



Original Article

Spinal Tuberculosis in Non-HIV-Infected Patients: 10 Year Experience of a Medical Center in Central Taiwan

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BACKGROUND/PURPOSE: Tuberculosis (TB) is an endemic disease in Taiwan and it usually affects the lung. Spinal TB accounts for 1–3% of all TB infections. The purpose of this study was to investigate the clinical manifestations, management, outcomes and drug susceptibility of *Mycobacterium tuberculosis* in non-HIV-infected patients with spinal TB.

METHODS: From January 1998 to December 2007, we retrospectively reviewed the medical charts of adult patients with a diagnosis of spinal TB. Only those with positive culture results and/or characteristic pathologic findings were enrolled. Demographic data, clinical manifestations and susceptibility to anti-TB drugs were reviewed and analyzed.

RESULTS: During the study period, 38 patients (23 men, 15 women) with spinal TB were identified and the mean age was 68 years. The median duration of symptoms was 60 days (range, 3–720 days). Amongst the 38 patients, back pain (100%) was the most common clinical symptom, followed by weakness (53%) and numbness (26%). The lumbar spine (15 patients, 39%) was the most commonly involved site, followed by the thoracic spine (14 patients, 37%). Concomitant pulmonary TB was found in 12 patients (32%). Three patients (8%) had concurrent bacterial or fungal infections. Almost all of the patients (35 patients, 92%) were successfully treated with surgery and anti-TB medications. The erythrocyte sedimentation rate was followed up in 16 patients before and after therapy and a significant decline was observed after treatment ($p=0.004$). No mortality was related to spinal TB.

CONCLUSION: Insidious clinical course and ambiguous manifestations of spinal TB often delay and hinder the accuracy of diagnosis of spinal TB. In addition to pyogenic osteomyelitis, spinal TB should be

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included in the differential diagnosis especially in elderly patients with chronic back pain accompanied by elevated erythrocyte sedimentation rate, and those living in the TB endemic area.

KEYWORDS: drug resistance, osteomyelitis, treatment outcome, tuberculosis

Introduction

Tuberculosis (TB) is an emerging international problem despite advances in the methods of diagnosis and treatment. The resurgence of TB can be expected to be associated with a concomitant increase in the incidence of extra-pulmonary TB, including Pott's disease.¹⁻³ There are a number of publications regarding spinal TB in other countries,^{4,5} but in Taiwan only a few studies on spinal TB have been conducted, and most of them focused on the image features of diagnosis.^{6,7} The clinical characteristics of adult spinal TB have never been thoroughly reviewed in Taiwan. Hence, the purpose of this 10-year retrospective study was to characterize the clinical manifestations, microbiological features and the treatment outcome of patients with spinal TB.

Methods

Patients

We retrospectively reviewed the medical charts of all patients diagnosed with spinal TB at China Medical University Hospital, Taichung, Taiwan from January 1998 to December 2007. All enrolled patients were adults (≥ 18 -years-old), and non-HIV infected. Spinal TB was diagnosed when the following criteria were met: (1) presence of osteomyelitis at one or more vertebral segment; (2) presence of *Mycobacterium tuberculosis* isolated from the abscess of a tissue biopsy specimen; and (3) histology of tissue specimen demonstrating caseating granuloma or granulomatous inflammation with positive acid-fast bacillus smear. Patients who fulfilled criterion (1) and criterion (2) or (3) were included in this study. Probable cases that we could not confirm microbiologically or pathologically but responded to anti-TB therapy were excluded. Patients' demographic data, underlying diseases, duration of symptoms, laboratory results, radiographic findings, culture results, histopathologic findings, treatment regimen and clinical outcomes were reviewed and analyzed.

Laboratory methods

Various culture and identification systems were used during this study period. Before 1998, Lowenstein-Jensen medium (Becton Dickinson, Sparks, MD, USA) was used for TB identification based on traditional biochemical reactions (nitrate reduction and niacin test). In 1999, the BACTEC MGIT 960 system (Becton Dickinson) was introduced, then clinical specimens were processed and the centrifuged sediment was inoculated in Lowenstein-Jensen medium (Becton Dickinson) and Middlebrook 7H9 broth (Becton Dickinson). The cultures were incubated at 35°C in 5% CO₂ for up to 8 weeks. The identification of TB was based on morphology and biochemical reactions. In 2004, the Protec ET system (Becton Dickinson) replaced the traditional biochemistry reaction methods of TB identification. Once growth was detected, the *M. tuberculosis* complex was confirmed by the Protec ET system and drug susceptibility subsequently performed.⁸

Statistical analysis

Statistical Package for the Social Sciences version 13.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Data were presented as mean \pm standard deviation (median value for data not distributed normally). We used paired *t* tests to examine differences between laboratory data before and during treatment. Qualitative variables were compared using Fisher's exact test. A *p* value < 0.05 was considered statistically significant.

Results

Clinical and laboratory data

During this 10-year period, 3,240 pulmonary TB and 404 extra-pulmonary TB cases were diagnosed. Among the extra-pulmonary TB cases, 38 patients (23 men, 15 women) with spinal TB were identified, and the mean age of all patients was 68 years (3 patients were younger than 50 years). The majority of patients ($> 50\%$) were older than 65 (Table 1).

The median duration of symptoms before diagnosis was 60 days (range, 3–720 days). Nine patients (24%) had no specific underlying diseases, and 29 patients (76%) had comorbidities as described in Table 1. Two patients had a previous history of pulmonary TB. Another two patients with chronic obstructive pulmonary disease and systemic lupus erythematosus received long-term corticosteroid therapy before the diagnosis of spinal TB. At the time of diagnosis, nine patients (24%) had constitutional symptoms. Twelve patients (32%) had concomitant pulmonary TB. Four cases had other extra-pulmonary site involvement, including pleurae (3 cases) and liver (1 case). Back pain was

the most common clinical complaint (38 patients, 100%), followed by weakness (20 patients, 53%) and numbness (10 patients, 26%). The mean value of C-reactive protein (CRP) level at presentation was 4.25 mg/L. In addition, most patients (89%) had elevated erythrocyte sedimentation rate (ESR; > 20 mm/hr) with an average ESR value of 62 mm/hr. Sixteen patients had serial ESR follow-up data, with a mean follow up of 10.8 months. A significant decline in ESR value was found between the pre- and post-treatment ESR values (pre-treatment mean ESR=64 mm/hr, post-treatment mean ESR=31 mm/hr; $p=0.004$).

Table 1. Demographic characteristics, clinical symptoms/signs and initial laboratory finding of 38 spinal tuberculosis patients^a

Characteristics	Value
Age (yr)	68 (36–86)
Age distribution (yr)	
< 65	12 (32)
≥ 65	26 (68)
Sex, M/F	23/15
Comorbidities, <i>n</i>	
Hypertension	16
Diabetes mellitus	7
Chronic kidney disease	7
Cardiovascular disease	5
Hepatitis B/hepatitis C	3/3
Others ^b	4
Duration of symptoms (d)	99 (3–720)
Clinical symptoms and signs	
Pain	38 (100)
Weakness	20 (53)
Numbness	10 (26)
Fever	6 (16)
Constitutional symptoms	3 (8)
Hematological and biochemical data	
Leukocyte count (cells/μL)	8,521 ± 3,403
Hemoglobin (g/dL)	12.1 ± 2.3
ESR (mm/hr)	62 ± 31
C-reactive protein (mg/L)	4.25 ± 4.21

^aData presented as mean (range), *n* (%) or mean ± standard deviation;

^bothers included chronic obstructive pulmonary disease, Systemic Lupus Erythematosus, malignancy (gastric cancer), and Gouty arthritis. ESR=erythrocyte sedimentation rate.

Image findings

Image findings are summarized in Table 2. Magnetic resonance imaging (MRI) was the most frequently used imaging modality in evaluating spinal lesions (35 patients, 92%); ten (26%) of these patients also received osteomyelitis scans, and the results demonstrated comparable findings to MRI. The lumbar spine was the most commonly involved site (15 patients, 39%) and the cervical spine was less commonly involved. The numbers of vertebral bodies involved per patient ranged between two and five (mean=3.5). One-third of patients had ≥ 3 vertebral bodies involved. Additionally,

Table 2. Imaging characteristics of 38 spinal tuberculosis patients^a

	<i>n</i> (%)
Location	
Cervical	1 (2)
Thoracic	14 (37)
Thoracolumbar	3 (8)
Lumbar	15 (39)
Lumbosacral	4 (11)
Skipped lesion (T, L)	1 (2)
Vertebra involved	
2	26 (68)
3	8 (21)
4	1 (2)
5	3 (8)
Imaging findings	
Disc space involvement	32 (84)
Paraspinal abscess	19 (50)
Epidural compression	27 (71)

^aData presented as *n* (%).

more than half of the patients had disc space involvement, epidural compression or paraspinal abscesses.

Diagnostic methods and microbiological findings

The majority of patients (32 patients, 84%) were subjected to surgery and the remainder of the patients underwent either computed tomography (CT)-guided needle biopsy or CT-guided drainage. The overall sensitivity for biopsies, including surgical and CT-guided biopsy was 84% (32/38) for granulomas, 58% (22/38) for the acid-fast bacillus smear on Ziehl-Neelsen's stain and 63% (24/38) for TB culture. There was no significant difference between each technique (Table 3).

Of the 24 *M. tuberculosis* isolates from the clinical specimens, 18 (75%) were susceptible to first-line anti-TB drugs including isoniazid (INH), rifampicin, ethambutol, pyrazinamide and streptomycin. Three patients (13%) were resistant to INH, one was resistant to streptomycin and another was resistant to both INH and rifampicin.

Treatment and outcomes

Among the 38 patients, 32 (84%) received surgical intervention combined with medical treatment. Surgical intervention was chosen for patients who had symptoms of epidural compression or joint instability problems. Three patients had co-infection with other microorganisms, including *Propionibacterium*, methicillin-sensitive *Staphylococcus aureus* and *Candida parapsilosis*; all of these patients received appropriate antibiotic treatment. Only four patients received medical anti-TB therapy alone due to a less extensive disease state. The choice of therapeutic regimens was based on the recommendations proposed by the American Thoracic Society, the Centers for Disease Control and Prevention, and the Infectious Diseases Society of America.⁹ The median treatment duration was 11 months (range, 6–32 months).

Thirty-four patients were followed up after completion of anti-TB treatment, and the Frankel Scale system¹⁰ was used to evaluate the functional recovery of these patients. Most patients (24 patients, 71%) were classified on the Frankel scale as D and E (Table 4), which meant that they had nearly complete recovery without motor or sensory deficit in daily activities. One patient was lost to follow up and four patients died during treatment. The cause of death in these four cases was not related to spinal TB itself, and no relapse was reported during follow up (mean duration = 10.6 months).

Discussion

Spinal TB was first described in 1782 by Sir Percival Pott.¹¹ It accounts for 50% of skeletal TB,^{12,13} and 1–3% of all TB cases.^{14–16} In our institution, spinal TB made up 1% (38/3,644) of all TB cases. Unlike other reports,^{17,18} our subjects were elderly, with 55% of patients over the age of 70 years. In other countries, the average life expectancy for the general population is shorter than in Taiwan.¹⁷ Similar to other

Table 4. Neurological grades, Frankel scale

	Definition	n (%)
A	Complete motor and sensory loss below the lesion	5 (14.7)
B	Incomplete, some sensory loss below the lesion	3 (8.8)
C	Incomplete, motor and sensory sparing, but the patient is not functional	2 (5.8)
D	Incomplete, motor and sensory sparing, but patient can stand and walk	19 (55.9)
E	Normal, complete functional recovery	5 (14.7)
Total		34 (100)

Table 3. Yield of computed tomography-guided biopsy/drainage and surgical biopsy for the diagnosis of spinal tuberculosis^a

	CT guided biopsy/drainage (n=6)	Surgical biopsy (n=32)	Total (n=38)	p ^b
Positive granuloma	6 (100)	26 (81)	32 (84)	1.000
Positive AFB smear	4 (67)	18 (56)	22 (58)	1.000
Positive culture	4 (67)	20 (63)	24 (63)	1.000

^aData presented as n (%); ^bFisher's exact test. CT=computed tomography; AFB=acid-fast bacillus.

studies,^{4,17} back pain was the most commonly presented symptom, followed by weakness and numbness. Unlike pulmonary TB, spinal TB is seldom accompanied with symptoms such as fever, body weight loss or night sweating,⁴ and this was clearly demonstrated in our study. Considerable variation in the duration of symptoms¹⁹ was also observed in the present study, and this may be due to the insidious clinical course and nonspecific manifestations of spinal TB.^{4,19} Analogous to other reports,^{20,21} the percentage of combined spinal and pulmonary TB was 32% in this study. Similar to the results of Pertuiset et al,¹⁸ the thoracic and lumbar spines were nearly equally affected and contributed 76% of the spinal regions.

In contrast to the report by Schlesinger et al,⁴ our patients had a more extensive disease state with paraspinal abscess and epidural compression. The different severity levels between the present and previous study⁴ may be due to the presence of nonspecific symptoms of spinal TB in the elderly, and a delay in diagnosis. In this population, degenerative joint disease or inflammatory changes were usually considered to be the causes of back pain and this may delay early and accurate diagnosis of spinal TB.²²

MRI and CT are still the most useful modes for detecting spinal lesions, especially MRI, which has good sensitivity and specificity,^{23,24} a total of 92% of our patients were diagnosed by MRI. Ten patients in this study received osteomyelitis scans and all the results were comparable to MRI findings, which is similar to the results from a prior study.²⁵ Osteomyelitis scans can provide a less expensive method, and assist with localizing the lesions in the diagnostic work-up.

Compared with other studies,¹⁸ more patients in this study received surgical intervention (32 patients, 84%). Although our patients were elderly and had relatively extensive diseases, most of them recovered well postoperatively and no surgical mortality was recorded during a 10-month follow-up. Images, clinical symptoms, ESR and CRP are the most commonly used parameters to follow up the therapeutic response of osteomyelitis.²⁶ In addition to the image studies and clinical symptoms, ESR was followed serially in 42% of our patients before and after treatment. There was a significant decline in the ESR value after adequate management. Similar to other authors' observation,²² CRP level was not initially elevated in our study, and the role of this parameter in following up the therapeutic response

of osteomyelitis remains to be defined.^{26,27} Therefore, comparison with CRP, ESR may provide clinicians more useful information in evaluating the treatment response of spinal TB.

It is interesting to note that 8% of the patients had co-infection with other pathogens, a finding which is infrequently reported in other articles.¹⁵ This phenomenon should remind clinicians that if the treatment response is not as expected, poor compliance to treatment, drug resistance, inadequate debridement and/or co-infection with other pathogens should be considered.

In conclusion, in elderly patients with chronic back pain and elevated ESR, spinal TB should be included in the differential diagnosis. Early diagnosis with less invasive modalities, such as CT-guided biopsy may reduce the patient's morbidity and improve the quality of life in these patients.

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