Tuberculosis of Spine

Muhammad Tariq Sohail, Raza Elahi Rana, Muhammad Hanif

ABSTRACT

Involvement of spine in tuberculosis has serious implications if not diagnosed and treated in time. Paraplegia of different grades is not uncommon. The disease is more common in developing countries but in the developed countries it is also seen, majority of the patients being immigrants from TB endemic countries. Diagnosis is based on clinical judgement aided by variety of investigations, MRI being the imaging modality of choice. Treatment must be started as early as possible following WHO guidelines and patients must be followed till the eradication of the disease. Decision of surgical intervention should be taken carefully as not all patients are candidates for conservative management.

Key words: Tuberculosis, Spondylitis, Mycobacterium

INTRODUCTION

Mycobacterium tuberculosis MTB infection was known as "consumption" to the world because of the associated weight loss and anorexia. It is one of the leading causes of morbidity and mortality across the globe [1]. Involvement of spine is commonly termed as Pott's disease as Sir Percival Pott for the first time described it in 1776 [2]. However, the disease has been present in humans since ancient times and it is one the oldest documented diseases. Evidence of the disease has been found on Egyptian mummies [3]. Tuberculous Spondylitis is the most common form of musculoskeletal Tuberculosis and accounts for almost 40 % all infections of spine [4,5].

Spinal tuberculosis may lead to serious complications [6]. If not treated in time, it can progress to destruction of vertebral body, which leads to collapse of that particular segment. Most commonly vertebral body is affected and posterior elements remain spared. As a result abnormal angulation develops in sagittal axis and characteristic Gibbus is formed [1]. Majority of the lesions (about 90%) are found in the thoracolumbar spine [7].

Untreated infection leads to abscess formation, which remains localized beneath anterior longitudinal ligament and extends posteriorly to the spinal canal through intervertebral foramina and cause spinal stenosis [8,9]. Neurological impairment develops with the passage of time, incidence of which varies from 23% to 76% [10] and the disease has the potential to end up in paraplegia [11].

Department of Orthopaedics,
Doctor's Hospital, Lahore
Correspondence: Muhammad Tariq Sohail
Email: drtariqsohail57@gmail.com

Despite of development of effective vaccination and improved socioeconomic conditions, tuberculosis still remains a serious public health problem [12]. 8.7 million cases of tuberculosis were estimated to exist in 2011 with 1.4 million deaths associated with tuberculosis [13].

The worst form of tuberculous lesion is involvement of spine because of devastating complications [14]. This review highlights the various aspects of involvement of spine in tuberculous in the light of studies done in the past years and also identifies some of the controversies in the treatment.

EPIDEMIOLOGY

Tuberculosis is known to be associated with lower socioeconomic status population and a disease of developing countries. The incidence is also alarmingly high in immunocompromised patients particularly HIV infected patients. According to a study the number of Tuberculosis patients in Africa doubled within two years with the spread of HIV/AIDS [1]. Throughout the world tuberculosis is the commonest opportunistic infection in Acquired Immune Deficiency Syndrome [15].

Even though it is quite uncommon in developed countries, with more and more immigrants pouring in from developing countries where tuberculosis is endemic the number of patients is also increasing. Data of Musculoskeletal tuberculosis reviewed in United Kingdom showed that 74% of patients were immigrants from subcontinent [16]. Worldwide increase in diagnosis of active tuberculosis is estimated by USA Center for Disease Control (CDC). The department predicted rise from 7.5 million cases per year to 11.8 million per year. Similarly associated mortality is expected to rise 2.5 to 3.5 million per year [1].

10% of extrapulmonary tuberculosis patients have skeletal involvement and out of these 50% have spinal tuberculosis [17]. In a study conducted in France on patients suffering from vertebtal osteomyelitis, the infectious organism was found to be *Mycobaterium tuberculosis* in 31% of the patients [18].

The pattern of age distribution of spinal tuberculosis patients was also found to be different in developing and developed countries. It was found to be more common in children in low socioeconomic population in contrast to adults in Middle East and Western countries [19].

PATHOPHYSIOLOGY

Tuberculous spondylitis is a secondary infection. The primary site of infection is pulmonary or genitourinary lesion. The causative organism, the anaerobic weakly gram-positive bacillus, Mycobacterium tuberculosis, reaches the highly vascular area of cancellous bone of the vertebral bodies through the blood circulation. In the subchondral region of vertebra there is a rich vascular plexus formed by the anterior and posterior spinal arteries. There also exists a venous paravertebral plexus of Batson, which is a valve-less system in which there is free, flow of blood in either direction depending on the intrathoracic or intra-abdominal pressures. Therefore the spread of the organism may take arterial or the venous route [20].

Hypersensitivity immune response is generated following phagocytosis of bacteria by the macrophages. Participation of other inflammatory cells leads to the formation of granuloma, the center of which becomes necrotic and ultimately the lesion start to destroy the bony architecture of the vertebra. This process initially takes place in the anterior inferior portion of the vertebral body and subsequently spreads to the disk or the central part of the body. Mycobacterial infections lack proteolytic enzymes and therefore the anterior and posterior longitudinal ligaments remain relatively unaffected and the infection spreads to the multiple contiguous vertebra [21].

Because of the variation in the pattern of blood vessels in vertebrae of young and old, the pattern of involvement may also vary. The paradiscal space is more vascularized in young patients and so the disc is more frequently involved. On the other hand due to avascularity seen in the same area of old age patients, disc involvement is also less. Involvement of multiple vertebrae is also frequently seen as the segmental arteries supply two adjacent vertebrae [22,23].

KYPHOTIC BEHAVIOR AND SPINE AT RISK

Involvement of thoracic spine in tuberculosis leads to kyphosis in almost all cases, whereas in cervical and lumbar region it results into loss of lordosis before the development of kyphosis. As the line of transmission of body weight passes through the anterior half of the dorsal spine, in the same half where disease activity initiates, pathological fracture and subsequent collapse of anterior half leads to development of kyphosis.

The resultant kyphosis continues to progress at variable rate even if the treatment is started. The rate of progression can be minimized with the help of braces but cannot be stopped. Tuli reported 150 increases in kyphotic angle with conservative management while 5% of the patients ended up in angle more than 600 [24]. In adults, once the bony fusion develops, no further increase in the kyphotic deformity has been seen. However, in the children, kyphotic deformity continues to progress with growth despite of complete healing of the vertebral lesion [25].

The instability produced by disruption of posterior ligament complex leads to the progression of deformity. Radiological signs known as “Spine at Risk signs” are the signs of instability of the spine and may predict the behavior of the deformity.

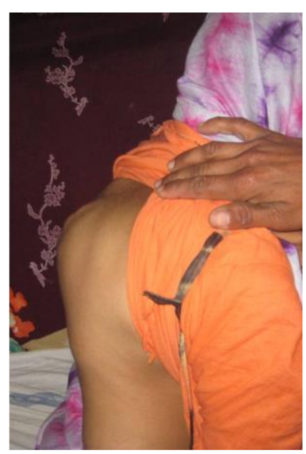


Fig: Gibbus Formation

Spine at Risk Signs [26]

1. Subluxation or dislocation of facet joints at the apex of deformity (a)
2. Posterior retropulsion of vertebral body fragments (b)
3. Lateral Translation of vertebral column (c)
4. Toppling or the tilt of upper normal vertebra over the lower normal vertebra (d0

NEUROLOGICAL INVOLVEMENT/ PARAPLEGIA

Disrupted local architecture and expansion of abscess cause compression over the neural elements and manifested clinically as radiculopathy, myelopathy or paraplegia. Pott's paraplegia was classified into two types by Hodgson. Type one was termed as early onset paraplegia and the other type as late onset paraplegia or paraplegia of healed disease [27].

Early onset paraplegia develops because of the destruction of vertebral body and the disc in the active form of the disease. In some cases there is compression fracture without involvement of the disc (Concertina collapse) and paranchyma of the cord is compressed. Meningomyelitis may also develop due to direct involvement of the cord and cause paraplegia. In some rare cases there may be infective thrombosis of the vascular supply of the cord leading to paraplegia. Tuberculoma of spinal cord or Syringiomyelia may also develop in few cases. However, the prognosis of this early onset paraplegia is good if active treatment is started timely.

The late onset paraplegia develops decades after active Infection. It has poor prognosis because of the fibrosis of the dura (pachymeningitis) and formation of tough fibrous membranes around the cord or transverse ridges of bones.

Predisposing factors to the above all pathological process are same as that of primary tuberculous lesion i.e low socioeconomic status, nutritional deficiency, diabetes mellitus, contact with patient suffering from tuberculosis, alcoholism, HIV infection and treatment with immunosuppressive medication [4]. Alavi identified old age, male gender, peritoneal dialysis, imprisonment and contact with tuberculous patients as specific risk factors for spinal tuberculosis in Iran [28].

CLINICAL PRESENTATION

Patients having spinal involvement of tuberculosis present very late to the spine surgeons. In a report by Sternbach, the average delay time period was of one and a half years from the onset of symptoms and establishing the diagnosis [29]. Patients belonging to low socioeconomic status only they develop deformity, neurological symptoms or severe pain takes proper medical advice.

The most frequent symptom with which patients present is back pain (More than 80%) [30].

Malaise, low-grade fever, loss of appetite and fatigue are some of the classical constitutional symptoms of tuberculosis. However, in musculoskeletal Patients with tuberculous spondylitis also present with local tenderness, stiffness of muscles, fluctuant non-tender swelling (cold abscess), angular kyphosis (gibbus) and sometimes discharging sinus [10].

The cold abscess depending on the site of its origin presents in its characteristic pattern. In cervical spine, cold abscess accumulates beneath prevertebral fascia and forms retropharyngeal abscess. In this case the patient may present with dysphagia, breathing problems (Millar Asthma) or change of voice (hoarsness). Cold abscess formed in the lumbar spine may present as fluctuant swelling in groin, thigh or the gluteal region [4].

In rare cases where cervical spine is involved, the patient may present with quadriplegia. Large vessels around cervical spine may get eroded and TB related sudden death (TBRSD) has also been reported [31].

Increased muscular tone and exaggerated spinal reflexes are seen when the disease affects the thoracic spine and paraplegia of lower motor neuron type when the affected area is lumbar spine. The neurological deficit is reported in a range from 12.5 % to 100% [30].

INVESTIGATIONS

Complete blood count may reveal anemia, raised acute phase reactants (ESR and CRP) and hypoproteinemia. Mantoux test is a screening tool for TB but not diagnostic, particularly in patients already exposed sub clinically to the disease or have been vaccinated with BCG. It also may give false negative result in immunocompromised patients e.g HIV infected or low CD 4 T cell count [32]. This is being replaced by another relatively new test known as Interferon Gamma-Release Assay (IGRA) with sensitivity up to 90%, but has the disadvantage of not being able to differentiate active from treated infection [33].

Plain radiography of the spine in suspected cases is a very basic and effective tool, which show characteristic tuberculous lesion in more than 90% of the cases [34]. Magnetic resonance imaging is the imaging modality of choice in tuberculous spondylitis, which can detect the exact site and dimensions of the bony as well as soft tissue lesion. Status of the neural structures, disc and sub ligamentous spread is more accurately defined [32]. Bony lesions not seen in plain radiographs are detected in MRI because bony lesions may not be apparent on radiographs until there is 30% of mineral loss from the bone. Unsuspected noncontiguous lesions in TB spine are also visualized [35].

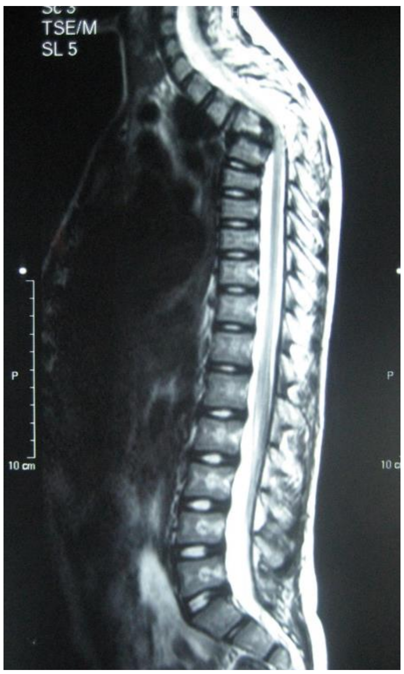


Fig. T2 Weighted image of patient with tuberculous involvement of upper thoracic vertebra with angular kyphosis

Table 1: Differential Diagnosis

Metatstatic Disease
Multiple Myeloma
Pyogenic Spondylitis
Lymphoma
Fungal Infection
Brucellar spondylitis
Inflammatory Spondyloarthropathy
Sarcoidosis
Osteoporotic collapse
Degenerative disc disease

CT scan can also be very helpful in describing the pattern of bone destruction and in few cases its role becomes essential in obtaining biopsy [36]. 3D reconstruction CT is helpful in the planning of surgical management of the deformity.

Bone scans, even though has lesser sensitivity and specificity, may be useful in detecting the activity level of the lesion in tuberculous spondylitis. It may also help in differentiating between metastasis and tuberculosis as uptake of radioactive material is seen at multiple sites in the former [37].

There are certain pathologies of spine which mimic tuberculous spondylosis [38], Table 1.

Histological confirmation is essential before starting the long medical course of medical or surgical treatment. In spinal tuberculosis CT guided biopsy is the gold standard technique for the early diagnosis of the disease [39]. Mondal successfully diagnosed 34 cases out of 38 patients having vertebral tuberculosis by fine needle aspiration biopsy 40]. In some cases where needle biopsy technique fails or there is inadequate sample, open biopsy has to be carried on. In such cases decompression and/or arthrodesis is done at the same time.

The tissue obtained is sent to the pathological lab for histopathology and microbiology. Acid-fast bacilli seen on the smear (seen in 52% cases) or histological evidence of tubercle or epithelioid cells seen in biopsy material confirm the diagnosis. Mycobacterium tuberculosis culture in Lowenstein-Jensen medium is another method with 83% sensitivity. However, it takes 4-6 weeks to produce result [41].

Chen, in his review article, emphasized on the importance of early diagnosis of spinal tuberculosis and identified various laboratory findings including positive interferon gamma release assay (IGRA) [42]. These immunodiagnostic tests are non-tissue based tests which can quantitatively measure interferon gamma produced by lymphocytes specific to Mycobacterium Tuberculosis [43]. However, these rapid biomarker-based tests are relatively new methods which are not available in the developing countries and their accuracy in different populations is yet to be determined.

Polymerase chain reaction is an effective rapid diagnostic tool with sensitivity up to 98%, which requires relatively small sample from any part of the diseased tissue [44]. Nucleic acid amplification tests (NAATs) of Mycobacterium tuberculosis are also commercially available and their role in confirming tuberculous meningitis and pleuritic has been established [45]. However, in Tuberculous spondylitis, obtaining tissue specimen remains hurdle at the present.

CLASSIFICATION

For selection of treatment methods for spinal tuberculosis and for documentation and record keeping, widely accepted classification system was not found in our literature search. Noordin [46], in a retrospective study proposed a scoring system based on patient's physical examination, laboratory and radiological investigation and site of the lesion. The calculated score was expected to be helpful in decision making regarding mode of treatment i.e, conservative or surgical. The study revealed that higher proportion of patients having thoracic involvement required surgical intervention as compared to patients with lumbar involvement.

Mehta and Bhojraj [47] also proposed a classification system of tuberculosis of thoracic spine based on MRI findings to plan appropriate surgical treatment. Patients in their study were divided into four groups: Group A with stable anterior lesion with no deformity, Group B & C with global lesion and instability and Group D with isolated posterior lesions. Different types of surgical intervention were undertaken depending on the group, which included anterior debridement and grafting, posterior instrumentation and anterior grafting or only posterior instrumentation.

Despite of the endeavor to completely describe all the features of tuberculous spondylitis, such classifications fail to give guidelines to the clinicians for the management. More satisfactory classification system is still required.

TREATMENT

The primary goal of the treatment is to save life of the patient by eradication of the infection. The secondary goal is to correct deformity of the spine and prevent paralysis.

The gold standard treatment for tuberculous spondylitis is the antituberculous chemotherapy, which can cure the disease in majority of the patients. Ferrer in a systemetic review of tuberculous spondylitis case series, found spontaneous fusion in 80% of cases treated with Antituberculous therapy [48]. Response to medical management is not only evident in terms of pain relief but decrease in the neurological deficit and correction of spinal deformity were also observed [49,50,51].

Combination of drugs, prolonged and uninterrupted administration is essential for the desired results. Treatment should be started as early as possible in all diagnosed cases. In cases where there is strong clinical suspicion, treatment should be instituted without waiting for the etiological diagnosis to be established.

Clinicians around the globe have successfully treated the disease with different drugs and variable duration of time and endorse their own recommendations. Standard regime has not yet been established [52].

However, we follow the WHO recommendations here in Pakistan, which divide medical management into two phases Table 3

Table 3: First line Anti-tuberculous Drugs

Initial Intensive Phase: 2 months		
DRUG	**Dosge**	**Administration**
Isoniazid	5mg /kg	Oral
Rifampicin	10mg/kg	Oral
Streptomycin	1 gm	Parenteral
Pyrazinamide	25-30mg/kg	Oral
Continuation Phase: 4-7 months		
Isoniazid	5mg/kg	Oral
Rifampicin	10mg/kg	Oral

The WHO recommended duration o treatment is 9 months for bone and joint infection of tuberculosis. However, it is important to follow patients on regular interval to detect any adverse effects of the drugs and determine the parameters of regression of the disease before stopping the treatment. The duration of the disease may be extended up to 12 to 24 months depending on the response of the disease to anti-tuberculous chemotherapy [53,54].

There are certain concepts, which have been changed over the time in the management of tuberculous spondylitis. Prolonged bed rest and brace immobilization, both are no more recommended [18].

Role of corticosteroids has also not been established in tuberculosis management, However, in a few cases of paraplegia due to tuberculous arachnoiditis where bony involvement is not seen, use of corticosteroids proved to be beneficial [55].

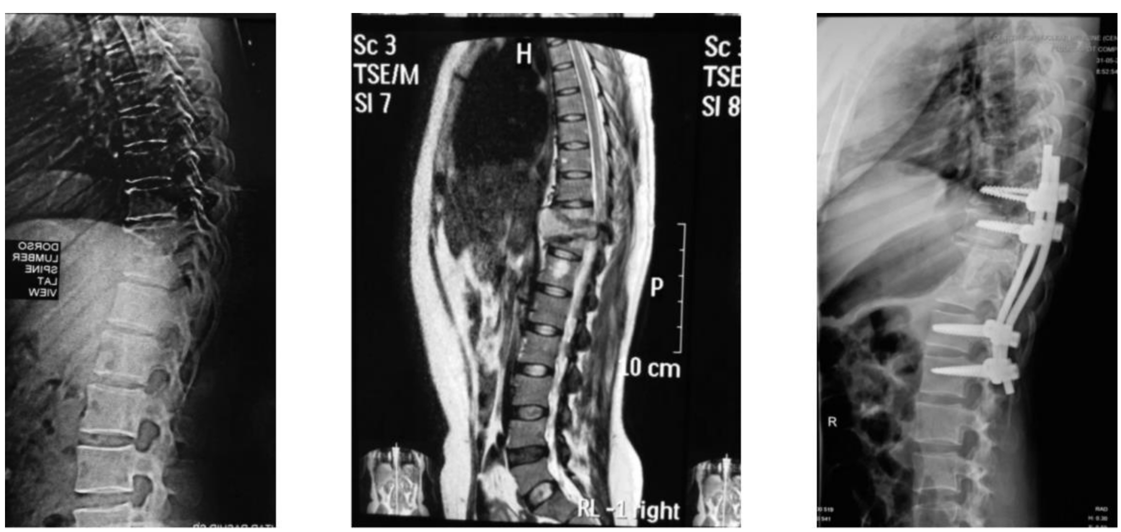
DRUG RESISTANT TUBERCULOUS SPONDYLITIS

Resistance to multiple antituberculous drugs is not uncommon as 7 to 15% of cases have been reported to have resistance for *Mycobacterium tuberculosis* [56]. Osteoarticular tuberculosis like Tuberculous spondylitis is a paucibacillary disease and therefore sensitivity of AFB smear and culture is very low [57]. To establish the diagnosis of multi drug resistance in caries spine becomes even more difficult due to the fact that the radiological signs of healing lag behind the actual healing by months. Therefore, a high index of suspicion is needed to diagnose the problem. The protocol of management of drug resistance in spinal tuberculosis has not been established yet [58].

Jain reported 15 cases of MDR tuberculous spondylitis patients. Surgical decompression was done in 12 patients and tissue obtained was analyzed. All patients were treated with initial first line antituberculous drugs followed by the second line ATT. The treatment given included: Rifampicin, Isoniazid, Ofloxacin, Ethiomamide, Cycloserine, and Injection Kanamycin/Amikacin. Most of the patients showed clinical improvement after 2 years. The author concluded that since it is a man-made problem, prevention is better than cure. In suspected cases surgery should be carried out to procure tissue for diagnosis followed by administration of proper combination of drugs [59].

SURGERY

Even though according to a Cochrane Data Base review[45] there is no convincing evidence that surgical management is superior to the medical management, in some circumstances surgical intervention is indicated. "Middle path regimen" described by Tuli in his classical paper in 1975 suggested conservative management and surgery reserved for patients not responding to the medical management. Neurological deficit was not the criteria for surgery; however, his study revealed that only 6% of patients without neurological deficit needed surgery where as 60% of patients with neurological deficit required surgery [60].



A B C

Fig. A: Tuberculous Spondyilitis of D10 and D11 of a young female patient presenting with backache for one year and on examination having upper motor neuron signs in the lower limb.
B: T2 weighted image of MRI of the same patient showing vertebral collapse, para spinal abscess and encroachment of the neural canal.
C: Posterior instrumentation, followed by costo transversectomy of D10 and D11 on left side, anterolateral decompression and placement of strut rib graft in the dead space.

Surgical intervention may be considered when no positive response is seen with conservative management, in the presence of large abscess, deteriorating neurological deficit, acute onset of paraplegia, instability and deformity [61]. There are certain advantages of surgery over conservative management. Return to previous activity state is quicker, pain relief and neural decompression is dramatic, time taken for bony fusion also decreases and delayed complications like deformity and neurological deficit can be avoided [62].

Debridement of the diseased tissue, decompression of the neural element and stabilization of the unstable spine are the basic objectives of surgery. Corrective osteotomies of spine can be done in healed rigid deformities [45].

Hodgson described "The Hong Kong operation". This radical surgery included debridement of diseased tissue and decompression of neural elements. Bleeding cancellous bone was exposed proximal and distally and tricortical iliac crest or portion of excised rib was used as strut graft for fusion. The unstable spine was instrumented posteriorly [63]. As an alternative to the bone grafting in the diseased area, surgeons have been instrumenting the defect created after debridement with cage and bone graft, for immediate stabilization and better deformity correction [64].

In the past instrumentation was avoided in the face of infection and two staged surgeries have been done. Debridement in the first and delayed instrumented fusion in the second.[65] Presently, in the management of tuberculous spondylitis, implants are routinely used. Studies have revealed that Mycobacteria do not colonize on stainless steel as much as Staphylococcus does. Infection risk is even lower when titanium alloy implants are used [66].

Depending upon the expertise of surgeon and type of implants, surgical intervention on the tubercular spine may be done by several approaches. Surgical approach maybe anterior, posterior, combined, anterolateral or transforaminal.

Surgical correction of thoracic or thoracolumbar kyphosis in active disease is done when the angle of kyphosis is more than 60 degrees. This severity of the kyphosis is related to the number of vertebra involved, usually three or more. Kyphosis also progresses in children younger than seven years of age with involvement of multiple vertebra or those who have two or more 'spine at risk signs'. Therefore, surgical correction is indicated in these cases [67].

Correction can be done in a single stage with transpedicular approach (closing wedge osteotomy) [68] or extrapleural anterolateral approach [69]. It can also be achieve in two stages i.e anterior decompression and bone grafting in the first and posterior fixation in the second. Anterior decompression can very well be done by transthoracic transpleural or retroperitoneal approach with the advantage of being able to expose both anterior and the posterior columns. Bone graft or cage can be placed in the defect created after curettage of the diseased segment. Moon et al achieved significant correction of kyphosis both with two staged procedure and with single stage procedure [70].

Corrective surgery in healed caries spine is a major undertaking as risk of neurological deficit is high and the degree of correction of deformity is low. Yau et al [71] attempted correction in multiple staged surgeries and distraction with halo-pelvic ring followed by anterior and posterior fusion. However, the study found this not very rewarding with respect to the complexity of the procedure. Moon discussing the challenges and controversies in management suggested that correction of severe kyphosis in healed disease should be avoided unless there is some life threatening indication like severe pulmonary complications due to deformity [1].

RECENT ADVANCES

Minimal Invasive Spine Surgical Techniques offer potential benefits of decrease surgical trauma, lesser blood loss and short operative time. In a series of 25 patients diagnosed with septic spondylitis, anterior debridement and cage fixation followed by posterior MIS screw fixation, Korovessis showed the benefits of MIS [72].

CONCLUSION

Tuberculosis is a contagious disease and affects the quality as well as the quantity of life. Patients suffering from tuberculous spondylitis also suffer social, mental and economic trauma. At the same time it can be cured completely provided it is diagnosed early. In this review we pointed out the clinical presentation and methods of early detection of the disease as well different management tools. Antituberculous medicine remains the gold standard and clinicians must make sure that the exact protocol of dosage, mode of administration and duration of treatment is followed. Decision of surgical intervention should be taken according to the behavior of the disease.

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