Current Concepts In Diagnosis & Management Of Osteoarticular Tuberculosis

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Abstract

Tuberculosis is common worldwide and in endemic in India. Musculoskeletal tuberculosis, involving spine and other joints is seen in 1% to 3% of patients with tuberculosis. The disease has varied clinical presentation & lack of charateristic radiographic findings leading to delayed diagnosis and treatment. Early confirmed diagnosis & proper medical treatment are essential for control of the disease.

This review article based on the recent literature review discuss the clinical presentation, diagnosis and management of osteoarticular tuberculosis.

Keywords: Tuberculosis, osteoarticular, tubercular osteomyelitis

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Introduction

Worldwide, tuberculosis (TB) is one of the top ten causes of death & the leading cause from a single infectious agent. In 2017, TB caused an estimated 1.3 million deaths (range, 1.2–1.4 million) among HIV-negatives & additional 0.3 million deaths among HIV-positive people [1]. Pulmonary TB (PTB) is most common form of tubercular disease but can affect extra-pulmonary sites exclusively or in combination with PTB [2].

Musculoskeletal tuberculosis, although relatively rare, is observed in 1% to 3% of patients with TB, out of which approximately one-half show spinal involvement & the remaining involves the extraspinal osteoarticular joints [3-6]. Tubercular tenosynovitis & arthritis is usually monoarticular & the organism can be isolated from the joint [7].

Patients generally have mild local & constitutional symptoms, frequently leading to significant delays in diagnosis, due to its varied clinical presentation & frequent lack of charateristic radiographic findings [8,9]. This delay in diagnosis & treatment, may result in additional bone or joint destruction [8-11]. Therefore, early diagnosis & treatment are essential. We therefore performed a review of these topics based on the recent literature review regarding clinical presentation, diagnosis and management of osteoarticular tuberculosis.

I. Clinical Presentation: TB arthritis is characteristically monoarticular, most commonly affecting spine & weight-bearing joints as knee, hip & ankle. Synovial type of TB arthritis is more common in these joints [12]. Multiple sites involvement is rare & is observed in 5-30% only [13,14]. Reactivation of old tubercular lesion after treatment occurs in 17-34% & is most common in hip joint [7,15].

It commonly presents with chronic joint pain & swelling with minimal signs of inflammation & restriction of movements. Effusion, painless periarticular cold abscess, chronic sinus

formation, regional muscle wasting & deformity occur late. Systemic constituional symptoms of fever, weight loss, loss of apetite, malaise & night sweats may or may not be present during active TB synovitis & arthritis. They may also have hypersensitivity phenomena such as erythema nodosum, episcleritis, uveitis & Poncet's arthritis. 50% of individuals may have active pulmonary TB at the time of diagnosis [16]. Thus patient with clinicoradiologically suspected osteoarticular tuberculosis should also be screened for active pulmonary or other primary extrapulmonary foci.

Table 1. Clinically, TB of joints have been classified into 5 stages [17-19].

Stage	Type	Movement	Clinical	Radiological	Prognosis
I	Synovitis	>75%	Soft tissue swelling	Haziness of articular margins & rarefaction	Excellent
II	Early arthtitis	50 to 75%	pain & spasm	Rarefaction, osteopenia, marginal bony erosions mild joint space reduction	Good with mild stiffnes
III	Advanced arthritis	> 75 % loss in all direction	Pain, spasm, loss of ROM	Marked diminution of joint space & destruction of joint surfaces	Fair with notable loss of motion
IV	Subluxation / dislocation	III + Gross restiction	a. III + deformity	Pathological dislocation Hip - w&ering /migrating Knee - triple deformity	Poor
V	Treminal arthritis & deformity	IV + Ankylosis	IV + gross deformity	Deformity with degenerative arthrosis	Poor

Specific involvement of tubercular arthritis:

1. Hand & wrist: Common in children < 5 years, but can affect any age group. Hand or wrist gradually becomes painful & swollen with joint effusions, synovial thickening & restricted range of motion. Systemic symptoms as fever, weight loss, anorexia or regional lymphadenopathy may be seen. In advanced case, wasting of hand & forearm muscles, deformity, enlargement of digits/metacarpals (sausage finger/spina ventosa), discharging sinuses, tubercular ulcers, cold abscess & compound palmar ganglia may be present. Rarely, patients have carpal tunnel syndrome, or involvement of nails.
2. Elbow: Can affect any age group. Patients present typical with local & constitutional features as swelling, pain, limitation of motion, synovial thickening etc. Rarely, ulnar nerve or posterior interosseous nerve palsies may be presenting feature. In advanced stage, wasting of arm & forearm muscles, elbow deformity in flexion/extension, pathological dislocation, discharging sinuses & cold abscesses may develop.
3. Shoulder : Can affect all ages, but is more common in adults than children. Patients present with pain, restricted shoulder movements (particularly limited external rotation & abduction) and muscle wasting (particularly deltoid & supraspinatus). In advanced case, there may be marked destruction of humeral head & glenoid with muscle atrophy or deformity (particularly, fibrous ankylosis with humeral head pulled up against glenoid & arm fixed in adduction & internal rotation). Systemic constitutional features, discharging sinuses around shoulder & cold abscess are uncommon. "Caries sicca" is the most common form – which is a dry arthropathy (rather than exudative). Relatively rare, it usually presents in the advanced stage with disabling symptoms that may mimic more common pathologies such as neuropathic shoulder, rheumatoid arthritis, & adhesive capsulitis.
4. Hip: Can affect any age, but most common in children & young adults. Three stages are
   a) Synovitis - characterized by gradual hip pain, limping (antalgic gait), fullness around hip caused by joint effusion, restricted range of movement & deformity (affected limb is flexed, abducted & externally rotated with apparent lengthening).
   b) Early arthritis - characterized by pain with every hip movement, muscle spasm, atrophy, bony destruction and deformity (affected limb flexed,

adducted & internally rotated with apparent limb shortening).

c) Advanced arthritis - characterized by very painful joint movements, grossly restricted movement and limb shortening. Pathological dislocation or subluxation may occur due to bony destruction of acetabulum/femoral head.

5. Knee: Can affect any age group. Patients present with painful, swollen, tender knee which is warm to touch, with limping & reduced range of motion. Systemic symptoms and regional lymphadenopathy may be seen. In advanced case, the joint may feel boggy due to synovial thickening, with joint effusion & wasting of thigh muscles. Discharging sinuses, cold abscess or deformity ranging from mild flexion deformity to severe triple deformity (flexion, posterior subluxation, external rotation & valgus) may be present.
6. Spine: Patients present with localized back pain, tenderness & constitutional symptoms along with or without signs of spinal cord compression. Advanced disease may have severe pain, spinal deformity, paraspinal muscle wasting & neurological deficit.

II. Laboratory investigations & Imaging

1. Blood: Low haemoglobin, relative lymphocytosis, raised erythrocytic sedimentation rate (ESR) are often found in active stage. Raised ESR, however, is not necessarily a proof of activity of infection. Its repeated estimation at 3 to 6 months intervals gives a valuable index to the activity of the disease [20].
2. Mantoux test: Stantard dose of 5 tuberculin units (TU-0.1 ml) is injected intradermally & read 48 to 72 hrs later. Person who has been exposed to the bacteria is expected to mount an immune response in skin containing bacterial protiens. A positive reaction (induration more than 10 mm) is present in tuberculous disease. A negative test, in general, rules out the disease. The tuberculin test may be negative in disseminated T.B, after vaccination, recent viral infection or steroid therapy, or in immunocompromised individuals [20]. This test in not recommended, currently.
3. Immunological test: Interferon gamma release assays (IGRAs by quantiferon assay), blood – based assays rely on the stimulation of host blood cells with M. tuberculosis-specific antigens & measure the production of interferon gamma. Although it more specific than the montoux test, but they are currently unable to distinguish between active disease & latent TB infection & hence not recommended [21,22].
4. Ziehl-Neelsen staining: This test is rapid, easy & requires minimal infrastructure; however, minimum load of 5,000-10,000 bacilli/ml is required & species differentiation is not possible. It may be helpful in sputum smears, but as osteoarticular TB is paucibacillary, hence this test has limited value [23].
5. Fluorescence microscopy: It utilizes fluorescent dye to stain the organisms and when excited by UV light using special microscope, bacteria appear as bright rods in a dark back ground. It is used successfully for rapid diagnosis of pulmonary TB; but in osteoarticular TB, particularly paucibacillary disease, use is not clearly established. Fluorescence microscopy is faster & more sensitive than conventional light microscopy, but the expense, need for a dark room & poor specificity limit its usefulness [23].
6. Culture: Isolation of organism on culture is gold standard for diagnosis of TB. Culture media used are egg based (Lowenstein – Jensen medium), agar based (Middlebrook 7H10,7H11) or liquid based (Mycobacterium growth indicator tube). Culture can detect as little as 10 bacilli/ml of sputum, differentiate different mycobacterial species, can be used for drug senstivity testing & is useful in symptomatic smear negative cases. But drawbacks of conventional culture methods are time consuming (6 to 8 weeks) & require strict quality control. Rapid culture methods like BACTEC which detect mycobacteria based on metabolism

(detects C14 labelled CO2 & reports as growth index(GI) value) rather than visible growth give results within 7-14 days. MGIT(mycobacteria growth indicator tube) method, detects growth early in 7 to 12 day by nonradioactive detection system using flurochrome for detection & drug screening, hence is useful for drug susceptibility testing [23].

7. Tissue biopsy: TB guidelines TAC subcommittee for bone & joint TB recommends that wherever possible, all patients should have a biopsy of the lesion, to provide a specimen for culture to confirm the diagnosis, perform drug susceptibility testing, and to rule out other diagnoses. Tissue biopsy can be done under radiological guidance, arthroscopy or via open surgical biopsy. Arthroscopic biopsy is advantageous as it visualizes the lesion, helps excision of affected tissue for diagnostic testing, & simultaneous therapeutic intervention if required. Percutaneous CT-guided biopsy is preferred, but some patients may require open biopsy. Regional enlarged lymph nodes / sinus tract curettage/edge biopsy can be sent for culture & histopathology, but microbiological result may be misleading due to contamination/colonization/2^0 infection. Biopsy is not needed for culture and microbiologically confirmed TB, but if patient is microbiological negative for TB then percutaneous biopsy is advised and if the foci is not easily accessible percutaneously or needs surgical management, then should undergo open surgical biopsy. Specimens should also be collected, when therapeutic invasive procedure is done. Specimens collected should be sent for:
   a. Microscopy & culture for pyogenic bacteria
   b. Microscopy & culture for MTB
   c. Histopathology / cytology.

   Histopathology shows, mononuclear, granulomatous reaction pattern i.e. granulomas with or without central caseation necrosis. Inflamatory reaction patterns on histopathologic examination of tissue are of secondary importance because other conditions such as fungal infections, foreign body reactions & sarcoidosis may be associated with granulomatous inflammation. Direct demonstartion of organism in tissue section by ZN staining is difficult to do, compared to do in direct smears. Thus histopathologic evidence for diagnosis of TB is adjunctive, always circumstantial & never a replacement for culture [23].
8. Cytological examination of smears: Direct smears may be stained with May-Grunwald-Giemsa (or Romanowsky dyes) & ZN stain for cytopathologic examination allowing recognition of inflammatory patterns & acid – fast organisms and making a tentative diagnosis in a day, but the diagnosis is always circumstantial and never definitive. This can be done for intraoperative consultation also [23].
9. Serological testing: This test can be used for antigen & antibody detection; however serological tests are expensive, require trained personnel, have low senstivity, are affected by BCG vaccination, previous infection & cannot distinguish between MTB & non-tubercular mycobacteria. Serological tests have so banned in India for TB [23].
10. Molecular methods: Detection & identification of mycobacteria directly from samples can be done by polymerase chain reaction (PCR) & nucleic acid amplification test. PCR provides rapid diagnosis within 48 hrs, has high senstivity, can identify the species & requires very small volume of specimen; however it cannot differentiate between live & dead mycobacteria. High cost, availability & infrastructure required limits its usage. Another molecular assay LPA (line probe assay) is based on reversed hybridization principle. DNA material is hybridized with specific oligonucleotide probes & after addition of enzyme substrate complex with chromogen results in purple/brown precipitates, which is visually interpreted. It is useful to detect resistance against rifampicin & isoniazid [23]. Gene Xpert (CBNAT) MTB/RIF automates & integrates sample processing & PCR in a single disposable plastic

cartridge, giving accurate results within 2 hrs. It simultaneously detects MTB & resistance to rifampicin. WHO recommends its use as initial diagnostic test in adults & children suspected of having MDR-TB or HIV associated TB [24-26].

11. Roentgenographic findings: Bone & joint TB is a slowly developing disease, which takes 3-4 months of disease process to show radiological features. First radiological sign of an active disease is localised rarefaction/osteoporosis. The speed of decalcification depends on reactive hyperemia, which is most intense in exudative infections. In synovitis stage, x-rays will show epiphyseal & metaphyseal decalcification and swollen synovial shadow. As the disease advances, the articular margins loose sharpness & become fuzzy. X-ray findings in arthritic stage are joint space narrowing secondary to destruction of articular cartilage and small zone of osteolytic area suggestive of granular foci surrounded by diffuse osteoporosis. Even if the lesion is located in one carpal/tarsal bone, remaining carpals/tarsals also rapidly decalcify, suggesting on x-ray that the infection affects all [23]. Tuberculous cavity at center may show a sequestrum of bone or calcification of caseous tissue which is irregular soft, feathery and coke –like sequestrum, which is surrounded by an osteolytic ring representing the fibrous wall. Bone is osteoporotic/normal/or dense, depending on the defence reaction. Radiological signs at this stage resemble as osteomyelitis. Joint effusion is seen as soft tissue shadow and abscesses may be seen as vague irregular densities in surrounding soft tissues. Advance destructive process may produce collapse of bone /subluxation/dislocation/migration & joint deformities. Damage to growth plate produces angular deformities due to irregular growths. The synovitic lesion, near epiphysis stimulates osteogenesis of epiphyseal growth plate, which may lead to premature appearance/enlargement of the ossific nuclei and may stimulate longitudinal growth. When it damages the growth plate & encroaches on the area of endochondral ossification, growth is irregularly retarded & deformity results. Spinal tuberculosis shows erosion & fuzziness of the paradiscal margins, disc space reduction & regional osteoporosis. There is an increased soft tissue shadow/paravertebral shadow (fusiform, spindle shaped, bird nest appearance, saw tooth appearance), destruction/collapse of vertebral body & kyphosis of vertebral column [23]. New bone formation (periosteal reaction) /ossification are seen in tuberculosis of hand and foot as the foci is superficial and it may encircle & enlarge the diaphysis in small long bones of hand/foot [23]. With treatment, recalcification is seen, suggestive of reduction of disease activity. Secondary to healing, the peri-focal bone is thickened as a calcified ring, as the decalcified trabeculae start calcifying [23].
12. Computerised tomography: It detects disease earlier even when destroyed areas of bone erosion is small and in areas of skeleton not appreciated on plain X- rays as craniovertebral spine, cervicodorsal spine, rib, sternum, sacroiliac joint and posterior elements of vertebrae. Intraspinal encroachement & dystrophic calcification is well appreciated by CT scan. CT guided biopsy/aspiration provides tissue for histological/cytological/microbiological diagnosis. Further, swelling in soft tissues caused by edema, granulations, exudations or abscess formation can be demonstrated, earlier. Calcification in abscess, as seen on CT is pathognomic of TB [23]
13. MRI: It is more sensitive & specific than X-rays & CT scan to detect tuberculous lesion and can diagnose disease in pre-destructive stage. MRI can show abscess/granulation tissue/caseous tissue, localized tuberculoma & generalized granuloma in multiple planes & can delineate soft tissue masses in both sagittal & coronal plane. The spinal cord changes, such as cord edema, atrophy,

syringomyelia, arachnoiditis myelitis, myelomalcia, syrinx, can be appreciated. It shows the extent & spread of tubercular debris under anterior & posterior longitudinal ligament, subligamentous spread of a paraspinal mass, abscess which shows low signal on T1 & high signal on T2 weighted images, encroachment of vertebral canal, compression of spinal cord by granulation material, bone or disk, identifying cranial & caudal level of obstruction and can evaluate for spinal tumor syndrome [23].

14. PET-CT scan: It helps in picking, residual inflammation in cases where the signs of healing are ambiguous on contrast MRI. SUV max (maximum standardized uptake value) of early phase PET-CT scanning is statistically significant in differentiating tuberculous from pyogenic spondylitis. It has high sensitivity & specificity for detecting & identifying the process of inflammatory activity in spondylitis [23].
15. Ultrasonography (USG): It is a useful non-invasive modality to detect soft tissue mass (solid or liquid), deep-seated abscesses & to perform USG guided aspiration. It is particularly useful in follow-up evaluation of psoas abscess when patient is under cover of ATT to document resolution of psoas abscess [23].

Diagnosis

Key principles of diagnosing osteoarticular TB as stated in INDEX TB guidelines are:

(a) High suspicision in patients with signs of joint infection with insidious onset & charaterisitic imaging features.
(b) Refer such patient to orthopaedian who can assess the joint & perform a biopsy for culture & histopathology
(c) Whenever possible and safe for patient take pus/fluid/aspirate/specimens and sent it for microscopy, culture (for all mycobacterial, pyogenic and fungal testing) and histopathology because it confirms diagnosis; drug susceptibility testing can be done to guide ATT and alternative diagnoses can be picked up [11].

The hierachy of evidence for the diagnosis of TB [23]

1. Culture
2. Molecular testing, PCR, other tests in development.
3. Demonstartion of AFB in direct smears or tissue sections.
4. Tissue reaction patterns: granulomas necrotising/non–caseating, necrosis without AFB
5. Radiological examination & imaging studies.
6. Physical examination of the patient.
7. Therapeutic response

III. Principles Of Management

Tuberculosis is a systemic medical disease. The mainstay of treatment remains uninterrupted antitubercular chemotherapy.

a. **Pre chemotherapy era:** The treatment was orthodox conservative treatment. During the Atharva veda period (3500 BC -1800 BC) "sipurdu" a herbal medicine was used along with good food, sun exposure, fresh air, rest & immobilization, given in specialised rooms called 'sanatoria'. Hippocrates (400 BC) & Galen (131-201 AD) used forceful maneuvers & manipulations to correct deformities. In late 19th & early 20th century, HO Thomas, Sir Robert Jones & Dame Agnes Hunt, also supported 'The sanatoria concept", in which patients were kept for 1-5 years, as the natural course of diseases was 3 -5 years. Only in one third patients the aim was achieved, rest of patients used to die or remained severly crippled. Surgical drainage of abscesses usually lead to persistent discharging sinus & rise of death.

b. **Post Chemotherapy era:** Antitubercular drugs (streptomycin 1947, para amino salicylic acid 1949, isoniazid 1952, pyrazinamide 1956, ethambutol 1962 & rifampicin 1967) changed the outcome of tuberculosis in general. The treatment was classified along chemotherapy in three philosophies:
(a) Universal surgical extirpation was advocated by Hodgson, Fellander &

Mukhopadhaya, where surgery under cover of ATT was done in all cases.
(b) Middle path regimen where a long course of drugs was advocated for all & surgery only for complications.
(c) Modified middle path regimen where a short 6-9 month course of antitubercular drugs was advocated for all & surgery only for complications.

Middle path regimen as per Tuli includes rest, antitubercular chemotherapy (streptomycin 1 gm/day for 3 months, para-amino salicylic acid 12 gm/day for 18 months & isoniazid 300 mg/day for 24 months), regular supervision, gradual mobilization after 6-9 months with braces/calipers for next 18-24 months, minor surgical procedures when required like aspiration of abscesses, excision of sinus tract etc [23].

c. General treatment

General care: It includes rest, high caloric & high – vitamin diet, fresh air or living in warm dry climate, daily heliotherapy, good hygienic & nursing care [27].

Rest, Mobilization & Brace: All patients of spinal tuberculosis are advised to sleep on hard bed. In craniovertebral, cervical & cervicothoracic lesions, traction is used in early stages to put diseased part at rest, particularly for cases with neural deficit & with pathological subluxation/dislocations. In active stage, joints given rest and braced in functional position. In presence of gross destruction especially in hip, knee & ankle cases, continuation of immobilization may lead to spontaneous sound ankylosis. Later they are started on intermittent guarded active & assisted exercises under cover of antitubercular drugs to retain useful functional range of movements.

Traction: In presence of deformities, traction is used to correct deformity, maintain the limb in functional position, hold inflamed joint surfaces apart, offer unhindered observation and local response to treatment & permit repetitive guarded assisted & active joint motion. This maintenance of traction & intermittent active & assisted joint motion during healing and post synovectomy/debridement/excisional arthroplasty stage encourages cells to develop into of healthy synovial membrane & well lubricated useful fibrocartilage adapted to the function of the joint. This permits return of reasonable function even in damaged joint & maintain lasting healed status [28].

Ambulation: Initial stage is without weight bearing. As the disease heals & pain subsides, weight bearing is permitted accordingly, under observation. If symptoms or signs increases, patient goes back a stage; if there is steady progress he goes forward (Thomas' test of recovery), but movements or degree of weight bearing is never forced beyond tolerable discomfort (functional treatment) [28]. Guarded weight bearing for lower limbs is started 3-6 months after subsidence of signs of activity, and braces/appliances are gradually discarded after its use in about 2 years [28].

d. Antitubercular chemotherapy

Invasive diagnostic procedures for confirming diagnosis are not always practicable & in such circumstances, clinician judgement is needed as to whether ATT should be started without a microbiological/histopathological diagnosis, or whether a period of observation is appropriate. Index-TB guidelines assert that in TB-endemic areas, it is reasonable to start ATT in patients with strong clinical & radiological evidence of TB of bones & joints & to monitor their progress. It also assert that that all bone & joint TB should be treated with extended courses of ATT with intensive phase consisting of 4 drugs (isoniazid, rifampicin, pyrazinamide & ethambutol) for 2 months, followed by continuation/maintenance phase consisting of 3 drugs (isoniazid, rifampicin, ethambutol) lasting 10–16 months, depending on site of disease, patient's clinical course & response.

1. Rifampicin: is semisynthetic antibiotic, acts on dormant intracellular mycobacterium, has good absorption in empty stomach. It causes red-brown discolouration of body fluids. 10mg kg is daily recommended dose with adult dose between 450-600 mg [11].

2. Isoniazid: has ability to penetrate cell which contain tubercle bacillus. Toxic effects include rashes, fever, vitamin B- deficiency & neurologic effects on reflexes & bladder function. The daily recommended dose is 3-8 mg/kg [27].
3. Pyrazinamide: it is bactericidal drug, which is well absorbed orally & eliminated by hepatic metabolism. It may cause nausea, flushing, arthralgia & hepatotoxic reactions. It is prescribed as 35 mg/kg/day [27].
4. Ethambutol: has replaced para-amino salicylic acid (PAS) as it has fewer toxic reactions & is well tolerated. Dose is 2.5 mg/kg for 60 days, then 15 mg/kg single daily dose [27].
5. Streptomycin: it acts best at 9.0 pH & so it should be accompanied by a buffered alkaline solution when injected intra synovially. Permanent toxic effects are related to 8th nerve palsy causing deafness & vertigo. The daily recommended dose is 1gm [27].

e. Abscess, Effusion & Sinuses

For palpable abscesses & large joint effusions, treatment is aspiration & instillation of one gram streptomycin alone or combined with injectable isoniazid at each aspiration. Local instillation is not necessary, if sufficient local concentration of antibiotics is achieved after parenteral administration. If aspiration fails to clear, then open drainage of abscesses is performed. All radiologically visible abscesses don't require drainage, if under ATT. Drainage is done for very large paravertebral abscess which increase in size in spite of ATT, prevertebral cervical abscess causing dysphagia or dyspnoea, incidentally during decompression for paraplegia or during debridement of diseased vertebrae for active tuberculosis. Sinuses usually heal within 6-12 weeks under ATT. 1% may require longer treatment & excision of the tract with or without debridement. It is important to note that sinus ramification is always greater than appreciated, complete surgical excision is indeed impracticable & fortunately unnecessary [28].

f. Surgery in Tuberculosis of Bones & Joints

Surgery is only adjunct and supportive to systemic antitubercular therapy and is not a substitute for prolonged course of antitubercular drugs. A trial of conservative treatment is justified in most of the cases before surgery is contemplated. Nonoperative treatment is usually adequate in pure synovial tuberculosis (without articular involvement), low grade, early arthritis & even advanced (stage III, IV) arthritis, especially in upper extremity. Operative procedures should be done after stabilization of general condition of patient under protective cover of ATT & before the development of drug resistance. The interval could vary depending on case, in general minimum 1-4 weeks of ATT & general treatment is advisable before any major surgical intervention [28]. In general, at any stage of disease, if lesion is not responding favourably to effective antitubercular drugs, there is doubt in diagnosis, or it is a case of refractory recrudescence of infection, exploration & appropriate operation is considered mandatory.

Extent & Type of Surgery

Arthrodesis is now rarely indicated as a primary mode of treatment. Reconstruction, reposition of joints, juxta-articular osteotomies, soft tissue releases & arthroplasties to obtain, mobile, stable joints with biological control of disease is now considered as rational treatment in tuberculosis.

Excision of focus is done, if juxtaarticular osseous focus is threatening the joint, despite adequate ATT. Synovectomy partial or total along with joint debridement limited to infected synovium, sequestra, pockets/cavities of pus & sinuses only is indicated in nonresponsive cases of tubercular synovitis & early arthritis. In advanced arthritis of hip & elbow in adults (nonresponsive cases or cases who did not obtain acceptable range of movements) excisional arthroplasty followed by frequent repetitive active & assisted movements of the operated joint to obtain a functional arc of movements is given.

Arthroplasty in patients with active tuberculous disease has proved disastrous. In advanced knee arthritis (& rarely in ankle, hip & wrist) in adults, for gross deformity & pain, compression arthrodesis should be performed by any of the standard techniques of arthrodesis extra or intra-articular may be adopted in tubercular arthritis under cover of modern drugs. In cases of healed disease with painless ankylosis in deformed position a juxta-articular corrective osteotomy is performed (for hip, knee & ankle or any joint) to bring the joint to best functional position. Following surgery, immobilization in plaster cast is continued till solid fusion is obvious radiologically (3 to 6 months) [28].

g. Outcomes & healed stage: Monitoring of treatment response in patients is done by:-

A) **Clinical** - General improvement in well-being, resolution of fever, weight gain, increase in appetite resolution of sinus/ulcer

B) **Haematological** – increase in Hb & RBC count, decrease in ESR

C) **Radiological** – shows appearance of remineralisation and sharpening of margin.

D) **Imaging** – MRI shows resolving collections, reduction in marrow edema & replacement of marrow by fat seen as high signal in T1 & T2 images & no contrast enhancement [27].

Thus patients diagnosed as confirmed/probable bone TB with improved clinical, haematological and imaging features as above, on completion of ATT and no relapse of disease are labelled healed status, and can stop ATT [11].

h. Presumptive treatment failure

Treatment failure should be suspected for bacteriologically confirmed or clinically diagnosed bone TB, when after completing at least 5 months ATT have -

a) Persisting or worsening local & systemic symptoms & signs

b) No improvement or deterioration of the lesion on repeat imaging

c) Appearance of new lesion/new abscesses/lymphadenopathy

d) Non-healing ulcer/sinus or wound dehiscence post-operatively.[11]

Possible causes of deterioration on treatment or failure to improve on treatment are poor adherence to ATT, drug resistance, paradoxical reaction, immune reconstitution syndrome associated with HIV or alternative diagnosis.

Such patients of presumptive treatment failure should undergo complete blood count, inflammatory markers such as ESR, liver enzymes, urea & electrolytes, fasting blood glucose/HbA1c & HIV test, repeat imaging & repeat diagnostic sampling or biopsy, which should be send for a) staining for AFB & culture for MTB with drug susceptibility testing b) Gram's stain & bacterial & fungal culture c) histopathology. PCR-based tests have variable sensitivity in bone TB & there is uncertainty in previously treated TB [11]. These groups of patient with bacteriologically confirmed or clinically diagnosed treatment failure should be treated by specialist team and by carefully monitoring empirical treatment with second-line drugs, guided by drug susceptibility testing [11].

Resistance: Multidrug Resistant (MDR) tuberculosis is defined as tuberculosis resistant to isonizid & rifampicin [24]. Extensively Drug-Resistant (XDR) tuberculosis is defined as tuberculosis resistant to isoniazid & rifampicin & any fluoroquinolone & at least one of the three second-line injectable drug (capreomycin, kanamycin, & amikacin) [24]. When strains are resistance to all first & second line anti –TB drug, then it is known as extremely drug resistant TB (XXDR-TB) or totally drug resistant TB (TDR-TB) [24].

Accurate & rapid detection of drug resistance are critical for improving patient care & decreasing the spread of TB. The main Drug Susceptibility Testing (DST) methods are absolute-concentration method & Proportion Method (PM) on Lowenstein-Jenson (L-J) medium, but both methods take some weeks for the results. Automation of culture using BACTEC MGIT 960 (M960) and Xpert MTB/RIF assay, which enables simultaneous detection of Mycobacterium Tuberculosis (MTB) &

Rifampicin (RIF) resistance are now widely used [26]. Xpert result that is positive for rifampicin resistance should be carefully interpreted & take into consideration the risk of MDR-TB for given patient with high prevalence for MDR-TB.

Paradoxical reaction: A patient with confirmed or probable skeletal TB on ATT, who initially improves & then subsequently has worsening of constitutional symptoms or signs of TB in the absence of another diagnosis or drug resistance, is paradoxical reaction. Features are same as for treatment like increased size of lesion, appearance of new lesions, recurrent fever & night sweat or development of another form of TB except that these show initial improvement. In drug-resistant cases, patient fails to improve or deteriorate from the start of ATT and shows no improvement until an effective second-line ATT regimen is started, whereas in paradoxical reaction, there is usually an initial improvement, followed by deterioration. In such patients, ATT should not be stopped or altered, but supplemented by NSAIDS & other supportive treatment, which are usually sufficient and patient usually begin to improve again [11].

Conclusion

Tuberculosis is common and endemic in India. Due to its varied clinical presentation and lack of characteristic radiographic findings, the diagnosis and treatment is delayed. Tuberculosis should be suspected in patients with signs and symptoms of joint infection with insidious onset and characteristic imaging findings along with presence of constitutional features and these patients should be investigated. The mainstay of treatment is antitubercular chemo-therapy and surgery is only adjunct and reserved for unresponsive cases.

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