

Chapter 15

Complications and Management in Tuberculosis of the Spine



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Abstract Tuberculosis of the spine is a severe form of extra-pulmonary tuberculosis and poses a challenge to physicians worldwide. Left untreated, it can lead to severe complications with significant patient morbidity. In this chapter, we discuss the most common complications of spinal tuberculosis and their management, including cold abscesses, kyphotic deformity, and neurologic deficits, in addition to the specific challenges posed by late onset symptoms. Adverse reactions to anti-tuberculosis drug therapy as well as medicolegal challenges in treating spinal tuberculosis are also highlighted.

Keywords Spine · Tuberculosis · Complications · Kyphosis · Neurologic deficit · Drug reaction · Cold abscess · Legal · Litigation

15.1 Introduction

Spinal tuberculosis accounts for approximately half of musculoskeletal tuberculosis cases and remains a challenge for physicians worldwide [1]. Left untreated, it can lead to serious sequelae and significant patient morbidity [2]. It usually begins in an insidious fashion as a secondary infection, with the *Mycobacterium tuberculosis* (*M. tuberculosis*) pathogen seeding the anterior aspect of the vertebral body most commonly hematogenously [3–5]. In the early stages, patients often present with varying degrees of axial pain, with multiple studies demonstrating 90–100% of patients reporting back pain as a symptom [6–8]. Constitutional symptoms are only present in about 20–30% of patients, with weight loss being quoted as the most consistent constitutional feature, although fevers, night sweats, and malaise can also be present but are more common in patients with concomitant pulmonary tuberculosis [5, 6, 9].

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The slow onset of progression often leads to a delayed presentation. This is especially an issue in countries with a high tuberculosis burden, where many patients have limited access to healthcare facilities, resulting in initial presentation at an advanced stage [5, 10]. Although the presentation and natural history of spinal tuberculosis can be variable, it usually presents with three main clinical complications: cold abscesses, neurologic deficits, and kyphotic deformity [3]. The timeline at which these complications arise are variable. Neurologic deficits can present early and late in the disease process, even decades after the initial infection, while kyphotic deformity is usually a late presentation of spinal tuberculosis.

15.2 Cold Abscesses

Cold abscesses are purulent collections that form as a result of caseous necrosis which follows the inflammatory response to the *M. tuberculosis* complex [3, 6]. They are found in 48–70% of patients with spinal tuberculosis and are characterized by slow growth and subligamentous spread [3, 11]. These abscesses often grow unnoticed until their mass effect causes symptoms, frequently leading to a delayed diagnosis. On imaging they are best seen on magnetic resonance imaging (MRI) and computed tomography (CT) scans, although even plain radiography may provide evidence of a cold abscess as a soft tissue shadow, increased cervical pre-vertebral soft tissue space, or mediastinal widening. At later stages they can fistulize, and their wall can become calcified due to the lack of proteolytic enzymes in *M. tuberculosis* [1, 4, 12].

They are most commonly para-vertebral but can also be found in a pre-vertebral or intra-osseous location [6]. About 90% of abscesses are found in the lower thoracic or lumbar spine, and 10% are found in the cervical and upper thoracic spine [3]. Initial presentation depends largely on the location and size of the cold abscess. Abscesses in the cervical region can be retropharyngeal and lead to dysphagia, hoarseness, or difficulty breathing [5]. Those in the thoracic spine are often fusiform paravertebral and rarely symptomatic. Those in the lumbar region can involve the iliopsoas muscle leading to groin swelling and pseudo-flexion hip deformity, and can even track down below the inguinal ligament into the medial thigh compartment [3, 5, 9].

Historically, management of cold abscesses frequently involved drainage with the goal of reducing disease burden and preventing further complications. However, with modern highly penetrating anti-tuberculosis drug therapy, abscesses are commonly successfully resorbed and eventually fill in with new bone following non-operative therapy [3, 4, 13]. Drainage is indicated however when abscesses lead to dysphagia, respiratory compromise, pseudo-flexion hip deformity, or neurologic deficits. Occasionally, draining a large abscess maybe performed while obtaining a biopsy in order to facilitate drug penetration [5].

15.3 Neurologic Deficits

Neurologic symptoms in the setting of spinal tuberculosis can be seen in approximately 10–20% of patients in developed countries and 20–41% in developing countries [14]. Neurologic deficits are often defined as early-onset or late-onset [3, 14, 15]. Early-onset deficits are those occurring while the disease is active (usually within the first 2 years of active disease) and result from direct or indirect compression by an abscess, granulation tissue, or debris onto the spinal cord parenchyma or instability leading to cord compromise [4, 6]. Late onset deficits are those which occur with healed disease and can present many years and even decades after the initial infection [15]. This is usually attributed to spinal cord damage secondary to a transverse bony ridge at the apex of the kyphotic deformity and dural fibrosis [4, 6]. Less common causes of neurologic deficits include infective spinal artery thrombosis, tuberculosis myelitis, and arachnoiditis [4].

Signs and symptoms can range from radicular pain, weakness, and paresthesias to myelopathy and even para- or tetraplegia if left untreated depending on the involved anatomic location [3, 4]. The mainstay treatment remains medical, as medical treatment effectively treats the majority of neurologic deficits from active disease [5, 16]. However, the original Medical Research Council trials which demonstrate the efficacy of conservative therapy only considered patients with limited disease, mild to moderate neurologic deficits, and mild deformity [17]. Recently, studies have found that decompression may lead to faster pain relief and functional recovery as well as decrease the risk of late-onset neurologic sequelae when compared to medical therapy alone [5, 14, 18]. As such, surgery is indicated in specific situations involving severe or rapidly worsening deficits at presentation, as this can indicate the presence of instability, as well as cases that are unresponsive to anti-tuberculous drug therapy [6, 14].

Prognosis after surgical decompression is generally favorable in patients with active early-onset disease with most showing neurologic recovery [19]. This is thought to be related to the low energy and relatively longer timeframe of cord compression with tuberculosis as opposed to trauma and other pyogenic infections [5, 14].

15.4 Kyphotic Deformity

Kyphosis is a late manifestation of spinal tuberculosis, reported in about 29% of patients. It develops as a result of destruction of the anterior aspect of the vertebral body in the thoracic spine. Collapse of the anterior column can lead to a focal gibbus deformity or a globally rounded kyphosis depending on the number of vertebrae involved [5, 6]. Progression of deformity is dependent on multiple factors including

age, involved region, and the extent of disease [9, 11]. In children, kyphosis can worsen during periods of growth even following cure of the disease. In contrast, in adults the final deformity is mostly determined by the extent of vertebral changes during the active disease stage [6]. The spine-at-risk radiographic signs (Fig. 15.1) described by Rajasekaran et al. help identify children at risk of developing progressive kyphosis [9, 20].

Surgery is indicated for a severe established deformity or spinal instability leading to a high risk of future deformity or neurologic deficits [5, 6]. In adults, a kyphosis of $>60^\circ$ is generally managed operatively as these usually progress and are associated with a high risk of late-onset neurologic deficits [21]. In children, however, a lower threshold of 30° is suggested due to the higher risk of future progression [1]. In addition, surgery is indicated when there are signs of spinal instability such as three column disease involvement; loss of >1 thoracic vertebral body or >1.5 lumbar vertebral body; pedicular destruction with posterior arch involvement; or two or more “spine-at-risk” signs in children [6].

Historically, surgery for spinal tuberculosis, including debridement and reconstruction, was performed mostly using an all-anterior approach from the principle that tuberculosis is predominantly an anterior column disease. However, with the development of pedicle screw instrumentation, the posterior approach has become more popular. Studies have demonstrated similar pain and neurologic improvement compared to the anterior approach along with improved deformity correction [22, 23]. In addition, current drug therapy regimens can result in satisfactory resorption of anterior abscesses, which makes a more extensive anterior debridement less necessary and permits use of a posterior approach [3]. Combined approaches can also be used for more complex deformities and can be performed in one or two stages [24].

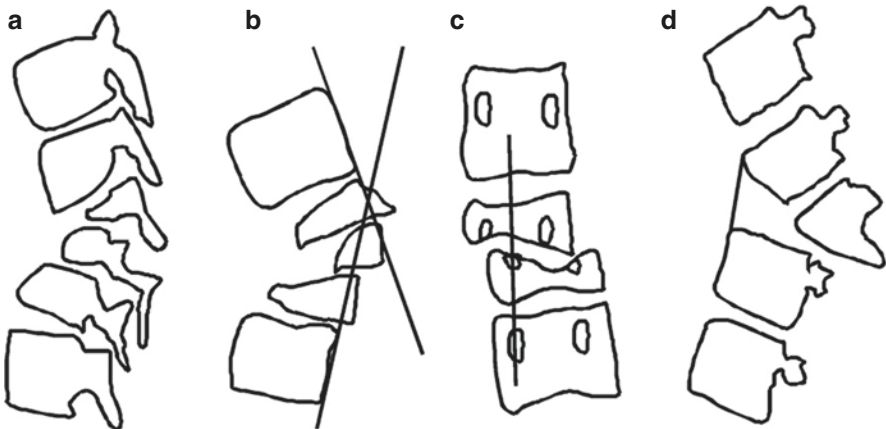


Fig. 15.1 Spine-at-risk signs assessed in a radiograph, demonstrating separation of the facet joint (a), retropulsion (b), lateral translation (c), and toppling (d). The presence of >2 signs indicate instability and a high risk of progression in deformity (Reproduced with permission from Jain et al. [9])

15.5 Challenges in Late-Onset Tuberculosis Symptoms

Although tuberculosis can be cured with medical therapy, treatment of late sequelae which are either due to late patient presentation or late symptom onset is challenging and often fraught with complications. Previous studies have demonstrated that in countries with high tuberculosis burden and limited access to healthcare, rates of surgical intervention are higher than in countries with a more developed healthcare system [1]. This reflects the challenge in treating patients who present at later stages of the disease process.

Patients who present with late-onset neurologic deficits at the healed stage of the disease often have a worse prognosis when it comes to neurologic recovery when compared to patients who present with early-onset deficits. This is also true for patients who present with long-standing neurologic deficits that have not been addressed in a prompt matter [14]. In both cases however, surgical decompression may offer the best chance for a potential recovery, but the patient must be advised that recovery is less predictable. In addition, late-onset deficits present a unique diagnostic challenge as one should differentiate whether such a deficit is associated with a healed lesion versus reactivation. Reactivation usually presents with more severe and rapidly developing deficits compared with healed lesions, and detailed review of advanced imaging, including CT and MRI, may reveal disease activity at or around the internal gibbus [14]. Patients with reactivation can be treated with debridement with or without stabilization, while patients with healed disease often require excision of the internal gibbus with or without deformity correction [9]. In addition, patients with reactivation have more favorable outcomes following surgical decompression compared to patients with healed disease [25].

Another challenge is the late development of kyphotic deformities. Deformities of 60° or greater has been observed in approximately 3–5% of patients with spinal tuberculosis treated with medical therapy alone [6]. Deformity correction in healed disease is more difficult and is associated with higher rates of complications compared with active disease. Patients with healed disease who present with a kyphotic deformity greater than 60° often require a combined anterior-posterior approach to correct the deformity, which is a major undertaking compared to a posterior or anterior only approach [9, 14, 24].

15.6 Adverse Drug Reactions

Medical management with anti-tuberculosis drugs remains the mainstay treatment of spinal tuberculosis, which is considered a severe form of extrapulmonary tuberculosis and hence falls under the World Health Organization's (WHO) Category-I treatment. Although protocols may vary by country or institution, the recommended WHO two-phase protocol involves an intensive 2-month phase of isoniazid, rifampicin, ethambutol, and pyrazinamide followed by a continuation phase of isoniazid

Table 15.1 First-line anti-tuberculosis drugs with the most common adverse reactions and their incidences (adapted from Forget et al. [28])

Drug	Reaction (incidence)
Isoniazid	Transaminitis (11%), hepatitis (0.4%), neurologic (1–3%), dermatologic (1%), gastrointestinal (2%), hypersensitivity (0.1–17%)
Rifampicin	Transaminitis (3–9%), hepatitis (1%), dermatologic (0.5–3%), gastrointestinal (1–8%)
Pyrazinamide	Hepatitis (1–5%), dermatologic (2–5%), gastrointestinal (1%)
Ethambutol	Neurologic (0.2–0.3%), dermatologic (0.15%), hepatitis (rare reports)

and rifampicin for a total treatment time of 9 months [4, 26]. Given the relatively long duration of therapy, awareness of adverse drug reactions is paramount, especially with the increasing prevalence of multi-drug resistant tuberculosis leading to the use of second-line drugs which have a greater toxicity profile [6, 27].

Side effects and interactions with other medications are both important considerations. Side effects of common first-line anti-tuberculous drugs and their incidence can be found in Table 15.1 [28]. Transaminitis with asymptomatic elevation of liver function tests up to five times the normal limit is common and can be serially observed without discontinuation of therapy. Neurologic side effects vary, with peripheral neuropathy common with isoniazid treatment and ocular toxicity being the main neurologic adverse effect of ethambutol [29, 30]. Second-line therapies tend to be more toxic. For example, fluoroquinolones are associated with QT prolongation predisposing to torsades de pointes, and aminoglycosides are associated with nephrotoxicity leading to oliguric renal failure [27].

Both rifampicin and isoniazid may also interact with other medications. Rifampicin is a potent inducer of drug metabolism and as a result reduces the level of other medications such as warfarin, contraceptives, corticosteroids, phenytoin, and theophylline, potentially resulting in subtherapeutic anticoagulation, birth control, and seizure prophylaxis. Isoniazid, on the other hand, can increase levels of warfarin, phenytoin, and carbamazepine [31]. The relatively common side effects and multitude of interactions of anti-tuberculosis drug therapy regimens serve to emphasize the importance of proper medical follow-up and monitoring of spinal tuberculosis patients by a multi-disciplinary team.

15.7 Medicolegal Issues

Throughout this chapter, we highlight the importance of early diagnosis and treatment of spinal tuberculosis before complications arise. Along with the immeasurable cost of patient suffering from the complications of delayed treatment, there is also a significant medicolegal cost.

Medicolegal issues arise from both the medical evaluation and therapy of spinal tuberculosis, as well as the complications related to its surgical treatment. Malpractice litigation has been reported when there is a failure to diagnose spinal

tuberculosis, delay in starting anti-tuberculosis therapy, incorrect treatment, inadequate monitoring, drug interactions with other medications, and failure to refer to a spinal surgeon [32, 33]. A review by Quraishi et al. from the United Kingdom's National Health Services Litigation Authority database showed that missed spinal infections accounted for 11.8% of all successful claims of alleged negligence with average damages paid out amounting to 433,206 British pounds [34]. As such, adherence to well-established national and international guidelines when evaluating and treating tuberculosis is of utmost importance as it avoids poor outcomes and also helps reduce the incidence of multi-drug resistance [32, 35]. Further, the importance of patient education and informed consent are critical in this setting. For all the aforementioned reasons, it is recommended that the treatment of spinal tuberculosis is undertaken at specialized healthcare centers with proper established protocols and a multi-disciplinary team that is familiar with both the medical and surgical aspects of the disease.

15.8 Conclusion

Tuberculosis of the spine poses a challenge to spinal surgeons worldwide. Left untreated, it can lead to severe complications with significant patient morbidity.

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