

Case Report

Unusual case of recurrent bony pain and swelling in a child – a case report

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ABSTRACT

Prolonged fever in children is a vexing problem. High grade fever with multiple joint pain and swelling can be seen in infections, inflammatory conditions, connective tissue disorders and malignancies. Peri articular pain and fever can be seen in enthesitis, osteomyelitis and malignancy whereas articular pain can be seen in hereditary arthropathies, infectious and inflammatory conditions. Arthritis is defined as presence of pain, swelling, redness, warmth and diminished range of motion. Involvement of more than four joints is taken as polyarthritis. Tuberculosis is an important differential diagnosis in this situation. Here we present a case of a 11-year-old boy with complaints of prolonged fever of 5 months duration with progressive pain, swelling and restriction of mobility of multiple joints. Investigations to rule out inflammatory arthritis, malignancy and infections were done in this child which were initially not pointing to a specific diagnosis. At times, even after best efforts, microbiological diagnosis cannot be established and we have to resort to advanced imaging, techniques and rely on a constellation of clinical and radiological, cytological and microbiological clues to clinch the diagnosis.

Keywords: Pyrexia of unknown origin, Arthritis, CRMO, Tuberculosis

INTRODUCTION

Tuberculosis (TB) is a very important cause of prolonged fever in children in India. There are two presentations---pulmonary and extra pulmonary. Extrapulmonary TB often has an insidious presentation with fever of unknown origin (FUO) or nonspecific symptoms in children, often causing a clinical dilemma.¹ The risk of complications is more in high-risk children, age below 5 years age and in those with immunocompromised conditions. The diagnosis of TB was established by the careful analysis of clinical signs and symptoms, history of recent TB contact, positive tuberculin skin test and suggestive radiological findings. This association may not be well evident in many cases of disseminated TB. Currently, CBNAAT is considered as the investigation of choice for the microbiological diagnosis of TB. However, microbiological diagnosis of TB in children is often

difficult as the disease is pauci bacillary in children and they are unable to produce sputum effectively. Mantoux test is not done now and CY TB test which is a next generation highly specific antigen-based skin test is approved only for those above 18 years of age. At times, even after best efforts, microbiological diagnosis cannot be established and we have to resort to advanced imaging, techniques to clinch the diagnosis especially in disseminated skeletal tuberculosis.²⁻⁴

CASE REPORT

A 11-year-old boy presented with complaints of prolonged fever of 5 months duration. The fever was high grade. He also had pain in both elbows along with fever. No swelling or restriction of mobility was noted initially. He was admitted in a local hospital and received treatment for 5 days. As fever was persisting, he was referred to a tertiary

care hospital and admitted there for 2 weeks. Child had weight loss after the onset of fever. No history of contact with tuberculosis. Investigations were done and the results were as follows (Table 1).

Table 1: Table showing investigation reports.

Name of investigation	Initial values
Hemoglobin	10.9
Total count	12680
Differential count	P71L24E2
ESR	99
MCV	74.8
Dengue IgM	Negative
Lepto IgM	Negative
Scrub typhus IgM	Negative
malaria	Negative
Blood culture	Sterile
ANA, anti ds DNA	Negative
RA Factor	Negative
HLA B 27	Negative
LDH	Normal
ferritin	35
Mantoux test	Negative
Sputum CBNAAT	Negative

Bone marrow examination was done and malignancy was ruled out. Investigations to rule out tuberculosis including Mantoux test, chest X-ray and sputum CBNAAT was done and was negative. Iv antibiotics and naproxen were started and given for 10 days. Child became afebrile with decrease in joint pain and was discharged. He was on naproxen for 2 weeks following discharge.

Repeat blood tests were done and values are shown in Table 2.

Table 2: Table showing investigation reports after 1 month.

Investigations	Values
Hemoglobin	10.2
Total count	11000
Differential count	P74L21E2
ESR	105

Fever subsided partially and there was decrease in joint pain after this. 2 months later, he had pain and swelling on the dorsum of right foot. He consulted a local orthopedician and X-ray was taken which showed a hair line fracture and plaster cast was applied. But pain and swelling increased and pus drainage was noted for which incision and drainage was done several times from local hospital. As symptoms were persisting paediatric surgery and orthopedic consultations were done. In view of persistent fever, pain, swelling and pus discharge, child was admitted under orthopaedic department. Multiple incision and drainage procedures were done with pus taken

for culture followed by sequestrectomy. Child also developed pain and swelling of both elbows of 2 weeks duration with restriction of mobility.

Child was admitted under the department of paediatrics due to these symptoms.

On examination, child had mild pallor. There was no generalised lymphadenopathy, bleeding or hepatosplenomegaly. The child was underweight (BMI-12.2). height was above 50th centile. There was no rash, nail involvement, ulcers, photosensitivity or bleeding. There was no family history of similar illness. He had normal development milestones and was fully immunised. He was completely vaccinated as per national immunisation schedule and a BCG scar was present.

Swelling, tenderness and restricted mobility was noted over both elbows with a palpable soft tissue mass possibly inflamed synovium. Swelling and tenderness was also noted over the right foot at the site of the initial lesion. Examination of other joints were normal. CVS, CNS and GIT examination was normal. Ophthalmological examination including slit lamp examination was normal.

Management and outcome

As symptoms were persisting, blood investigations were repeated (Table 3). Investigations also showed normocytic normochromic anemia with few microcytes, increased rouleaux formation, showed persistently raised counts, CRP and ESR.

Table 3: Repeated investigations.

Name of investigation	Values
Hemoglobin	8.6
Total count	12400
Differential count	P56L29E1M8
ESR	128
MCV	73.8
Sputum CBNAAT	Negative
Chest Xray	Normal
Blood urea	12
Serum creatinine	0.46
SGOT	34
SGPT	33
Serum albumin	2.7
Serum globulin	4.8
Serum sodium	133
Serum potassium	4.1
Serum calcium	8.8
Serum phosphorus	4.1
ALP	128
TSH	2.89
Blood culture	Sterile
ANA, anti-ds DNA, RA Factor	Negative

Investigations to rule out tuberculosis, juvenile idiopathic arthritis were done. ANA negative, RA factor—negative, ESR remained high-128. USG abdomen was normal. 2 blood cultures and pus cultures were sterile. HIV – negative. Child was started on iv ceftriaxone, along with clindamycin and naproxen was also started. CRP—64 which decreased to 41 after starting treatment. X ray of right elbow was shown in Figure 1.



Figure 1: X-ray of right elbow.

Ultrasonography (USG) both elbow and right foot showed synovial thickening with bony erosions. Magnetic resonance imaging (MRI) showed well defined T1 hypointense and T2 hyper intense lesions with surrounding oedema in calcaneum and 1st metatarsal bone with diffuse soft tissue edema. Biopsy of elbow synovial tissue — showed necrotising granulomatous lesion with epithelioid granuloma, CBNAAT was negative (Figure 2).

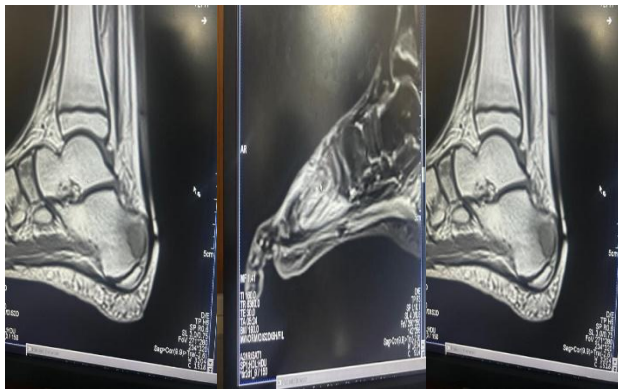


Figure 2: MRI of foot.

At that point we were considering the possibility of chronic recurrent multifocal osteomyelitis as repeated tests for tuberculosis were negative and multiple cultures were sterile.

Child became symptomatically better with subsidence of pain and decrease in swelling CRP which was 64 which decreased to 41 after starting treatment. He was discharged on oral antibiotics and naproxen.

When he came for follow up after 2 weeks, child developed an ulcerative lesion on the biopsy site along with pain and swelling over right wrist and lumbar area. Figure 3 shows image of right elbow.



Figure 3: Right elbow.

In view of multiple bony involvement with pain, swelling and restriction of mobility, PET computed tomography (CT) scan was taken after consultation with rheumatologist.

PET CT showed metabolically active irregular lytic lesions involving lower cervical, dorsal and lumbar vertebra with associated prevertebral, paravertebral and intraspinal collections. Metabolically active chronic osteomyelitis was noted in the right calcaneum with lysis, involucrum extending to the skin.

Metabolically active multiple lytic lesions were also noted in the distal tibia, right navicular bone, distal femur and right fibula. Metabolically active peri articular tissue was noted in bilateral elbow joints. Metabolically active multiple small to enlarged lymph were also found in bilateral cervical, axillary, retroperitoneal and pelvic areas. With these findings, the possibility of tuberculosis was reconsidered.

Excision biopsy of ulcerative lesion was done and specimen was sent again for CBNAAT, MGIT, fungal culture. CBNAAT became positive for mycobacterium tuberculosis which was rifampicin sensitive in the biopsy specimen and ATT was started. In view of disseminated tuberculosis with severe multifocal skeletal involvement, possibility of immunodeficiency and mendelian susceptibility for mycobacterial disease was entertained and samples were sent for genetic study which turned out to be negative.

After starting ATT, the child improved gradually. On follow-up the child became afebrile and gained weight with good compliance and without any ATT-related adverse events reported.

DISCUSSION

Skeletal TB accounts for 10-35% of pediatric extra-pulmonary TB. The lesions can develop more than 10

years after the initial infection and occur primarily in older children, particularly during the first two decades of life.⁵ The systemic symptoms are found in only 33% of children and more common in the immunocompromised host.⁶ Early detection is crucial to prevent bone and joint destruction.⁷ Radiologic imaging plays an important role in diagnosis, characterization, evaluation of extent, and follow up. Skeletal TB typically presents with solitary bony lesion with local signs of inflammation and less than 50% of patients have concurrent pulmonary TB. Common skeletal manifestations are spondylitis (50%), arthritis and osteomyelitis (11%).

Tuberculous spondylitis or potts disease is the most common among these and involves the intervertebral disc only late in the disease.¹ Subligamentous spread of the infection may lead to multiple levels of vertebral body involvement that may either be continuous or skipped. Extension of the disease into the paravertebral or extradural space may occur. Lower thoracic and upper lumbar spine are frequently involved. TB spondylitis results from venous spread in the paravertebral Batson's venous plexus. Clinical manifestation of TB spondylitis is intermittent, relatively long bouts of fever, with insidious progression, compared to acute onset of high fever in pyogenic etiology.⁷ MRI is beneficial to differentiate between pyogenic and TB spondylitis. TB spondylitis shows multiple body involvement, well defined paraspinal soft tissue with contrast enhancing walls, vertebral intraosseous abscess with relatively disc preservation, and severe bony destruction resulting in gibbus deformity. Pyogenic spondylitis has less than 2 vertebral body involvement, with thick and irregular abscess wall, ill-defined enhanced margin of paraspinal soft tissue, moderate to complete disc destruction, disc abscess, and infrequent bony destruction

Tuberculosis involving hips and knees present with monoarticular disease with juxta-articular osteoporosis, osseous erosions, and joint space narrowing.⁸ Jungling's disease (multifocal bone lesions) is secondary to hematogenous spread. It can mimic rheumatoid arthritis when hands and feet are involved. TB arthritis usually results from metaphyseal osteomyelitis with transphyseal spread or the organism can be directly deposited onto the joint synovium.

A careful suspicion of the diagnosis of tuberculosis is paramount in children with chronic or subacute monoarticular arthritis, even in absence of a positive tuberculin test or abnormalities on chest radiograph. needle biopsy of the synovium may be required.⁹

There are four radiographic findings of TB osteomyelitis: cystic, infiltrative, focal erosions and spina ventosa.^{10,11} TB osteomyelitis demonstrates lack of sclerosis, less sequestra and reaction as compared to the pyogenic osteomyelitis. Other differential diagnoses include Ewing's sarcoma, fungal and subacute pyogenic

osteomyelitis, cartilaginous tumors or eosinophilic granuloma.

Tuberculous osteomyelitis can appear as cystic, well-defined lesions, infiltrative lesions or spina ventosa which is a term used to describe a form of tuberculous osteomyelitis where underlying bone destruction, overlying periosteal reaction and fusiform expansion of the bone results in cyst-like cavities with diaphyseal expansion. As per study by Agarwal et al, subtalar ankylosis can develop and subtalar joint involvement was a poor prognostic factor.¹² Radiographs are still the mainstay of evaluation of patients with bony lesions.¹³ Ultrasonography can detect soft-tissue extension of the bony lesions and guide drainage or biopsy procedures. CT accurately demonstrates bony sclerosis and destruction, especially in areas difficult to assess on radiographs such as the posterior elements of the vertebral body. MRI is the modality of choice in evaluating early marrow involvement and soft-tissue extension of the lesion.

The clinician should try to obtain as much pathological material while planning a biopsy from a probable tubercular lesion.¹⁴ An image guided biopsy may yield better tissue for diagnosis. Possible tissues can be skin edge, pus, granulation tissue, soft tissue, bone curetting, lymph nodes, joint fluid, synovial tissue, and other involved sites. Whenever feasible, these samples should be subjected to multiple laboratory tests (acid fast staining, culture, histopathological examination, molecular analysis) The entire sample should be processed for the laboratory investigations.

The main treatment for extrapulmonary TB is multidrug antitubercular chemotherapy (ATT)- a 2-month intensive phase consisting of four drugs (isoniazid, rifampicin, pyrazinamide and ethambutol), followed by a continuation phase lasting a minimum 10 months [2RHZE/10RHE] (which is extendable to 18 months on a case-by-case basis, depending on the site of disease and the patient's clinical response).¹⁵

Analgesics, rest, immobilization, splintage, braces are also necessary in early stages. As soon as inflammation and pain were controlled, patients should be encouraged to start joint mobilization to regain/retain useful range of motion.¹⁶ Tubercular osteomyelitis, if advanced, requires protection to prevent pathological fractures. Most patients also require nutritional therapy.

Surgical intervention may be needed if there is gross neurological deficit at presentation, neurological deficit is of very recent origin, there is evidence of instability or when the neurological deficit interferes with patient mobilization/nursing (e.g. quadriplegia or paraplegia) and for correction of post tubercular kyphotic or scoliotic deformities, both in acute and late stages.¹⁶ Late onset neurological deteriorations often also need surgical decompressions.

CONCLUSION

11-year-old boy presented with fever of unknown cause and joint swelling, pain and restriction of mobility. Here the diagnosis of disseminated TB is often difficult due to atypical presentation and the paucibacillary nature of paediatric TB. The case highlights the difficulty in diagnosing disseminated TB and the need for additional imaging techniques to clinch the diagnosis. In regions with high TB prevalence like India, TB needs to be considered as a clinical possibility of fever of unknown origin and must be ruled out after thorough clinical and laboratory evaluation. Repeated detailed clinical and laboratory examinations must be considered to reach a definitive diagnosis. In regions with high TB prevalence like India, TB needs to be considered as a clinical possibility of fever of unknown origin and must be ruled out after thorough clinical and laboratory evaluation.

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