

CASE OF THE MONTH

Multi-drug Resistant Tuberculous Osteomyelitis of the First Carpometacarpal Joint Presenting as Unmasking Immune Reconstitution Inflammatory Syndrome

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Abstract

Tuberculosis (TB) is an important cause of significant morbidity and mortality, particularly in patients living with human immunodeficiency virus (HIV) infections. The co-infection of TB and HIV coinfection is further complicated by a relatively higher frequency of extra-pulmonary TB and upsurge of drug resistance. Musculoskeletal TB is a relatively less common form of extrapulmonary TB; involvement of carpometacarpal joint as an initial manifestation is even rarer. We herein present a retro positive patient who presented with low-grade fever, constitutional features and swelling of the base of the left thumb. On evaluation, he was found to have axillary and inguinal lymphadenopathy with lytic destruction of carpometacarpal joint as well as D10-D11 vertebrae. Fine needle aspiration (FNA) of synovial fluid was negative for tuberculosis but geneXpert from FNA of axillary node revealed *Mycobacterium tuberculosis* with rifampicin resistance. This case highlights the rarity of carpometacarpal joint involvement in TB as the initial manifestation and the importance of meticulous search of alternative sites for sampling in difficult situations such as osteoarticular TB. It also highlights the rising prevalence of drug-resistant TB and a definitive need for microbiological diagnosis wherever feasible.

in D10-D11 with destruction of intervening disc along with an epidural abscess. Aspirate of joint fluid (metacarpal joint) was negative but fine needle aspiration cytology from the left axillary node was positive for *Mycobacterium tuberculosis* and resistant to rifampicin on GeneXpert (Cepheid). The patient was started on Category IV antitubercular therapy (ATT) according to the national program i.e. kanamycin, levofloxacin, cycloserine, ethionamide, pyrazinamide and ethambutol. Nevirapine was changed to efavirenz to avoid hepatotoxicity due to concurrent administration of nevirapine and ATT. On follow up after one year of initiation of ATT, he had no fever, his appetite was normal, and there was almost complete resolution of joint and lymph node swelling.

Case Report

A 50-years old male patient, without any previous comorbidities, presented to an outside hospital with complaints of intermittent low grade fever for one year associated with loss of appetite and weight. There was no history of cough, hemoptysis, respiratory distress, abdominal complaints, headache or any bowel/ bladder disturbances. On evaluation, he was found to be positive for HIV-1 antibodies. He was started on zidovudine, lamivudine and nevirapine on which he showed initial improvement. Three months into the treatment, he started complaining of fever and noticed a gradually progressive painful inflammatory swelling in his left thumb (1st carpometacarpal joint). He took symptomatic treatment for these complaints but did not show any improvement. He presented to our clinic with non-resolving symptoms.

On general physical examination,

lymphadenopathy was noted in the left axillary and bilateral inguinal region. The nodes were discrete, firm in consistency, and were not attached to underlying or overlying structures. Local examination of left hand showed soft, fluctuant and tender swelling at the base of the thumb. There was restricted range of motion in the affected joint. On systemic examination, mild spinal tenderness was noted at lower thoracic spine. Rest of the systemic examination was normal. His routine laboratory hematology and biochemistry were normal (Table 1). CD4 count was 392 cells/ul. Chest X-ray was normal.

Plain radiograph of right-hand (Figure 1) showed lytic destruction of carpal bone and base of 1st metacarpal. MRI dorso-lumbar spine revealed contiguous vertebral body destruction

Table 1: Laboratory parameters of the patient with reference values

Laboratory parameters	At admission	Ref. values
Haemoglobin (g/dl)	12	12-15
Total leucocyte count (/mm ³)	7700 (Neutrophil 66%, Lymphocyte 25%, Monocyte 8%)	4000 - 11000
Platelet count (/mm ³)	2,54,000	150000 - 400000
Total bilirubin (mg/dl)	0.8	0.8-1
Aspartate transaminase/ Alanine transaminase (IU/l)	32/24	Up to 50
Urea/Creatinine (mg/dl)	32/0.7	0-40/0-1
HBsAg/Anti-HCV	Negative	
VDRL	Non-reactive	
Urine routine	Normal	

*g/dl- gram per deciliter, mg/dl- milligram per deciliter, mm³ -per cubic millimeter, IU/l- international units per litre

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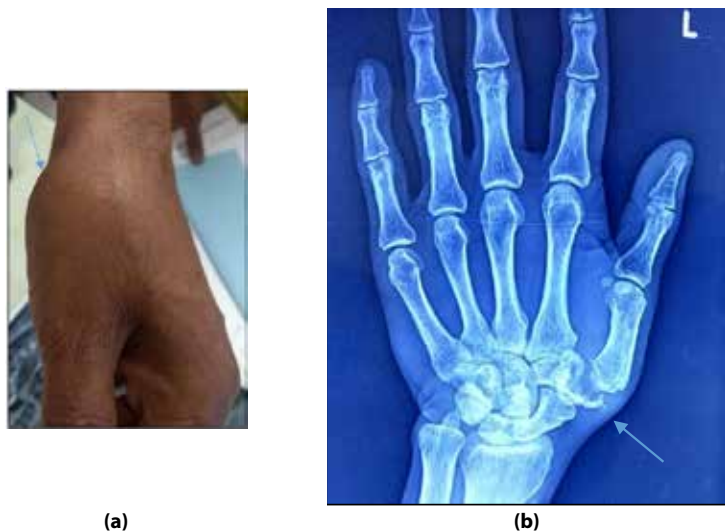


Fig. 1: (a) Picture of left hand showing swelling at first metacarpal joint (arrow); (b) Radiograph of left hand PA view showing erosive arthritis involving first carpometacarpal joint (shown by arrow) with periarticular soft tissue swelling

Discussion

Tuberculosis (TB) is one of the commonest illness in patients living with Human immunodeficiency virus (HIV). HIV infection is associated with increased risk of re-activation of TB. Also, initiation of anti-retroviral drugs (ART) may lead to reactivation of underlying latent infection (usually within three months), a phenomenon called as unmasking Immune reconstitution inflammatory syndrome (IRIS). In HIV positive patients, incidence of both extra-pulmonary (EPTB) and multi-drug resistant tuberculosis (MDR-TB) is increased. In those with EPTB, musculoskeletal involvement is a less common presentation. We report a rare case of TB involving the first carpometacarpal (CMC) joint.

IRIS is a condition associated with initiation of antiretroviral therapy (ART) leading to a state of overwhelming inflammatory response due to immune recovery.¹ IRIS may lead to reactivation of underlying latent infection i.e. unmasking infection, which occurs within few months after ART initiation or paradoxical infection, which occurs when patient is already on ATT and is started on ART leading to flare up. As per International Network for the Study of HIV-associated IRIS (INSHI) consensus definition, unmasking TB IRIS usually occurs within three months of ART initiation.¹ We considered the possibility of unmasking TB IRIS in our case, as he developed symptoms within 3 months of ART initiation. On further

evaluation, he was found to have involvement of 1st CMC joint, lumbar spine and peripheral lymph nodes.

Musculoskeletal system TB is an uncommon manifestation of extra-pulmonary TB (EPTB); it accounts for around 2.8% - 14% of EPTB cases.²⁻⁴ Within the spectrum of skeletal TB, involvement of carpometacarpal joint (CMC) is very rare; there is scanty literature on CMC joint TB arthritis as initial manifestation. To the best of our knowledge, there is only one more case of TB of 1st carpometacarpal joint reported from India.⁵

The diagnosis of musculo-skeletal TB is commonly based on clinical and radiological findings but with increased incidence of MDR-TB, especially in HIV positive patients, the role of microbiological diagnosis becomes very important. In our patient, although the diagnosis of TB was clear based on the radiological findings and it is a common practice to empirically start ATT in such situations, we went for invasive sampling. The aspiration of joint fluid was negative for tuberculosis but the lymph node FNAC yielded positive results and he was started on appropriate treatment. This emphasizes the importance of meticulous search for possibility of dissemination and involvement of other sites which can be sampled for diagnostic purpose and may provide information relevant to diagnosis and management. Another important lesson learnt from this case was the fact that the diagnostic accuracy of GeneXpert is variable in

different samples. Its sensitivity is higher in tissue aspirates as compared to that in the body fluids like synovial fluid.^{6,7} According to studies from India, prevalence of MDR-TB (newly diagnosed or previously treated for TB) in PLHIV varies from 12.5% to as high as 47% in a study in ART clinic attendees.⁸⁻¹⁰ MDR TB is generally associated with poor outcomes unless diagnosed early and initiated on appropriate treatment. Therefore, high index of suspicion is extremely important.

This case also highlighted the fact that TB in endemic countries may present with unusual presentation or unusual sites like first carpometacarpal joint.

Conclusion

Extra-pulmonary involvement at unusual sites and multi-drug resistance is common in immunosuppressed patients living in endemic areas. Establishment of microbiological diagnosis by invasive sampling of appropriate site (with higher yield) is of utmost importance for adequate management.

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