

# Retrospective Analysis of Varied Clinical Presentations and Delayed Diagnosis in Tuberculosis affection of Extremities

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## Abstract

**Introduction:** Tuberculous involvement of extremities is not rare (50% of osseous disease which is 1-8% of extrapulmonary tuberculosis. These are commonly seen in larger joints followed by foot joints. These are termed milder form of tuberculosis as they are paucibacillary and have low chance of spread of infection. Also due to this nature they are often mis-diagnosed and mistreated. Invasive procedures to yield biological sample may be required to diagnose it.

**Case Report:** We report a series of 7 cases with involvement of extremities. Anatomical sites involved were lateral humeral condyle, flexor tenosynovium, distal femur, knee joint, calcaneum, ankle skin. They were initially treated as tennis elbow (arthritis elbow), carpal tunnel syndrome (flexor tenosynovitis, Rheumatoid arthritis), plantar fasciitis (calcaneum osteomyelitis), pyogenic osteomyelitis and non-healing ulcer (osteomyelitis distal femur and ankle ulcer respectively). Average age was 46.3 years and all patients were males. Average duration of detection from the onset of symptoms to diagnosis was mean 16 months, much longer in upper limb (mean 29.3 months) and shorter in lower limb (6 months). ESR was elevated in all cases with mean value of 63.4. Chest radiograph was negative (71.4%) in all except two. AFB culture and Mantoux test were positive in 2 cases. Histopathology showed granulomatous inflammation in all specimens and all patients were started on AKT on basis of this. All cases responded well to anti-tuberculous regimen with no recurrence at last follow up.

**Conclusions:** Monoarthritis, recurrent compression neuropathies due to synovitis, non-healing osteomyelitis, sinuses and ulcers must be viewed with caution. The usual hematological investigations are not very reliable, but a moderately raised ESR is useful findings to suspect and intervene. Appropriate specimens from the suspected site of involvement should be obtained for microscopy, culture and histopathological examination to increase the detection rate. Anti tuberculous drugs can be started if there is evidence of granulomatous synovitis in histopathological examination and if there is no other obvious causes.

**Keywords:** tuberculosis, delayed diagnosis, granulomatous inflammation, extremities.

## Introduction

The focus of tuberculosis (TB) control program in India has been on pulmonary TB and rightly so, as it is a major

public health problem[1]. Extrapulmonary involvement of TB (EPTB) is noted in approximately 14% of patients, with 1% to 8% having osseous disease [2]. Approximately 30% to 50% of patients with osseous disease have vertebral involvement, extremity involvements is less common. Less frequently observed appendicular involvement usually affects major weight bearing joints of the lower extremity, most commonly the hip and knee, followed in frequency by the foot, elbow, and hand [2]. There are six layers in extremity that can be affected by

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Fig 1: Radiograph of Case 1 showing lytic lesion in lateral condyle of humerus.



Fig 2: Radiograph of second case showing lytic lesion in distal femur



Fig 3: Radiograph of third case showing lytic lesions in calcaneum

TB and atypical mycobacterial infections: the skin, subcutaneous tissues, tenosynovium, bursa, joints and bone [3]. Under Revised National Tuberculosis Control programme, it is recommended that EPTB should be diagnosed bacteriologically, histopathologically or on clinical judgment of treating specialists [4]. International Standards of Tuberculosis Care (ISTC) also recommends that for all patients suspected of having EPTB, appropriate specimens from the suspected site of involvement should be obtained for microscopy and, where facilities and resources are available, for culture and histopathological examination [4]. EPTB is a milder form of disease in terms of infectivity as compared to pulmonary TB due to low bacterial load. This combined with difficulty in getting appropriate specimens from extrapulmonary sites causes delayed diagnosis [4]. Many of the affected sites may require an invasive procedure to get a biological sample to arrive at the diagnosis. Also due to lack of diagnostic resources and poor yield of conventional diagnostic methods, there is a considerable delay in starting the treatment [1]. Thus with atypical presentation and difficult diagnostic methods, TB in extremities are generally misdiagnosed, with considerable delay in treatment. A high

index of suspicion might help in these cases and this is seen in the cases described below.

### Case History

A retrospective review of all cases of extremity TB at our institute in last two years was done. Data was collected from hospital record sheets. Age, sex, socioeconomic status, site and side of involvement, associated constitutional symptoms, co-morbidities, predisposing conditions and previous invasive surgical procedures undergone were noted. Routine investigations like ESR, Lymphocyte count, Mantoux test, AFB culture with Lowenstein Jensen medium, radiograph of the local part and chest radiograph were done for the evaluation of each patient and reports were noted.

First case: 37 year old male, known diabetic since 10 years (on Insulin) presented with pain and swelling of right elbow of 3 years duration. He was initially treated as a case of tennis elbow and has undergone needle aspiration from the elbow. Mantoux test was negative, ESR was 66mm/1st hr, chest radiograph was negative and local radiograph showed lytic lesion in lateral condyle. Debridement and histopathological examination (HPE) showed granulomatous affection



Fig 4: a,b-MRI of case 5 showing flexor tenosynovitis. c- Intraoperative picture showing granulomatous inflammation of the synovium.

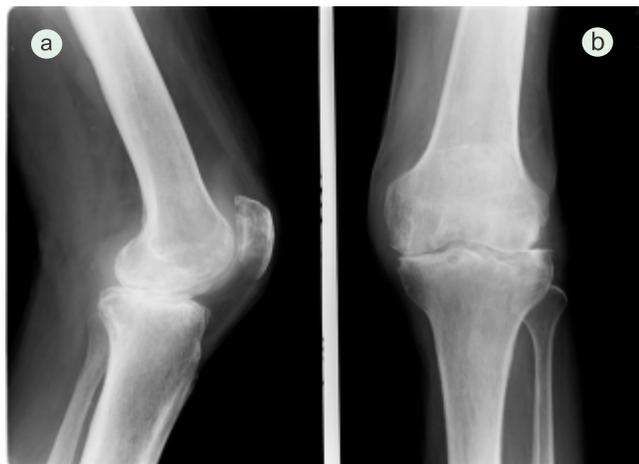


Fig 5: Radiograph of case 6 showing lytic lesion in proximal tibia.

of synovium, but mycobacterium culture was negative.

Second case: 10 year old boy presented with left knee pain since 4 months. Radiograph showed lytic lesion distal femur. Mantoux test was negative, ESR was 74 mm/1st hr, chest radiograph was negative. Initial debridement showed nonspecific osteomyelitis, however patient did not respond to intravenous antibiotics for 6 weeks and developed nonhealing sinus at lower end of femur. Repeat debridement and HPE showed granulomatous infection, and mycobacterium culture was positive.

Third case: 40year old male presented with pain in heel since 10 months which was treated symptomatically, with poor response. Radiograph showed lytic lesion in calcaneum. Mantoux test was positive, ESR was 52 mm/1st hr, chest radiograph was negative. Debridement and HPE showed granulomatous affection of calcaneum, but mycobacterium culture was negative.

Fourth case: 59 year old man presented with pain and swelling followed by ulceration over right ankle since last 6 months. Ulcer was not responding to repeated debridement and dressing. He is a known diabetic on immunosuppressive therapy following renal transplant and this was taken to be cause of non-healing. Mantoux test was negative, ESR was 40mm/1st hr, local and chest radiograph was negative. Debridement and HPE showed granulomatous affection of skin, but mycobacterium culture was negative.

Fifth case: 52 year old man with pain, swelling left wrist, features of carpal tunnel syndrome of 16 months duration. He has been prescribed steroids irregularly for joint pain. Carpal tunnel release was done 1 year

back, but symptoms again recurred. Mantoux test was negative, ESR was 52 mm/1st hr, chest radiograph was negative. Debridement and HPE showed granulomatous affection of synovium, but mycobacterium culture was negative.

Sixth case: 66 year old man with pain swelling left knee followed by ulceration in popliteal region of about 4 months duration. He had low grade fever and weight loss. He was on treatment for pulmonary TB with anti TB drugs for the last 2 months. Mantoux test was positive, ESR was 70 mm/1st hr, chest radiograph was positive. Knee Debridement and HPE showed granulomatous affection of synovium, however mycobacterium culture was positive.

Seventh case: 60 year old man with pain swelling right wrist, flexor tendon ruptures [FPL,FDP(LF)], features of carpal tunnel syndrome for last 36 months duration. Mantoux test was negative, ESR was 90mm/1st hr, local radiograph was negative however the chest radiograph was positive. Debridement and HPE showed granulomatous affection of synovium, but mycobacterium culture was negative

Thus all patients had varied presentations; however with common feature of undiagnosed chronic complain of pain or ulceration (sign of chronic inflammation). All patients underwent HPE to reveal granulomatous inflammation. All the patients were then treated by First line anti TB drugs- four drug regime daily or thrice weekly directly observed treatment short course for 2 months followed by two drug regime(Isoniazid and Rifampicin) for minimum of seven months and maximum of 10 months. All the patients responded favorably to treatment and at last follow up (minimum 1 year) follow up after stoppage of therapy, were free of symptoms.

## Discussion

TB is a great masquerader and can mimic many diseases specially in endemic areas. The most striking feature of this series was the delay between the onset of symptoms and correct diagnosis. Average duration of presentation from the onset of symptoms to diagnosis was mean 16 months with upper limb having a much prolonged delay of mean 29.3 months and lower limb a shorter delay of 6 months. Similar delay in diagnosis was noted by Bush et al [5] in tuberculosis of hand and

wrist. Ruiz et al noted that the median time to diagnosis (time from the onset of symptoms to positive culture) was 8 months with an interquartile range of 3.5–24 months in non-endemic areas [6]. 4 out of 7 were subjected to previous surgical/invasive procedures, still diagnosis has delayed.

Pain is the most common presenting symptom, but only one had constitutional symptoms (one with pulmonary TB). 4 out of 7 had various predisposing factors causing immune deficiency (diabetes, steroid intake, renal transplant) although none of them have HIV infection. Predisposing factors are present in other reports in about 30–40% of patients, but some series have shown no predisposing factors and thus this can only be taken as a corroborative indicator in suspicion on tuberculosis. Anatomical sites involved were elbow, flexor tenosynovitis (2 cases), distal femur, knee joint, calcaneum, ankle skin. Majority have involvement of lower extremity. They were initially treated as Tennis elbow (TB arthritis elbow), carpal tunnel syndrome (flexor tenosynovitis, RA), plantar fasciitis (Calcaneum Osteomyelitis), pyogenic osteomyelitis and ulcer (Osteomyelitis distal femur and ankle ulcer respectively). In addition to a low suspicion level, the lack of a rapid hematological and microbiological diagnostic method increases the time needed to confirm the clinical suspicion.

Lymphocytes count was normal in all our cases making it a nonspecific indicator in our specific kind of tuberculosis. Average ESR in our series was 63.4mm/hr while that in series of González-Gay et al [7] was 55.7 +/- 29.0 mm/hr. This was elevated in all our cases and could be taken as an indicator, however it points more towards chronicity of the disease than any specific cause. Chest radiographs were positive for tuberculosis in 2 out of 7 (28.6%) cases in our series (19% by González-Gay et al [7]) and in cases with positive chest or local radiograph a high index of suspicion should be entertained.

Mycobacterium culture by Lowenstein Jensen medium was positive in 2 out of 7 (28.6%) cases in our series (.Jain et al -12%, Tuli et al- 30-60% [8]). All were mycobacterium tuberculosis. The improved BACTEC TB system is claimed to be rapid, sensitive, and efficient method for the isolation, differentiation, and susceptibility testing of mycobacteria in a clinical laboratory. The new rapid TB test - known as Xpert

MTB/RIF - has also reported to be sensitive and specific [9]. However in our retrospective series these methods were not used and may be use of these methods could have improved diagnostic accuracy. Mantoux test was positive only in 2 of 7 (28.6%) cases. Thus tuberculin test failed to play a reliable or auxiliary role in identifying TB disease and infection in the BCG-vaccinated population as shown by Feng et al [10].

Histopathological diagnosis of osteoarticular TB has been reported to be positive in the range of 72-97%. Histopathological positivity in Jain et al [8] series was 100%. Sometimes the results were inconclusive as the patients were already on Anti TB Treatment for many months before reporting to the hospital. The advantage of histopathology lies in the early results obtained, enabling the surgeon to embark upon the appropriate treatment.

There is no consensus among the orthopaedic surgeons about the duration of treatment. In a study by Agarwal et al [11], 42/52 respondents voted against short course (6 months) regimen. The mean value for duration of treatment with isoniazid and rifampicin treatment in the study was 12 months; for pyrazinamide, it was three months. There was almost no consensus over the duration of treatment with ethambutol. But many experts feel six- to nine-month regimen (two months of isoniazid [INH], rifampin, pyrazinamide, and ethambutol), followed by four to seven months of isoniazid and rifampin) is recommended as initial therapy for all forms of extrapulmonary tuberculosis unless the organisms are known or strongly suspected to be resistant to the first-line drugs. Extended therapy also may be required for patients with bone and joint tuberculosis, delayed treatment response, or drug resistance [12].

## Conclusion

Even though we are aware of the masquerading nature of tuberculosis, there may exist a striking delay between the onset of disease and diagnosis causing much morbidity to patient and his working capabilities. High level of suspicion and use of rapid and efficient microbiological and histopathological diagnostic methods can decrease this delay

### Clinical Message

Monoarthritis, Recurrent compression neuropathies due to synovitis, non-healing sinuses, osteomyelitis and ulcers must be viewed with caution. The usual investigations are not highly reliable, but a moderately raised ESR is useful findings to suspect and intervene. Exploration, debridement and histopathological evaluation gives the patient the best chance for early diagnosis and less morbidity. Anti tuberculous drugs can be started if there is evidence of granulomatous inflammation on histopathological examination.

### Abbreviations

FPL-flexor pollicis longus

FDP(LF)-Flexor digitorum profundus little finger.

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