

Case Report

Ten years follow up of a chronic tubercular osteomyelitis of the proximal tibia in infancy

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ABSTRACT

Primary tuberculous osteomyelitis accounts for less than 10% of extra pulmonary tuberculosis in childhood. In about 50% of the patients, the vertebrae are the sites of skeletal involvement. Solitary bone TB is rare in infancy and has non specific findings and can be misdiagnosed easily. A 12 month old infant, presented with fever, pain, swelling in left knee, difficulty in moving left lower limb and inability to bear weight for 15 days at Nizam's institute of medical sciences, Hyderabad, in 2010. She was managed conservatively with injectable antibiotics, initially. After 15 days fever and swelling recurred. A biopsy was performed which showed plenty of polymorphs. A month later with second recurrence she was operated by means of debridement and curettage. Subsequent biopsy and culture revealed active *Mycobacterial tuberculosis* infection. Anti-tubercular treatment titrated to her body weight was administered for 12 months and patient was followed up. The patient's general condition improved with betterment in laboratory parameters and resolution of the lesion, without any sequelae. Upon a close follow up of 10 years (2010-2020), no residual deformity was noted and excellent clinical outcome achieved. Skeletal TB without spinal involvement in children is rare and it does not have any pathognomonic radiographic or clinical characteristics. Physis can heal gradually and full range of motion of the adjacent joints can be maintained. Tuberculosis should be an essential differential diagnosis while addressing cases with similar presentation in endemic regions like India. As clinical and radiological findings may be indistinguishable from malignant disease, tuberculous osteitis should be excluded in infants presenting with undiagnosed bone lesions despite been vaccinated with Bacille Calmette Guerin at birth.

Keywords: Tuberculosis, Osteomyelitis, Infant, Proximal tibia

INTRODUCTION

Primary tuberculous osteomyelitis accounts for less than 10% of extra-pulmonary tuberculosis (TB) in childhood.¹ In about 50% of the patients, the vertebrae are the sites of skeletal involvement.² Solitary bone TB is rare in infancy and has non-specific findings and can be misdiagnosed easily.³ Skeletal lesions tend to be isolated to one anatomical site and multifocal tuberculosis with more than one tuberculous osteo-articular lesion is rare, especially in immunocompetent individuals.

In infants the epiphysis can be destroyed by bacterial infection spreading from a metaphyseal focus. At this young age transphyseal vessels provide a pathway for infection to spread.^{5,6} Skeletal Tuberculosis is often difficult to diagnose initially; several weeks or months may be required to diagnose it correctly. In the case reported by Chen SC et al, it took 80 days to confirm the diagnosis. The variable radiological appearance of isolated bone lesions in children can resemble various bone lesions including subacute and chronic osteomyelitis, simple and aneurysmal bone cysts,

cartilaginous tumors, osteoid osteoma, granulomatous lesions, hematological disease and certain malignant tumors. Surgical debridement and curettage is indicated for cases with diffuse bone destruction.⁴ To the best of our knowledge, tuberculosis of proximal metaphysis of tibia in infancy is very rare and not reported yet.

The objective of the study was to closely follow up the patient, identify any limb length inequality and angular deformities and treat those at the earliest.

CASE REPORT

A 12 month old infant, presented with fever, swelling, pain, difficulty in using the left lower limb and inability to bear weight for 15 days. At the first visit, clinically, the infant was mildly toxic with features suggestive of osteomyelitis of proximal tibia on the left side. No other joints were involved. Hematological parameters revealed raised total leucocyte count (TLC) 24,000 cells/cm³ with neutrophilia 82%, and erythrocyte sedimentation rate (ESR) 60 mm/hr, whereas C-reactive protein was within normal limits. Blood cultures were negative. Radiographically, lytic pathology was seen in and around the central part of the growth plate on the metaphyseal side. It was associated with attenuation of growth plate, with peri articular osteopenia, subchondral erosion, periosteal reaction and increased joint space of the left knee joint (Figure 1). Aspiration of the lesion, and gonocentesis was done by two separate portals by a thick needle and no organisms were isolated. Hence, she was managed conservatively initially with injectable antibiotics and slab support. The TLC came down to 17,900 cells/cm³ with neutrophils being 32% and ESR normalized to 6 mm/hr.



Figure 1: Radiograph taken on first visit; lytic pathology was seen in and around the central part of the growth plate on the metaphyseal side with attenuation of growth plate, with peri articular osteopenia, subchondral erosion, periosteal reaction and increased joint space of the left knee joint.

At the second visit, after 15 days, in view of recurrence of fever (2 episodes) and swelling, a proper biopsy was performed under anesthesia. Intra Operatively a pocket of purulent fluid was found. The biopsy showed plenty of polymorphs, with negative staining for acid fast Bacilli and fungal elements. No organism was isolated on culture. Histopathology revealed possible suppurative inflammation. At this juncture, chronic atypical Brodie's abscess and chronic recurrent multifocal osteomyelitis was thought of and continued with broad spectrum antibiotics with a wishful thinking of remission.

At the third visit, even after a fortnight with antibiotics, she was worsening (TLC 25,100 cells/cm³, neutrophils 40%, lymphocytes 50%, ESR 56 mm/hr) so we stopped the antibiotics to get a positive culture, and planned for a repeat biopsy. She was operated by means of thorough debridement and gentle curettage of the left proximal tibial metaphysis to mitigate the iatrogenic proximal tibial physal injury. Intraoperatively cheesy caseous material was found which was meticulously collected for biopsy and culture. The lesion was extending to the entire proximal tibia with involvement of the proximal physis. Once again culture and gram stain was negative and histopathology revealed chronic caseating granulomatous inflammation suggestive of *Mycobacterial tuberculosis* pathology (Figure 2). Simultaneously the material also subjected to TB culture, which showed growth of mycobacteria species in BACTEC-460 TB system at the end of four weeks, which was sensitive to all primary line of drugs.

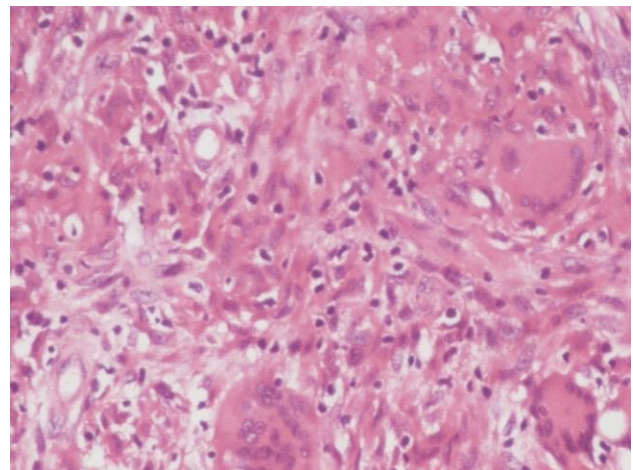


Figure 2: Photomicrograph showing plump epithelioid cells and Langhans type of giant cells forming ill defined granulomas. There is inflammatory infiltrate comprising macrophages and lymphocytes with few areas of necrosis.

Titrated anti tubercular treatment for her body weight was started immediately with four drugs after her biopsy report. She responded very well both clinically and radiologically. The TLC improved to 10,800 cells/cm³, neutrophils 49%, lymphocytes 42% and ESR was 32 mm/hr. The inflammatory signs disappeared and the

surgical wound healed uneventfully. At the end of one month the slab was removed and started with knee range of movement. Weight bearing was delayed till 10 weeks as radiologically we felt the involucrum was inadequate till then. Later on she was switched to maintenance therapy with two drugs rifampicin and isoniazid for next 10 months.

The patient made a dramatic recovery in relation to pain and tenderness. Radiologically the lesion showed features of healing and the laboratory parameters started to normalize (Figure 3). The TLC improved to 10,800 cells/cm³, neutrophils 49%, lymphocytes 42% and ESR was 32 mm/hr.



Figure 3: Radiograph taken upon 1 month of follow up after the debridement and curettage, showing resolution of the lesion with relative normalization of joint space.

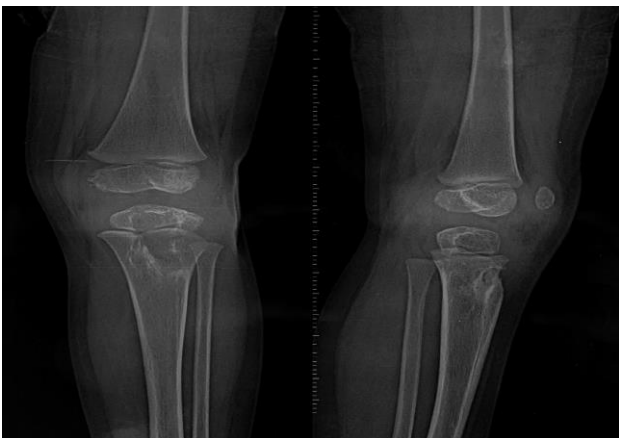


Figure 4: Radiograph at 1 year of follow up showing significant resolution of the lesion without physeal bar, without any bony deformity.

The patient was followed up regularly to identify and treat the sequelae of the infection as we expected growth disturbances, angular deformities and knee stiffness as the lesion was large, involving the physis, the patient

being an infant and proximal tibia being the main growing end of the bone. Lesion healed well with a significant decrease in the size of the lesion, without any formation of a physeal bar and no residual deformity (Figures 4 and 5).



Figure 5: Radiograph taken at 2.5 years of follow up, maintenance of joint space with further resolution of the lesion.



Figure 6: Radiograph taken at 10 years of follow up showing normal joint space and no bony sequelae.



Figure 7: Scannogram of both the lower limbs at 10 years of follow up showing normal mechanical and anatomical axis.



Figure 8: Clinical standing image of the child at 10 years of follow up with no gross deformity in lower limbs and excellent range of motion (0-130 degrees).

Over 10 years good remodeling was noted and the patient had excellent range of motion (0-130°), no limb length discrepancy and no angular deformity (Figures 6-8).

DISCUSSION

Tuberculous affection of bone in this part of the World is fairly common and tuberculosis is the greatest masquerader. One has to have high index of suspicion to pick up the infection early. Because of relative rarity of skeletal tuberculosis and non specific early clinical findings, the diagnosis is usually considerably delayed. The average duration of symptoms before treatment was 2.3 months (range 2 weeks to 6 months).⁸ Chen et al reported an average 6.6 month delay in the diagnosis of tuberculous osteomyelitis.⁹ Tekali et al reported an average delay in diagnosis of 10 months (range 10 days to 6 years), indicating the difficulty in making a prompt diagnosis. In our case it took 55 days, from the date of presentation to confirm the diagnosis.¹⁰ Despite tuberculosis being common, proximal tibial involvement in infancy is rare and sparingly reported. The common involvement at this region in infancy is hematogenous osteomyelitis.

The nearest differential was Brodie's abscess, but it was not typical as no sclerosis of the cavity was seen and the child continued to have progressive changes clinico-radiologically. Brodie's abscess presents in early childhood and it's relatively indolent and radiologically it does not progress rapidly. Its slow clinical course is similar to the course of patients with tuberculosis, thus, they are often mixed. Metaphyseal involvement is usually seen among children while diaphyseal involvement is seen among adults.¹¹ Vohra et al 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.¹²

In 75% of tuberculous osteomyelitis cases, causative organism in the lungs is spread via hematogenous ways.¹² The commonly affected sites in order of frequency are, Spine, femur, tibia and fibula.¹³ The clinical features did not support the diagnosis of acute or chronic osteomyelitis as the infant was not toxic or septicemic. The most common symptoms include pain, swelling and limp.⁴

Four types of lesions are observed in tuberculous osteomyelitis i.e. cystic, infiltrative, regional erosion and spina ventosa.¹³ They usually localize in the metaphyses of long bones or flat bones as single or, less commonly, multiple foci. The lesions are radiolucent, round to oval with slight marginal sclerosis. These 'cysts' can mimic lesions such as simple bone cysts and aneurysmal bone cysts, tumors and granulomatous bone lesions. Infiltrative lesions are diffuse areas of permeation with little or no periosteal reaction, resembling chronic osteomyelitis, benign and malignant tumors such as leukaemias, round cell tumors and Ewing's sarcoma. Pathological fractures usually occur with this radiological type.¹⁴

While treating these entities one should be aware of early stages of chronic recurrent multifocal osteomyelitis (CRMO) which may not be multifocal to start with. It was first described by Gideon in 1972 as an unusual form of multifocal bone lesions with subacute and chronic symmetrical osteomyelitis. The age of onset is childhood and it's again culture negative osteitis. These inflammatory conditions are characterized by episodes of systemic inflammation including serological signs of inflammation (CRP, ESR, interleukin-6, tumor necrosis factor- α) occurring in the absence of autoantibodies and antigen specific T cells.¹⁵ The treatment of CRMO is mainly anti-inflammatories and not antibiotics. The entire management of this entity revolves around good biopsy and culture. In this case the biopsy was repeated as the first biopsy couldn't yield anything and the appropriate treatment was delayed. A meticulous biopsy after studying the scans will entail us to procure the samples from the affected area. Some patients with CRMO may have a markedly raised CRP but these are likely to require a biopsy in order to execute an infectious agent. In cases of deep seated areas, MRI or PET CT scans do find a place in identifying the area of maximum involvement. Biopsies preferably should remain extra-articular and joint aspirations should not be clubbed with it. A properly executed biopsy will expedite the treatment and improves the outcome. 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.¹² Culture results are positive in only 29%-61% of subacute osteomyelitis cases. This rate decreases to 10%-30% in tuberculosis cases.¹⁴

The outcome of infections in growing bones is a matter of concern. The ill effects of physis affection due to infection will lead to growth disturbances, in form of angular deformities and limb length discrepancy. In this case, fortunately the child didn't have these problems despite the involvement of physis. We believe this is due to the chronic hyperemia caused by the infection and slow destruction by the mycobacterial infections and relatively early detection and treatment and patient's ability of child to remodel. Partial physeal destruction with chronic hyperemia may be the cause of no limb length discrepancy.

The destruction was in the central area which might have neutralizing effect in relation to angular deformities which is common sequelae after pyogenic infections. The knee range was not captured owing to its metaphyseal location. The lesion crossing the epiphyseal plate, but not involving the joint must have preserved the knee range. As the treatment was initiated early, natural progression of the disease process could be curtailed with good remodelling potential and sequential follow up. The ill effects of bone infection were not found in this case.

CONCLUSION

Skeletal Tuberculosis in infancy is extremely rare. In treating infections of bone, one has to have this entity in the thought process. Tuberculosis has very few clinical and radiological parameters to diagnose the problem. With a high index of suspicion the biopsy should be well planned and meticulous and always samples to be sent for mycobacteria. Tuberculosis should be an essential differential diagnosis while dealing with cases with similar presentation in an endemic region like India. For every case of osteomyelitis in infancy, tuberculosis should be ruled out. Long follow up is essential for monitoring the sequelae of the bone growth. As clinical and radiological findings may be indistinguishable from malignant disease, tuberculous osteitis should be excluded in infants presenting with undiagnosed bone lesions despite been vaccinated with Bacille Calmette Guerin at birth. Even if radiographs reveal a substantial destruction of the bony epiphysis and metaphysis, the appearance may be deceptive as the remaining chondro-epiphysis can restore the epiphysis and lead to normal joint development. In immature skeleton the lesion has to be followed till skeletal maturity to detect and treat the sequelae at the earliest.

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