ORIGINAL ARTICLE

AN ANALYSIS OF CLINICO-RADIOLOGICAL AND HISTOPATHOLOGICAL CORRELATION IN TUBERCULOSIS OF SPINE

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ABSTRACT

Background: In the recent past, the use of computerized axial tomography and magnetic resonance imaging has helped to differentiate spinal tuberculosis from radiologically similar lesions.

Objective: The objectives of the study was to assess how dependable clinical and radiological features are in establishing a diagnosis of spinal tuberculosis; and to identify other conditions which may have clinical and radiological features similar to those seen in patients with spinal tuberculosis.

Methodology: Two hundred and sixty-seven consecutive patients with clinical and radiological features suggestive of tuberculosis of the spine treated over a period of five years were analysed. This retrospective case series analysis was done in a tertiary care hospital. The clinical presentation, radiological features and the erythrocyte sedimentation rate were correlated with the histopathological diagnosis on tissue obtained by open biopsy in 130 cases during surgery and in 137 cases by closed vertebral biopsy.

Results: One hundred sixty-six cases were histologically proved as tuberculosis and 74 proved to be non-tuberculous lesions. Twenty-seven cases in which the biopsy was inconclusive were excluded from the study. The study demonstrated that tuberculous lesions were commoner in younger patients and the lesion was more often in the paradiscal region as compared to non-tuberculous lesions. However, all other clinical and radiological variables were not significantly different to enable reliable identification of tuberculous lesions on the basis of clinical and radiological features alone.

Conclusion: It is recommended that all vertebral lesions suspected to be of tuberculous origin not responding to empirical antituberculosis therapy should have a definitive histopathological diagnosis and radiological investigation to facilitate appropriate treatment.

Keywords: Spinal tuberculosis, non-tuberculous lesions, diagnostic criteria

INTRODUCTION

In the recent past, the use of computerized axial tomography and magnetic resonance imaging has helped to differentiate spinal tuberculosis from radiologically similar lesions. These imaging techniques have also helped in early detection of this lesions.[1-3] In less developed countries, routine access to these imaging modalities is limited and hence the clinical and plain radiological features remain the main-stay in the diagnosis of tuberculosis of the spine.[4]

The inherent risk of relying on clinical signs and plain radiography alone is that more sinister lesions could be mistaken for tuberculosis and treated inappropriately, leading to irreversible complications.

Since there is a paucity of reports[5] of the frequency of lesions that mimic spinal tuberculosis, this study was undertaken to: (1) Assess how dependable clinical and radiological features are in establishing a diagnosis of spinal tuberculosis and to (2) identify other conditions which may have clinical and radiological features similar to those seen in patients with spinal tuberculosis.

MATERIALS AND METHODS

Two hundred and sixty-seven patients who presented with clinical and radiological features suggestive of spinal tuberculosis over a period of 5 years formed the basis of this study. A detailed history regarding the presenting symptoms and their onset was obtained. Back pain being one of the most important complaints, its onset, aggravating factors, radiation and other characteristics were noted. In patients having fever (whether low grade or high grade), any diurnal variation (viz, evening rise of temperature) and its association with sweating was recorded. Any history of significant weight loss accompanied with loss of appetite was noted.

A careful clinical examination of the spine was carried out to record the deformity of the spine, site of maximal tenderness and paraspinal muscle spasm. Systemic and per abdominal examination was done to rule out other focus and cold abscess. A tentative diagnosis of spinal tuberculosis was made if, at least one each of the following clinical and radiological features were present.

(A) Clinical features: (i) Fever; (ii) back pain; (iii) neurological deficit.

(B) Radiological features: (i) Localized osteoporosis; (ii) vertebral lesions with or without paravertebral shadows: (iii) destruction of a vertebral body or its appendages.

If neurological deficit was demonstrated, the extent of neurological deficit was classified into four grades[6]:

(a) Grade I (negligible), the patient is unaware of neural deficit but the clinician detects spasticity, ankle clonus and/or a plantar extensor response.

(b) Grade II (mild), the patient has obvious spasticity and motor deficit but is able to walk with or without support.

(c) Grade III (moderate), the patient has spastic paraplegia or quadriplegia in extension with sensory deficit less than 50% and is bed-ridden.

(d) Grade IV (severe), paraplegia or quadriplegia with sensory deficit more than 50% and/or flexor spasm, flaccid paraplegia or quadriplegia, and/or bladder or bowel involvement.

All the patients had hematological investigations, which included a hemogram and erythrocyte sedimentation rate. Standard antero-posterior and lateral radiographs of the entire spine was taken. Tissue for histopathological diagnosis was obtained in all cases. Because of the length of the time taken to culture mycobacteria and the uncertainty of demonstrating acid-fast bacilli in paucibacillary spinal tuberculosis, histo-pathological diagnosis was taken as the confirmatory criterion for starting the antituberculous treatmen.[4,7-11] Tissue was obtained by closed vertebral biopsy in 137 patients with negligible or no neurological involvement and minimal pain. In the remaining cases, tissue was obtained by open biopsy at the time of surgery.

The material was also sent for culture and sensitivity. Culture reports were obtained only in 93 cases, after an average period of 9.7 weeks. Patients above the age of 40 years were also investigated for multiple myeloma which included total serum protein estimation with albumin/globulin ratio; serum alkaline phosphatase, calcium and phosphorous levels, protein electrophoresis and screening for Bence-Jones proteins in the urine. The confirmation or exclusion of myeloma was by bone marrow examination. Lesions identified on plain radiography were classified as central, paradiscal, anterior or posterior. When more than two contiguous vertebrae were involved, the lesions were termed as "multiple lesions, whereas when one or more normal vertebrae were present in between two lesions, they were termed as "skip lesions.

Additional radiological investigations were done in 96 cases. This included computerized tomography (CT) in 58 cases, magnetic resonance imaging (MRI) in 23 cases (Fig 1), myelogram in 15 cases, and isotope bone scans in 44 cases. Six patients had no identifiable vertebral lesion on plain radiographs but definite abnormalities were detected on the bone scan. These patients underwent CT or MRI scans and closed vertebral biopsy. Myelograms, CT scans and MRI scans were done in cases with demonstrable neurological deficit. All patients with a confirmed diagnosis of tuberculosis were treated with four drugs for 3 months (intensive phase) followed by two drugs for 9 months (continuation phase). Patients with non-tuberculous lesions were treated appropriately based on the histological diagnosis.

All patients were followed up for a minimum of two years. The patients in whom the histopathological diagnosis was inconclusive were either treated as tuberculosis or kept under observation for two years. These patients were excluded from the analysis. Univariate analysis for the categorical variables was done by Chi-square test and for continuous variables by the t-test. Multiple logistic regression was applied to identify the independent clinical and radiological variables that supported a diagnosis of spinal tuberculosis. A p-value less than 0.05 (two-tailed) were considered as significant.

RESULTS

Out of 267 spinal lesions studied, 166 were of tuberculous origin whereas 74 were established as being non-tuberculous. In 27 patients the histo-pathological examination was inconclusive. Pain was the most common presenting feature among both tuberculous and non-tuberculous lesions. The frequency of pain and other symptoms has been shown in Table 1.

Table 1: Frequency of Clinical Features at the Time of Presentation of Tuberculous and Non-tuberculous Vertebral Lesions

Clinical feature	Non-TB (n= 74)	TB (n=166)
Pain	72 (97.3)	155 (93.4)
Fever with constitutional symptoms	14 (18.9)	108 (65.1)
Tenderness, muscle spasm	65 (87.8)	161 (96.9)
Kyphosis	42 (56.8)	68 (40.9)
Cold abscess	Nil	34 (20.5)
Bladder involvement	9 (12.2)	16 (9.6)

Figure in parenthesis indicate percentage

Clinical and laboratory variables: Univariate analysis and multiple logistic regresion showed that there was no predilection for spinal tuberculosis to affect either sex (Table 2) but it was seen that tuberculosis was clearly more common in younger patients. The average age of patients with tuberculous lesions was significantly lower than that of patients with non-tuberculous lesions (40.68±18.63 *versus* 54.81±15.09 years; $p<0.0001$). Both univariate and multivariate analysis showed that eryt-

hrocyte sedimentation rate was not a reliable investigation to differentiate tuberculous from non-tuberculous lesions.

Table 2: Distribution of Clinical and Radiological Variables in Patients with Tuberculous and Non-tuberculous Vertebral Lesions

Clinical or radiological variable	Cases (%)		P value
	Non TB (n=74)	TB (n=166)	
Sex			
Male	44 (59.5)	95 (57.2)	0.747
Female	30 (40.5)	71(42.8)	
Grade of paraplegia			
Normal	58(78.4)	85(51.2)	0.001
I	3(4.1)	32(19.3)	
II	5(6.8)	27(16.3)	
III	5(6.8)	12(7.2)	
IV	3(4.1)	10(6.0)	
Site			
Cervical	2 (2.7)	6(3.6)	0.47
Thoracic	39(52.7)	69(41.6)	
Thoracolumbar	11(14.9)	23(13.9)	
Lumbar	22(29.7)	67(40.4)	
Sacral	0	1(0.6)	
Type of lesion			
Central	47(63.5)	31(18.7)	0.00001
Paradiscal	13(17.6)	90(54.2)	
Anterior	0	7(4.2)	
Posterior	6(8.1)	6(3.6)	
Multiple	4(5.4)	30(18.1)	
Normal*	4 (5.4)	2 (1.2)	

*Patients who presented with clinical features suggestive of vertebral lesions without any radiological abnormality; lesions were detected by bone scan; Figure in parenthesis indicate percentage

Table 3: Results of Multiple Logistic Regression Analysis to Identify Variables Facilitating a Diagnostic Differentiation between Tuberculous and Non-tuberculous Vertebral Lesions

Variable	Odd's ratio	95% CI	P value
Age	-	-	<0.001
Site *			
Cervical	1.75	0.21-14.85	0.61
Thoracolumbar	0.37	0.11- 1.18	0.09
Lumbar	1.44	0.61- 3.39	0.36
Sacral	**	**	0.91
Type *			
Central	0.07	0.03-0.16	<0.001
Anterior	**	**	0.78
Posterior	0.09	0.02-0.40	0.001
Paradiscal	0.64	0.16-2.53	0.53
Normal#	0.07	0.01-0.51	0.009
Grade *			
1	5.41	1.26-23.11	0.02
2	4.69	1.26-17.49	0.02
3	3.08	0.81-11.59	0.09
4	2.65	0.49-14.25	0.26

*Thoracic region among the sites, paradiscal among the types and normal neurologic status among the grade of paraplegia were considered as the reference category for the multiple logistic regression analysis; # Patients who presented with clinical features suggestive of vertebral lesions without any radiological abnormality; lesions were detected by bone scan; ** Number is too small for odd's ratio and 95% confidence interval (CI) calculations

Out of 97 patients who had neurological deficit, 81 had spinal tuberculosis and 16 were non-tuberculous. Almost half of the cases (49%) with spinal tuberculosis had neurological deficit of varying degrees.

Radiological variables: Both tuberculous and non-tuberculous lesions were encountered most commonly in the thoracic region. The site of the lesion was not helpful in differentiating tuberculous from non-tuberculous lesions (Tables 2 and 3). The types of the lesions in the vertebrae were as follows: 103 paradiscal, 78 central, 12 posterior and 7 anterior lesions. Univariate analysis and multiple logistic regression analysis suggest that the type of the lesion is useful in differentiating between tuberculous and non-tuberculous lesions. Of 103 paradiscal lesions, 90 turned out to be tuberculous whereas 47 out of 78 central lesions proved as non-tuberculous. Out of 34 multiple lesions 30 belonged to tuberculous group whereas only 4 were non-tuberculous (Tables 2 and 3). The histological diagnosis of the vertebral lesions which were of non-tuberculous origin is shown in Table 4.

Table 4: Distribution of Cases of Nontuberculous Lesions Diagnosed by Histopathology

Histopathological diagnosis	Cases
Metastasis	30
Multiple myeloma*	21
Pyogenic vertebral osteomyelitis	7
Non-Hodgkin's lymphoma	3
Osteoporotic fracture with callus	3
Plasmacytoma	2
Acute myeloid leukaemia	1
Neurilemmoma	1
Angiosarcoma	1
Angioblastoma	1
Haemangioma	1
Osteochondroma	1
Aneurysmal bone cyst	1
Gaint cell tumour	1
Total	74

* Patients presented with a solitary lesion in the spine, however post-biopsy bone scan revealed multiple skeletal involvement

DISCUSSION

Spinal tuberculosis is the commonest form of skeletal tuberculosis and constitutes about 50% of all cases of osteo-articular tuberculosis.[12-15] In developing countries it continues to pose a major public health problem.[4,16,17] Konstam and Blesovsky[17] and Tuli[7] noted that over 50% of their cases were seen in the first three decades of life. The predilection for younger patients to develop spinal tuberculosis was noted in the present study also.

The incidence of paraplegia among patients with spinal tuberculosis has been reported as between 10 and 30%.[12] Forty-nine per cent of the patients with spinal tuberculosis presented with varying degrees of neurological deficit. One possible reason for such a high frequency of neurological deficit in this series is because this centre is a tertiary referral centre, to which patients may be referred only when they develop complications

or do not respond to conventional treatment. Neurological involvement was also noted more frequently among patients with tuberculosis than with non-tubercular lesions. Though a statistically significant difference was noted between the ages of patients with tuberculous and non-tuberculous lesions, this clinical feature alone cannot be used with any degree of confidence to identify the cases of tuberculosis.

In this study tuberculous lesions were most frequently seen in the thoracic and thoraco-lumbar regions, which is similar to the findings of Tuli.[7] However, non-tubercular lesions were also found with equal frequency in these areas (Table 2). This study confirmed the observations of earlier author[7] that paradiscal lesions are the most common type in vertebral tuberculosis. However, 17.6% of the paradiscal lesions in this series proved to be non-tuberculous. The central type of lesion is due to the involvement of a single vertebral body producing a concertina collapse without any involvement of the disc space.

In the absence of a paravertebral shadow, this type of a lesion is difficult to differentiate from vertebral collapse due to other neoplastic conditions. Konstam and Blesovsky[17] noted less than 10% central type lesions among their patients with spinal tuberculosis. Even though central lesions favour the diagnosis of a nontuberculous aetiology it needs to be emphasised that 18.7% of central lesions in the present study proved to be due to tuberculosis. Skip lesions have been described in spinal tuberculosis but are considered to be rare.

Literature shows an incidence of 4-7% (Konstam and Blesovsky[17] and Tuli[7]). In the present series 10% of the patients with spinal tuberculosis had skip lesions. Out of 34 multiple lesions, 30 were proved to be tuberculous while only 4 were of non-tuberculous origin. These observations suggest that even though the type of lesion may point a definitive diagnosis, this should not be considered as confirmatory. Posterior element lesions are most difficult to visualise and diagnose by clinical and radiological methods. Babhulkar *et al*[5] reported only 22 lesions from a study spanning 10 years. We had 12 posterior element lesions out of which 6 were of tuberculous origin whereas remaining 6 were established as non-tuberculous.

Early diagnosis and treatment of spinal tuberculosis is essential to prevent complications like neurological deficit. The "gold standard" for diagnosis should ideally be isolation and culture of tuberculous bacilli. However, culture methods are slow and insensitive especially in cases of paucibacillary skeletal lesions.[7,18]

The shortcomings of these methods led to search for more sensitive and rapid detection methods. Polymerase chain reaction (PCR) is a comparatively simple technique and is widely used now. The high sensitivity of PCR has been widely acknowledged but the specificity of the test is poor.[18-20] In view of this it has been recommended that the decision to initiate or to stop antituberculous treatment should not be based on the results of the PCR.[18-20] We acknowledge that CT and MRI scans may have some definite advantages over conventional radiography, in pre-operative planning as they show the extent of the lesion and precise level of cord compression responsible for neurological deficit.[1-3] However, even MR findings may not always help in differentiating various types of spinal infections from one another and also from neoplasms. We agree with Watts and Lifeso4 and others[7-11] that diagnosis of vertebral tuberculosis should be primarily based on histopathological examination. Even though its classical clinical and radiological features have been described in the literature, spinal tuberculosis does mimic other lesions and can be missed, mistaken or misdiagnosed.

This was clearly noted in this study where several different conditions were initially thought to be spinal tuberculosis on the basis of clinical and radiological features. Nevertheless, young patients presenting with pain, fever, raised erythrocyte sedimentation rate and classical radiological features such as a metaphyseal lesion with paravertebral shadow may be empirically treated with antituberculous drugs. However, these patients have to be closely observed. In case they either do not respond to non-operative management or deteriorate clinically and neurologically attempt should be made to establish a histopathological diagnosis.

Spinal tuberculosis and a variety of other non-tuberculous spinal lesions may have similar clinical and radiological features. Lesions with a grave prognosis like myeloma or secondaries can mimic spinal tuberculosis and one cannot afford to delay a definitive diagnosis. In case of classical lesions without neurological deficit, a therapeutic trial with antituberculous therapy may be tried. However, if there is no response, these lesions should be confirmed by histopathological examination.

CONCLUSION

Both tuberculous and non-tuberculous lesions were encountered most commonly in the thoracic region. The most common lesion was paradiscal among the spinal tuberculosis. It is recommended that all vertebral lesions suspected to be of tuberculous origin not responding to empirical antituberculosis therapy should have a definitive histopathological diagnosis and radiological investigation to facilitate appropriate treatment.

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