Spinal tuberculosis (TB) remains endemic in many parts of the developing world and is increasingly seen in the developed world due to migration. A total of 1.3 million people die annually from the disease. Spinal TB is the most common musculoskeletal manifestation, affecting about 1 to 2% of all cases of TB. The coexistence of HIV, which is endemic in some regions, adds to the burden and the complexity of management.

This review discusses the epidemiology, clinical presentation, diagnosis, impact of HIV and both the medical and surgical options in the management of spinal TB.

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Spinal tuberculosis (TB) is one of the oldest diseases known to man having been identified in Egyptian mummies dated before 3300 BC1 and often referred to as Pott’s disease. Percival Pott described the associated paraplegia due to destruction of the anterior spinal column and progressive kyphosis, in 1779.2

Epidemiology

In 2015, there were 10.4 million new cases of TB globally, 11% of which were in HIV positive patients. In the same year, 1.8 million people died from TB.4 Spinal TB is more common in young adults and children and has been labelled “a disease of poverty”3 due to its higher incidence in lower income households and poorly developed countries. Although the incidence of TB is highest in the developing world, particularly southern Africa, where it approaches 1%, it is increasingly seen among immigrants in the western world.5

Extrapulmonary TB represents 10% of cases, of which half involve the musculoskeletal system. The spine is the most common musculoskeletal site representing between 1% and 2% of cases.6

The reason for the high incidence in Africa includes socioeconomic factors of poverty and poor access to health facilities and its association with HIV disease. Sub-Saharan Africa has 25.6 million HIV positive people, which represents 70% of the total number of HIV positive patients in the world.4 HIV reduces the cellular immunity required to control TB by preferentially targeting TB-specific CD4 cells. This increases the incidence of TB infection, the rate of reactivation of latent disease and of extrapulmonary disease. TB in turn accelerates the replication of HIV infected CD4 cells, increasing viral production.7 A genetic predisposition to spinal TB has been seen in Chinese patients with FokI polymorphism in the vitamin-D receptor gene.8

Spinal TB follows the haematogenous spread of mycobacterium tuberculosis into the cancellous bone of the vertebral bodies from lesions in the lungs or genitourinary system by venous or arterial routes.9 Haematogenous spread is facilitated by the arterial arcade that flows through the subchondral region of each vertebra, from posterior and anterior spinal arteries which form a rich local vascular plexus.10 The disease is characterized by the paradiscal destruction of a vertebral body leading to kyphosis with preservation of the disc until late in the disease process (Fig. 1). The kyphosis with epidural pus and disc and osseous debris can lead to compression of the spinal cord and neurological sequelae. Occasionally, concertina collapse may occur with compression at a single vertebral body without intervertebral disc involvement.11

Late-onset paraplegia may occur despite resolution of the active disease, due to severe persistent kyphosis with attenuation of the spinal cord over the internal gibbus. This leads to myelomalacia, which is irreversible, and poor neurological recovery despite subsequent surgery. Thus, early control or correction of kyphosis is required.12

Clinical features. The onset of spinal TB is insidious, typically progressing over four to 11 months. This, with poor access to health facilities in developing areas where TB is most
prevalent, results in delayed presentation. Weight loss is the most consistent constitutional feature. The frequently quoted fatigue, pyrexia, night sweats and generalized aches are generic and often ascribed to other ailments. Spinal TB usually presents with axial pain in the affected region with surprisingly varied intensity from a dull ache to a severe disabling pain. There is often an associated spinal prominence, a gibbus, due to collapse of the anterior column and kyphosis. Paraspinal abscesses may be large at the time of presentation. In the cervical spine, they may manifest as hoarseness, respiratory distress, or dysphagia. In the thoracic spine, there may be fusiform paravertebral collections, which are seldom clinically evident. In the lumbar area, abscesses form in the psoas muscle which may cause swelling in the thigh and groin. These can extend below the inguinal ligament into the medial compartment of the thigh.

Neurological deficit is common and reported between 23% and 76% of cases, with higher prevalence when cervical and thoracic regions are involved. It is usually incomplete with sensory preservation and varying motor involvement. Lumbar disease may present as weakness with limitation of mobility but due to pain from the spine destruction and psoas abscess rather than neurological impairment.

**Imaging**

Imaging may suggest the diagnosis, however, a definitive tissue diagnosis requires laboratory confirmation. Radiographs are frequently used as they are readily available in the under resourced areas where TB is most prevalent. The soft-tissue shadows of a thoracic paraspinal abscess may be the earliest radiographic sign. As the pus disseminates in the psoas muscles, the abscess may not be evident when the lumbar spine is involved. The fact that the height of the disc is maintained until late in the disease differentiates spinal TB from pyogenic discitis, in which there is early loss of disc height. The number of vertebral bodies involved may be underestimated, and careful review of the associated posterior elements is required to identify this number which may also predict the final thoracic kyphosis. The vertebral height may be divided into tenths. Using the total number of vertebrae which are involved, the thoracic kyphosis five years later may be predicted; thus: kyphosis = total vertebral involvement × 30.5° + 5.5°. Thus, two completely destroyed vertebrae predicts a 65.5° kyphosis at five years.

The use of CT scans allows earlier detection of vertebral involvement and more detail of the destruction. Epidural and central canal involvement and paraspinal abscesses with calcification may be identified, suggesting TB as opposed to pyogenic infection. Although CT has largely been superseded by MRI, it is still relied on in less well-resourced areas. MRI is the most sensitive and specific form of imaging in these patients allowing visualization of cord
compression by pus and debris, intrinsic cord signal, bone marrow changes and disc destruction. A full sagittal sequence of the spine allows detection of non-contiguous lesions, which occur in up to 16% of patients (Fig. 2).

Positron emission tomography (PET) may allow identification of sites of active disease and monitoring of the response to treatment, predicting possible drug resistance, and identifying appropriate sites for biopsy, but is not specific. Availability is usually a problem in areas where TB is endemic.

**Diagnosis**

Routine blood tests may be used to monitor and possibly exclude but not confirm the diagnosis. The ESR is markedly raised in spinal TB with an average in the 70s. The WBC count is usually normal. The level of platelets is raised and the differential count may show a lymphocytosis. Biopsy of the pathology is mandatory to acquire tissue or pus to differentiate the lesion from tumour and other infections. Tissue has a higher diagnostic yield than pus. Culture of mycobacterium tuberculosis remains the benchmark for the definitive diagnosis and allows sensitivity to antibiotics to be established. Unfortunately, culture takes up to six weeks to yield a result despite using accelerated culture systems such as BACTEC (BACTEC MGIT 960, BD Diagnostic Systems, Sparks MD, Franklin Lakes, New Jersey). As spinal TB is paucibacterial, acid fast bacilli (AFBs) are not always seen on microscopy. We have reported a 38% yield. Histological features assist if they show the typical features of caseating granuloma, giant cells, and occasional AFBs. In endemic areas, these features are often regarded as diagnostic but occasionally other conditions such as sarcoidosis and cat scratch disease cause similar granuloma. Histology will confirm spinal TB in 60% of cases.

Polymersase chain reaction (PCR) technology identifies the presence of genetic material of mycobacterium tuberculosis with specificities between 80% and 90%, and sensitivities of 95% with minimal delay. This technology is now available where it is needed most due to the recent development of GeneXpert cartridge-operated, hospital-based machines (Xpert MTB/RIF, Cepheid, Sunnyvale, California) and can provide a diagnosis within two days. It also allows the recognition of antibiotic resistance.

Further exciting developments include the use of interferon-gamma measurements in the blood using QuantiFERON-TB Gold (Cellestis Ltd, Victoria, Australia), with reported sensitivities and specificities of 84% and 95%. Unfortunately, they are not useful in areas with a high incidence of TB due to the populations exposure with asymptomatic latent (inactive) disease rather than active disease.

**Treatment**

Medical management is the mainstay of treatment of spinal TB, with surgery indicated for specific situations. Anti-tuberculous therapy should begin as early as possible. In poorly resourced, high-burden areas, it may be initiated empirically based on clinical findings while the diagnostic process continues, in order to avoid the inevitable delays in waiting for these investigations.

The relief of pain and resolution of a neurological deficit follows anti-tuberculous therapy in most patients. The World Health Organization has recommended treatment in two phases, an intensive phase and a continuation phase. The intensive phase of two months includes four drugs, isoniazid (H), rifampicin (R), ethambutol (E), and pyrazinamide (Z). This is reduced to two drugs, isoniazid, and rifampicin in the continuation phase. They recommend a total duration of nine months for patients with TB of the musculoskeletal
system. The American Thoracic Society recommends six months of treatment in adults and 12 months in children.

This is in contrast to the practice in countries with a high burden of TB. Recent guidelines from India recommend two months of intensive four-drug therapy (RHZE) and three drugs (RHE) for a continuation phase of between ten and 16 months.

As our patients are malnourished and frequently have HIV coinfection, and due to concerns about the antibiotic penetration of large abscesses or granulomas, when managed non-operatively, we use four drugs, a combination preparation Rifafour (Aventis Pharma Ltd, Johannesburg, South Africa) consisting of RHZE, for a minimum of nine months. This may be extended according to the clinical response, particularly the relief of pain and gain in weight with normalization of the ESR, and radiographic features of bone healing. Pyridoxine (vitamin B6) is added to prevent isoniazid-associated peripheral neuropathy.

Between 5% and 11% of patients with spinal TB are drug resistant. This may be mono or multidrug resistance. The GeneExpert cartridge-based system detects rifampicin resistance only, but we have not had a patient with drug resistance which did not include resistance to rifampicin. Following successful culture, sensitivity testing of all the drugs is performed. Should there be resistance, infectious diseases experts should be consulted for second-line therapy. This usually requires the addition of a quinolone and an aminoglycoside, necessitating prolonged daily injections. Multiple resistance is more common in HIV coinfection and has a poorer prognosis.

The side effects of the drugs need to be considered during routine follow-up. These include visual deterioration from ethambutol induced retrobulbar neuritis and hepatitis from HRZ. We use ESR for routine monitoring as it can be performed in the clinic within an hour, rather than relying on transport to a laboratory service. It will slowly return to normal in patients with spinal TB. It is, however, less useful in those with HIV coinfection.

The ‘directly observed treatment short-course’ (DOTS) method improves compliance of medical management with rates of completion of between 61% and 86%. A financially incentivized DOTS system has further increased completion to 91%.

**Surgery**

The indications for surgery include an established or predicted deformity, a neurological deficit, large abscesses and diagnostic biopsy if percutaneous options are not available.

Overall, paraplegia may recover in 40% of patients with spinal TB with medical management alone. The use of surgery remains controversial although it is generally advised in selected cases. Surgery relieves compression of the spinal cord, corrects kyphosis, may facilitate fusion, and leads to faster relief of pain compared with conservative treatment. Function may be improved sooner, with less bone loss and a lower risk of late-onset neurological deterioration.

In many areas where TB is endemic, interventional radiology biopsy services are not available. Thus, the surgeon is responsible for performing the biopsy, usually in theatre, and the opportunity may be used to drain large abscesses due to concerns about drug penetration and in order to expedite the resolution of symptoms. Surgical options may be determined by what is locally available, in terms of surgical skill and postoperative facilities. This is also moderated by the patient’s ability to finance the care where state-financed care is not available.

As the thoracic spine is most commonly involved, a costotransversectomy may be used where there is minimal deformity with a paraspinal abscess. The pus may be drained and anterior column debris debrided. This can be combined with a posterior fusion (Fig. 3).

Formal debridement and reconstruction of the anterior column is reserved for patients with severe kyphosis with cord compression. This can be performed by an anterior-only approach or posterior-based approaches. The T6-T11 area is easily accessed transthoracically, and the diseased vertebrae and discs are resected and reconstructed. Inexpensive allograft humeral shaft can be used with screw fixation to the vertebral body above and below. This is our preference. Some surgeons are concerned about postoperative pulmonary risks, especially where no intensive care facility is available.

The anterior column can be resected from a posterior approach after pedicle screw placement. This is achieved using a uni or bilateral costotransversectomy, sacrifice of one or two intercostal nerves, debridement, and the introduction of graft and a cage (Fig. 4).
Adequate decompression and correction of a kyphosis can be achieved with both approaches. Our preference is transthoracic, as complete debridement is easier and more effective without sacrifice of nerve roots. Although there may be some subsidence of the graft, the outcomes are good, with no need for postoperative ventilation or intra-operative single-lung ventilation as the lung is simply retracted.

The thoracolumbar region is biomechanically more challenging and surgery using only an anterior approach is not advised. The options are anterior debridement and reconstruction with posterior pedicle screws, or a posterior only approach. Here all may be undertaken using a posterior-based approach of pedicle screws and costotransversectomy with anterior column debridement and reconstruction, as it avoids intraoperative repositioning and enables a quicker procedure.

Our preference is to use allograft for reconstruction of the anterior column usually with humerus in the thoracic spine and femur in the lumbar spine. The fibula may be used in smaller patients, particularly children. This is extremely cost-effective. Our commercially available allograft humeral and femoral shafts cost between 5% and 10% as that of cages. They also integrate over time giving a biological solution (Fig. 5). In areas where commercial allograft is not available, the options include: fibula autograft, with associated morbidity and increased theatre time, the patient’s own ribs, which are frequently too weak and often fracture, or commercially available cages. There is no contraindication to the use of instrumentation, pedicle screws, or anterior cages in spinal TB as the mycobacterium does not create a biofilm.

The cervical spine can be managed with anterior debridement and reconstruction. If the residual endplates are soft from the disease, there may be subsidence due to poor fixation and posterior instrumented augmentation should be considered (Fig. 6).

**Spinal TB in HIV positive patients**

In many areas where TB is endemic, HIV disease is also endemic. Not only do these diseases drive each other, as discussed above, the coexistence complicates management. The immune reconstitution inflammatory syndrome (IRIS) manifests when HIV medication is initiated and the patient’s immunity improves and reacts to the TB. There may be an overwhelming inflammatory response, which can result in death. It is important to prevent this syndrome by treating the TB before the HIV. When the CD4 cell count in the blood is < 50 per cubic mm, highly active antiretroviral treatment (HAART) should be deferred for two weeks; when the CD4 count is > 50 per cubic mm, it should be deferred for eight weeks.

There are also pharmacological interactions where anti-TB drugs, specifically rifampicin, stimulate the cytochrome P450 system, increasing the metabolism of HIV drugs, and the dose may need to be increased.

**Prognosis**

The prognosis is generally good in spinal TB, with almost all patients having relief of pain and improved neurological deficits. As opposed to trauma, even patients with no sensory or motor function below the lesion usually improve due to the low energy nature of the cord compression. Most patients regain mobility following surgery. A poor prognosis is dictated by the general health status of the patient rather than the neurological deficit. Neurological recovery may be expected in most patients managed for active spinal TB and usually occurs within the first three months.

In conclusion, spinal TB is most prevalent in socioeconomically deprived communities with poor access to health care. It is, however, increasingly prevalent in the developed world, where it had been largely eradicated, due to population migration. With its insidious onset and vague
symptomatology, a high index of suspicion needs to be maintained. Coexistent HIV disease increases its incidence and complicates management. Although medical treatment is always required, surgery may expedite neurological recovery and allow a kyphosis to be corrected. The technique used needs to be tailored to the local skills and facilities. The prognosis is usually good, once the diagnosis has been made, and treatment initiated. Most patients have relief of pain and neurological improvement within three months of the onset of treatment.

Take home message:
- TB has its highest incidence in the developing world but with increased population migration is increasingly present in the developed world.
- The management is further challenged by the co-existence of HIV infection.
- Presentation can be insidious and a high level of suspicion needs to be maintained.
- Biopsy is mandatory to confirm diagnosis and antibiotic sensitivity.
- Medical management is the mainstay but surgery is indicated for predicted or established severe kyphosis, neurological deterioration and large abscess collection.
- Medical management needs to be adapted in the presence of HIV to avoid IRIS (immune reconstitution inflammatory syndrome).
- With optimal management, prognosis is good even with profound neurological impairment.

References


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