Chapter 10
Spinal Tuberculosis

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10.1 Introduction

Spinal infections include infections primarily affecting (1) the spinal cord; (2) nerve roots and meninges; or (3) the vertebrae, intervertebral discs, and epidural space. They are broadly classified as pyogenic or nonpyogenic, with the former category including vertebral osteomyelitis and discitis, while parasitic, fungal, and tuberculous infections constitute the latter category.

10.2 Definition

Tuberculosis (TB) is one of the oldest pathological conditions that affect mankind. It can affect several tissues outside the lungs. Five percent of TB cases affect the skeletal system, with 50% of those being located within the vertebral column [1] and causing a kind of tuberculous arthritis of the intervertebral joints. Spinal TB (STB) is also known as *Pott disease* (or *Pott's disease*), named after Percival Pott, who published the first description of it in 1779 [2].

10.3 Epidemiology

Tuberculosis is a global health problem, affecting one third of the world's population [3]. It is a widespread disease, with 8.7 million new cases annually, and worldwide rates of TB have increased in parallel with the incidence of acquired

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immunodeficiency syndrome (AIDS) [4]. The increase in TB has been witnessed not only in Africa and Asia but also in European countries. In addition, TB ranks second, just after human immunodeficiency virus (HIV) infection, among infectious causes of mortality. Hence, TB remains an important cause of morbidity and mortality worldwide [5]. Turkey has been reported to be a low-incidence country for TB [3].

When extrapulmonary TBSpinal tuberculosis (STB)epidemiology is taken into consideration, 10–35% of all TB cases [6]. In 2016 it was estimated that STB accounted for around 2% of all cases of TB and around 15% of extrapulmonary TB cases [7].

10.4 Risk Factors for Developing Spinal Tuberculosis

There are many predisposing factors for STB, including previous TB infection and malnutrition [8]. Population groups with an increased risk of STB include immunecompromised persons (with AIDS, lymphoma, leukemia, or organ transplants), diabetic persons, children, elderly persons, alcoholics, persons with a low socioeconomic status, persons with poor treatment compliance, migrants from developing countries, prisoners, nursing home residents, health care workers, and homeless people [9, 10]. In addition, hematological seeding from an infectious focus in the skin, genitourinary tract, gastrointestinal tract, or respiratory tract is considered an important risk factor for STB [11].

10.5 Pathophysiology

There are two types of STB: the classic form (or spondylodiscitis) and an increasingly common atypical form, which is spondylitis without disk involvement [12]. In adults, involvement of an intervertebral disc is secondary to spread from an adjacent infected vertebra, while in children it can primarily be due to the vascularized nature of the intervertebral discs. The basic lesion in Pott's disease is a combination of osteomyelitis and arthritis, usually affecting more than one vertebra. The anterior aspect of the vertebral body adjacent to the subchondral plate is commonly involved [13]. STB can include any of the following: progressive bone destruction, leading to vertebral collapse and kyphosis, spinal canal narrowing by abscesses, cold abscess formation (due to extension of infection into adjacent ligaments and soft tissues), or granulation tissue or direct dural invasion, resulting in spinal cord compression. These events lead to different neurological deficits [8, 12, 13].

10.6 Diagnosis

The diagnosis is based on the history, imaging studies of the spine, chest radiography, computed tomography (CT) of the chest, and laboratory values such as the white blood cell count and purified protein derivative tests.

10.6.1 Clinical Picture

10.6.1.1 Clinical Course

The involvement of spinal vertebrae results from hematogenous spread of *Mycobacterium tuberculosis* into the cancellous bone tissue of the vertebral bodies [7]. The primary infection site comes from either a pulmonary focus or another extrapulmonary focus, such as the gastrointestinal tract or lymph nodes [8].

10.6.1.2 Clinical Presentation

Delays in diagnosis of STB are common [7]. Patients with STB may present with a wide variety of symptoms [14].

The average time from presentation to diagnosis is 1 year and 7 months. Typically, the onset of symptoms is insidious, and the disease progression is slow. The duration of symptoms prior to diagnosis may range from 2 weeks to several years [15].

With regard to sex predilection in STB, 53% of STB patients are male [7].

The clinical presentation and findings of physical examinations depend on the site and stage of the disease, the presence of complications, and constitutional symptoms [16].

The most commonly reported symptoms are focal back pain, fever, weight loss, and neurological abnormalities such as motor or sensory root affection of the bowel/bladder dysfunction, and paraplegia [7].

Also, the patients have systemic symptoms of active TB, including cough, shortness of breath, fevers/chills, and night sweats.

10.6.1.3 Complications After Spinal Tuberculosis

The incidence of neurological deficit varies from 23% to 76% [7].

Complications include syringomyelia, permanent neurological deficits, and spinal osseous defects [17]. Paraplegia is considered the most devastating complication of STB.

10.6.1.4 Laboratory Tests

Hematological investigations such as a complete blood count, erythrocyte sedimentation rate, enzyme-linked immunosorbent assay, and polymerase chain reaction (PCR) are needed in the case of STB [7].

Microbiological evidence includes at least one of the following: isolation of *M. tuberculosis* in blood, bone, bone marrow, deep soft tissue, and/or (paravertebral, epidural, or psoas) abscess specimens; and positive microscopy for acid-fast bacilli from bone, bone marrow, deep soft tissue, and/or a (paravertebral, epidural, or psoas) abscess, or any sterile body tissue. Bone tissue or abscess samples stained for acid-fast bacilli, mycobacterial organisms isolated from culture, and CT-guided or ultrasonography-guided needle biopsy or surgical biopsy are also widely used [7, 15, 18]. That can be done by use of Ziehl–Neelsen staining. In addition, rapid culture by use Ziehl–Neelsen staining by using PCR for detection *M. tuberculosis complex* [3, 7, 19].

10.6.1.5 A Rapid Biomarker-Based Nontissue-Based Test

The accuracy of tools for immunological diagnosis of tuberculosis, using two mycobacterial proteins—culture filtrate protein-10 and early secretory antigenic target-6—has been evaluated [20]. With high sensitivity and specificity, the enzyme-linked immunospot (ELISPOT) assay, using CFP10/ESAT6 fusion protein as an antigen, is an effective technique for auxiliary diagnosis of STB [20]. These immunodiagnostic tests, the whole-blood interferon-g (IFN-g) enzyme-linked immunosorbent assay QuantiFERON-TB Gold (Cellestis Ltd., Chadstone, VIC, Australia), and the enzyme-linked immunospot assay T-SPOT.TB (Oxford Immunotec, Oxford, UK), can quantitatively measure IFN-g production by lymphocytes specific to *M. tuberculosis*–specific immunodominant antigens, which are encoded by the RD1 region of the pathogen. Another commercially available IFN-g release assay (IGRA), the QuantiFERON-TB Gold in-tube assay (QFTGIT) (Cellestis Ltd.), is able to measure IFN-g production specific to the immunodominant TB antigens early secretary antigenic target-6 and culture filtrate protein-10 [7].

10.6.1.6 Imaging Diagnosis

Spinal TB commonly manifests as tuberculous meningitis (TBM) and rarely as intramedullary tuberculoma [9]. However, plain radiography is performed initially in patients suspected to have STB, and plain radiograph images show a birds-nest appearance characteristic of an aneurysmal phenomenon [21].

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) abnormalities include spinal lesions that originate from the vertebral endplate, involve the anterior vertebral body corner, show evidence of subligamentous spread, exhibit multiple vertebral bodies but preserved disks, and show extensive paraspinal abscess formation, abscess calcification, and vertebral destruction or vertebral body collapse [9, 21].

In addition, there is extensive paraspinal abscess formation and abscess calcification [9]. CT is more effective for defining the shape and calcification of soft tissue abscesses than plain radiography, because CT provides much better visualization of the bony details of irregular lytic lesions, sclerosis, disk collapse, and disruption of bone circumference.

For radiolucent lesions to be visible on plain radiographic images, there must be 30% bone mineral loss [15].

Positron emission tomography (PET) can be useful in differentiating between STB and other pyogenic spondylitis [22]. However, MRI can be used for early detection of STB, which can reduce the complications of STB. A confirmatory diagnosis can be made only on the basis of biopsy or culture results [9].

10.7 Classification of Spinal Tuberculosis

Kumar introduced a four-point classification for posterior STB, based on the site of involvement and the stages of the disease [23]. One of the most important limitations attributed to this classification system is that it includes only posterior STB, which is relatively rare.

Mehta and Bhojraj introduced a new classification system for STB, using MRI findings. They classified patients into four groups according to the surgical technique employed. Group A consisted of patients with stable anterior lesions and no kyphotic deformity. Group B consisted of patients with global lesions, kyphosis, and instability. Group C patients had anterior or global lesions along with a high operative risk for transthoracic surgery, due to medical comorbidities and probable anesthetic complications. Finally, group D patients had isolated posterior lesions that needed only posterior decompression [23, 24]. This classification categorizes only thoracic lesions, which is the most important limitation of this system [13].

10.8 Treatment

Antituberculosis drugs have a main role in the recovery and response of patients with STB [25]. The efficacy of these drugs has been shown in several studies of STB treatment in the absence of a neurological deficit, instability, and deformity,

regardless of the presence of a paravertebral abscess [26]. Adequate and early pharmacological treatment can prevent severe complications [27]. A combination of rifampicin, isoniazid, ethambutol, and pyrazinamide for 2 months, followed by a combination of rifampicin and isoniazid for a total period of 6, 9, 12, or 18 months, is the protocol most frequently used for treatment of STB [17, 26, 27]. Short-course chemotherapy regimens have been demonstrated to have excellent results except in patients younger than 15 years and those with an initial angle of kyphosis of more than 30 degrees and whose kyphosis increases substantially [28]. Patients who receive medical management alone may receive CT-guided drainage of the target lesions [7].

Multidrug-resistant TB is defined as an organism that is resistant to rifampicin and isoniazid [25]. Such resistance is detected if there is a lack of clinical or radiological improvement, development of a new lesion or a cold abscess, or an increase in bone destruction despite medical treatment for 3–5 months [25]. Multidrug-resistant TB is a global concern; it is encountered in 3% of all new cases and in 12% of retreatment cases [13]. The recommended treatment for multidrug-resistant TB is an average of six anti-TB drugs for at least 24 months [29]. The most recent World Health Organization (WHO) guidelines recommend use of five drugs that are expected to be effective in the initial intensive phase and four drugs that are likely to be effective in the continuation phase. The duration of the initial phase is 6–9 months, and the total treatment period is 20–24 months [29]. Close monitoring of patients for development of adverse reactions is necessary [25, 29].

10.8.1 Surgical Treatment

The neurological status at the time of presentation is a critical factor for treatment decision making and patient outcomes. If the imaging results suggest that STB is present, the decision regarding operative management should be based on assessment of the risk of failure of medical treatment, according to the grading system for spondylodiscitis [30]. Surgery is often required for decompression [31], kyphosis correction, and maintenance of spinal stability [31, 32]. There is controversy as to the ideal surgical approach. An anterior approach allows direct access to the focus of infection, which is helpful for debridement. However, surgery with a single anterior approach could lead to unsatisfactory outcomes in terms of kyphosis correction and maintenance of spinal stability [33]. Surgery with a single posterior approach shows advantages in kyphosis correction and maintenance of spinal stability, but it does not allow complete debridement of an infected lesion in front of the vertebrae [32]. Thus, a combination of anterior debridement/bone grafting and posterior instrumentation, which overcomes the drawbacks of surgery via a single anterior or posterior approach alone, has become a common choice for treatment of STB [32]. With the development of minimal invasive spinal surgery, a technique of posterior percutaneous instrumentation is also employed to enrich the surgical methods of anterior debridement/bone grafting/posterior instrumentation [32].

10.8.2 Prognosis

The determinants of the success or failure of multidrug-resistant TB treatment are (1) progressive clinical improvement at 6 months following chemotherapy; (2) radiological improvement during treatment; (3) disease with *M. tuberculosis* strains that are resistant to use of up to three anti-TB drugs and use of up to four second-line drugs; and (4) no change in the drug regimen during treatment [29].

Some prognostic factors need to be defined before surgical intervention. Kyphosis can be defined as the occurrence of a negative Cobb angle, which can appear at the lumbar level on the basis of bone destruction. With regard to the physiological spinal curve, the lumbar vertebrae maintain a lordotic curve, with a Cobb angle range of 30–50°. In 137 cases with kyphosis caused by STB, the lordotic curve of lumbar vertebraeSpinal tuberculosis (STB)prognosis became kyphotic and the Cobb angle changed to a negative value as a result of bone destruction [30]. Yao et al. [34] identified nonparalysis, a shorter symptom duration, fewer involved vertebrae, and percutaneous instrumentation as favorable prognostic factors for recovery postoperatively. In the early postoperative stages (1–3 months), patients treated with percutaneous instrumentation achieved higher Japanese Orthopedic Association (JOA) scores than those treated with open instrumentation, but no significant difference in JOA scores was observed in the longer term (6–24 months). Moreover, the patients treated with percutaneous instrumentation had a shorter operation time.

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