset disc infection, which results in intervertebral space narrowing due to disc herniation into the collapsed vertebral body; this is regarded as an atypical radiologic feature of vertebral tuberculosis. In multiple vertebral body involvement, the characteristic gibbous deformity and paraspinal mass or collection are common. Posterior element involvement is a characteristic of vertebral tuberculosis. When severe, distinct loss of vertebral height can lead to moderate kyphosis with facet joint subluxation or dislocation. Preservation of disc space as well as posterior element abnormalities and multiplicity of vertebral body involvement in tuberculosis may lead to difficulty in distinguishing tuberclusis from tumoral processes (3-6).

To the best of our knowledge, 14 cases of scapular tuberculosis have been reported in the literature, with the scapula body being the most commonly involved, and the most common radiological findings were described as lytic lesions with sclerotic margins (7). Tuberculosis of the ilium constitutes less than 1% of all skeletal tuberculosis. A typical radiological feature of tuberculosis in cancellous bones is feathery sequestra or lytic lesions with irregular margins associated with mild surrounding sclerosis. Similarly, calvarial tuberculosis within the frontal and parietal bones, the most common site of involvement in the skull, is also rare with a typical pattern of inner and outer table involvement along with a sclerotic border and a central sequestrum (8).

An important factor in deriving the differential diagnoses of multifocal lytic bony lesions is to consider the patient's age. Langerhans cell histiocytosis, lymphoma, tuberculous osteomyelitis, and pyogenic osteomyelitis as well as metastatic neuroblastoma, Ewing's sarcoma, and enchondromatosis should be considered as the main differential diagnoses for multifocal lytic bony lesions in children. Although all of the abovementioned diseases have a relatively similar radiological pattern of bone involvement, bone scintigraphy, and cross-sectional CT and MR imaging can be helpful demonstrate disease distribution as well as any soft tissue or bone marrow involvement. Eosinophilic granuloma is a limited form of Langerhans cell histiocytosis with no extra-skeletal involvement, which could present in either monostotic or polyostotic form. When vertebra plana is present and the calvarium is involved, eosinophilic granuloma may have a clinical or radiological manifestation identical to that of tuberculous osteomyelitis, i.e., a painful soft-tissue swelling in a patient with well-circumscribed and pouched-out lesions. In this setting, a more destructive and aggressive appearance of the lesions in the eosinophilic granuloma may be a distinctive feature. Finally, the presence of a caseating granuloma on histological examination suggests tuberculosis, while microbiological and/or histological confirmation is essential for the definite diagnosis of vertebral tuberculosis.

To conclude, we have shown the radiological findings of a case of multifocal osseous tuberculosis, initially misdiagnosed as Langerhans cell histiocytosis. Familiarity with the imaging features of musculoskeletal tuberculosis and a high index of clinical suspicion are necessary for the correct diagnosis and proper treatment.

## Footnote

**Authors' Contributions:**Data acquisition: Hamidreza Haghighatkhah, Yousef Jafroodi, Afarin Sadeghian Dehkordy, Morteza Sanei Taheri. Data interpretation: Hamidreza Haghighatkhah, Yousef Jafroodi, Afarin Sadeghian Dehkordy, Ramin Pourghorban. Drafting of the manuscript: Afarin Sadeghian Dehkordy.

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