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## Spinal Tuberculosis: A Major Public Health Hazard in Isfahan

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**Abstract:** The purpose of this study is to review of spinal tuberculosis in three hospitals in Isfahan of Iran. We carried out a cross sectional study of 630 patients with tuberculosis and identified 100 patients with spinal involvement in the three hospitals. Tuberculosis was diagnosed based on one of a compatible clinical picture. A radiographic study of the spine with suspicious signs and skin tested were performed for each patient. Demographic data, sign, symptoms and site of spinal involvement were recorded. In all patients, a chest X ray and sputum smear and culture was performed for ruling out of pulmonary tuberculosis. Out of the 100 patients with spinal tuberculosis, 58% were male and 42% were female. Main symptoms were spinal deformity, local tenderness and neurologic deficits. Fever and constitutional symptoms were in 80% of cases. Only 68% had a positive tuberculin skin test. Three percent involvement were the upper thoracic spine, 23% the lower thoracic spine, 69% also the lower thoracic, T12 and upper lumbar spines, (thoracolumbar) and 5% the cervical spine. 40 cases underwent bone biopsy that 25% had a positive smear, whereas 62.5% had a positive culture. Histologic findings suggestive of tuberculosis involvement of the bone were found in 37 of the 40 biopsies. The most common age for spinal involvement were 20-40 years ( $p < 0.05$ ). Spinal tuberculosis may be missed in patients with no evidence of pulmonary. No pathognomonic imaging signs allow tuberculosis to be readily distinguished from other conditions. In this here, we discuss about clinical and histopathological findings in patients with spinal tuberculosis.

**Key words:** Isfahan, potts disease, spinal tuberculosis

### INTRODUCTION

Tuberculosis, caused by *Mycobacterium tuberculosis*, remains a major public health hazard, especially in developing countries in which poverty, malnutrition and the presence of drug-resistant strains have combined to aid the spread of the disease. Infection with HIV increases the risk of reactivation of dormant tuberculosis and the risk of acquiring the primary infection. In those, co infected, a high frequency of extra pulmonary disease has been observed (Bureau and Cardinal, 2001; Moore and Rafii, 2001; Bono, 2006). In developed countries, tuberculosis has been reduced in the past 30 years, as a consequence of a precocious diagnosis and mostly with anti-bacillary therapeutics (Almeida, 2005). Despite the reduction in the prevalence of tuberculosis since the advent of antituberculous drugs, the incidence of extrapulmonary tuberculosis continues to increase in industrialized countries. Osteoarticular tuberculosis represents between 3 and 5% of all cases of tuberculosis and between 10 and 15% of extrapulmonary forms (Le Page *et al.*, 2006). Spinal tuberculosis may be

missed in patients with no evidence of pulmonary tuberculosis (Schlesinger *et al.*, 2005). Spinal TB results in significant potential morbidity and mortality and delay in diagnosis is associated with increased frequency and severity of complications (Jain, 2002).

Tuberculosis of the spine (Pott disease) has plagued humankind since ancient times. Skeletal lesions of Pott disease have been found in 5000-year-old Egyptian mummies (Derry, 1938). Vertebral tuberculosis is the commonest form of the skeletal tuberculosis (Tuli, 1997; Sankaran, 1993; Hopewell, 1995; Sridhar, 1995). It accounts for more than 50% of musculoskeletal tuberculosis (Hodgson *et al.*, 1967). It is most common during the first three decades, though the disease may occur at any age between 1 to 80 years (Tuli, 1997). Most commonly, it affects the thoracic and thoraco-lumbar spine (Tuli, 1997; Sankaran, 1993; Sridhar, 1995). TB of cervical spine is most common in children. The clinical manifestations of Pott's spine are protean. The patient of Pott's spine under discussion was admitted with an extremely uncommon clinical finding of gluteal abscess (Tuli, 1997). In the developed countries, musculoskeletal

tuberculosis is uncommon, but its incidence is reported to be greater in older individuals (Moore and Rafii, 2001). Spinal tuberculosis is usually a secondary infection from a primary site in the lung or genitourinary system. Spread to the spine is thought to be hematogenous in most instances. Tuberculosis infection is characterized by a delayed hypersensitivity immune reaction. Typically, the infection begins in the anterior aspect of the vertebral body adjacent to the disk. The infection then spreads to the adjacent vertebral bodies under the longitudinal ligaments. Noncontiguous (skip) lesions are also occasionally seen (Davidson and Horowitz, 1970; Shivaram, 1985). The most frequent site of spinal tuberculosis is the thoracolumbar junction the incidence decreases above and below this level. Therefore, any segment of the spine can be involved. The relative rarity and varied presentations of spinal tuberculosis pose diagnostic difficulty, warranting its inclusion in the differential diagnosis of any spinal disorder (Davidson and Horowitz, 1970). However, immigration, an aging population and the association of spinal tuberculosis with HIV infection can be expected to increase its prevalence. MR imaging is usually performed to evaluate suspected spinal abnormalities and the disease may first be detected when symptomatic patients undergo this examination. The diagnosis of spinal tuberculosis is difficult and it commonly presents at an advanced stage. The management and follow up is complicated by a lack of guidance on the appropriate use and interpretation of spinal magnetic resonance studies (Cormican, 2006). The purpose of our essay is to review of clinical and pathological findings of spinal tuberculosis in Al-Zahra, Kashany and Amin Hospitals in Isfahan of Iran.

## **MATERIALS AND METHODS**

We carried out a cross sectional study of 630 patients with tuberculosis and identified 100 patients with spinal involvement in the three hospitals Medical School in Isfahan (Al-Zahra, Kashany and Amin). Tuberculosis was diagnosed based on one of a compatible clinical picture such as fever, night sweating, chills, malaise, back pain and restriction of movement. A radiographic study of the spine with suspicious signs was performed for each patient.

A diagnosis of spinal tuberculosis for the purpose of this study was defined as a positive culture of *Mycobacterium, Tuberculosis* on the finding of necrotizing or no necrotizing granulomas on histological study of tissue biopsy specimens in symptomatic patients with bone lesions on computed tomography scan or magnetic resonance imaging compatible with tuberculosis

(disc space narrowing, end plate erosions, vertebral collapse, cord compression, para spinal abscess). Additional patients were diagnosed with spinal tuberculosis and were found to have a positive Tuberculin Skin Test (TST) but did not have culture taken on histological studies done. These patients who clinically improved and their bone lesions improved with treatment of tuberculosis. All patients were skin tested using the Mantoux method performed by the intradermal injection of 0/1 mL of purified protein derivative tuberculin containing 5 TU (tuberculin units) into the skin of the forearm. Tuberculin skin tests of 5 mm duration in HIV-seropositive patients were read, as positive and TST 10 mm were positive read as positive in HIV-seronegative patients. All patients underwent magnetic resonance imaging as part of the evaluation for spinal involvement. The most common findings on imaging were bone destruction, disc space narrowing, with and without the presence of cold abscesses in adjacent muscle structures and, less frequently, compression of the spinal cord or cord roots. In all patients demographic data (sex, age), sign, symptoms and site of spinal involvement were recorded. Patients were classified into four age groups: Lower than 20 years as childhood and adolescence, 21-40 years as early adulthood, 41-60 years as middle adulthood and up to 65 years as late adulthood. In all patients, we took a chest x-ray and sputum smear and culture for ruling out of pulmonary tuberculosis. In addition, patients were classified into four subgroups according to type of spinal involvement: cervical (C1-C5), upper thoracic (T1-T5), lower thoracic (T6-T11) and thoracolumbar (T12-L5). The data obtained were analyzed using the Statistical Package for the Social Sciences (SPSS) version 11.5. Chi-squared test were used for multiple comparison. Differences in the p-value of <0.05 were considered significant.

## **RESULTS**

Review of tuberculosis surveillance data revealed that 630 tuberculosis cases were seen in three Medical hospitals in Isfahan. Of that number, we identified 100 cases as tuberculosis involving the spine. Of the 100 patients with spinal tuberculosis, 58% were male and 42% were female. Presenting symptoms included back pain, weakness, loss of appetite, weight loss and numbness with a duration ranging from 2 months to 3 years and main symptoms were spinal deformity, local tenderness and neurologic deficits such as weakness, numbness, gait difficulties (Table 1). Fever and constitutional symptoms were in 80% of cases. Thirty four patients had cord compression and two cases had neurogenic bladder. Only 68% were recorded with a positive tuberculin skin test.

Table 1: Signs and symptoms of spinal tuberculosis in isfahan

Sign and symptom	%
Back pain	99
Constitutional symptoms	80
Pulmonary symptoms	18
Neurologic deficite	34
Spinal deformity	70

The most common findings on imaging were bone destruction, disc space narrowing, with and without the presence of cold abscesses in adjacent muscle structures and, less frequently, compression of the spinal cord or cord roots. Twenty six of 100 cases (26%) involved only thoracic spine; 3 of 26 (11.5%) involved the upper thoracic spine; 23 (89.5%) involved the lower thoracic spine. Sixty nine cases also involved the lower thoracic, T12 and upper lumbar spines, (thoracolumbar); 5 of 100 (5%) involved the cervical spine (Table 2). Twenty of the 100 cases (20%) developed Para spinal abscesses. Only 18% of patients had extra spinal pulmonary involvement. Forty cases underwent bone biopsy with or without biopsy of the Para spinal abscess. Ten of the 40 (25%) biopsies had a positive smear, whereas 25 of 40 (62.5%) of biopsies had a positive culture. Histologic findings suggestive of tuberculosis involvement of the bone revealing granuloma formation, either caseating or noncaseating, were found in 37 of the 40 biopsies. Other patients (60%) were diagnosed with finding in MRI and CT SCAN together with positive tuberculin skin test and response to therapy.

The most commonest age for spinal involvement were 20-40 years ( $p < 0.05$ ). 11 of 100 cases had low than 20 years old, 47 patient in 20-40 years, 27 in 41-60 and 15 had up to 60 years. There were no differences between age and site of spinal involvements (Table 2). From 58 male patients 3 cases (5.2%) had cervical involvement, 3 cases (5.2%) upper thoracic, 12 cases (20.6%) lower thoracic and 40 patients (69%) had thoracolumbar involvement. From 42 female patients two cases (4.8%) had cervical involvement, 11 cases (26.2%) lower thoracic and 29 patients (69%) had thoracolumbar involvement. No patients had upper thoracic involvement (Table 3). There were no differences between sex and site of spinal involvement. All patients were managed with standard anti tuberculosis therapy consisting of Isoniazid, Rifampin, Pyrazinamide and Ethambutol during the initial 8-week intensive phase, followed by discontinuation of the Pyrazinamide and Ethambutol and continuation of the Isoniazid and Rifampin during the continuation phase of treatment. Therapy was given for an average of 12 months. In 50% cases with severe back pain or neurologic deficits suggestive of epidural or canal compression, adjunctive surgical therapy was used. Eleven percent of cases had serious complications, neurologic residuals and permanent kyphosis occurred secondary to therapy.

Table 2: Site of spinal involvement in tuberculosis in different age in Isfahan

Site of infection	Age				Total
	<20	20-40	40-60	>60	
Cervical	1	2	0	2	5
Upper thoracic	0	3	0	0	3
Lower thoracic	1	8	8	6	23
Thoraco lumbar	9	34	19	7	69
Total	11	47	27	15	100

Table 3: Site of spinal involvement in tuberculosis in different sex in isfahan

Site of infection	Sex	
	Male	Female
Cervical	3	2
Upper thoracic	3	0
Lower thoracic	12	11
Thoraco lumbar	40	29
Total	68	42

## DISCUSSION

Spinal tuberculosis may be missed in patients with no evidence of pulmonary. Vertebral tuberculosis is the commonest form of skeletal tuberculosis comprising about 50-70% of all bone and joint tuberculosis (Kumar and Chandra, 2003).

Davidson and Shivaram reported that the median age of patients with spinal tuberculosis was 39 years (Davidson and Horowitz, 1970; Shivaram, 1985). This is similar to the findings in our study (20-40 years old). Spinal tuberculosis is characteristically chronic and slowly progressive. Presenting symptoms are usually back and neck pain or pain at the site of involvement. Pain was noted in a majority (99%) of our patients. Neurologic deficits such as weakness, numbness, gait difficulties and incontinence occur less frequently (Tuli, 1997; Sankaran, 1993; Kumar and Chandra, 2003; Lippincott and Wilkins, 2005). However, were noted in 34% of our cases because of delayed diagnosis. Unlike pulmonary tuberculosis, which may present with a constellation of symptoms, including cough, weight loss, fever and night sweats, if tuberculosis only involves bone pain, it may be the only symptom. Fever, weight loss and night sweats, were reported in 80% of patients. Because of the nonspecific nature of the symptoms of spinal tuberculosis, a high index of suspicion is important in establishing the diagnosis of destructive spinal lesions. In spinal tuberculosis, different vertebral sites may be involved as seen in our cohort Tuberculosis of the spine has the following distribution-thoracic 42%, lumbar 26%, thoracolumbar and cervical each 12%, cervicodorsal 5% and lumbosacral 3% (Tuli, 1997). Involvement of the thoracic spine was reported in 50%, cervical spine in 25% and lumbar spine in 25% (Lippincott and Wilkins, 2005; Bloch *et al.*, 1989). This generally parallels present finding that most tuberculosis of the spine

involves the thoracic (26%) and thoracolumbar (69%) vertebrae. Simultaneous involvement of multiple sites in the spine was infrequent. Radiographically, the obliteration of the disc space was a common finding. The lesion in the spine is most often paradiscal in location with destruction of the disc, reduction of the disc space and concomitant destruction of the vertebral bodies on either side of disc space (Tuli, 1997; Sankaran, 1993). Tuli reported clinically palpable cold abscess in 20% cases and radiologically visible perivertebral abscess in 21% cases of Pott's spine (Tuli, 1997). That was lower than present study (30%).

A normal chest x-ray does not exclude the diagnosis of tuberculosis. Only one third of patients presenting with tuberculosis of the bone have a history of pulmonary disease (Sridhar, 1996; Daniel and DeBanne, 1987). Lippincott and coworker reported that 50% of spinal tuberculosis had pulmonary involvement (Lippincott and Wilkins, 2005). In our patient population, only 18% had pulmonary tuberculosis.

In evaluating a patient with a destructive spinal lesion, there should be a heightened sense of suspicion for spinal tuberculosis. This is particularly important if the patient has one or more risk factors. A positive tuberculosis skin test provides supporting evidence but by itself does not confirm the diagnosis. Over 90% of immunocompetent patients with skeletal TB have a positive intermediate strength tuberculin skin test (Berney *et al.*, 2002). We saw 68% PPD positive test. A Para spinal abscess (seen in eight of our patients) associated with the presence of pulmonary tuberculosis (seen in 15% of our patients) strongly suggests a diagnosis of spinal tuberculosis (Watts and Lives, 1996). Delay in diagnosis can be catastrophic in vertebral tuberculosis. The extension of disease process can cause compression of the spinal cord leading to severe and irreversible neurologic sequel including paraplegia (Hopewell, 1995). Ultimately, a bone biopsy with or without biopsy of the Para spinal abscess confirmed the diagnosis. All patients should be started on an appropriate treatment regimen when spinal tuberculosis is suspected. The most commonly used treatment is a regimen containing 5 mg kg<sup>-1</sup> Isoniazid per day, 10 mg kg<sup>-1</sup> Rifampin per day, 20 to 25 mg kg<sup>-1</sup> Pyrazinamide per day and 15 mg kg<sup>-1</sup> Ethambutol per day (Blumberg, 2003). Therapy should be continued for duration of 6 to 9 months. In all cases with severe back pain or neurologic deficits suggestive of epidural or cord compression, adjunctive surgical therapy may be necessary (Lippincott and Wilkins, 2005) but 50% of our cases needed surgery.

The differential diagnosis of the tuberculosis of spine includes pyogenic and fungal infections, sarcoidosis, metastasis and lymphoma. No pathognomonic imaging signs allow tuberculosis to be readily distinguished from other conditions. Typically, infectious spondylitis is characterized by involvement of the intervertebral disk. A history of chronicity and slow progression is suggestive of tuberculosis. Moreover, inflammatory collections tend to be larger in tuberculosis than in pyogenic spondylitis. In the central and posterior element forms of tuberculosis, only biopsy can achieve a provide diagnosis (Sankaran, 1993).

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