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CLINICAL AND HISTOPATHOLOGICAL CORRELATION IN TUBERCULOSIS OF SPINE BIOPSIES

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ABSTRACT:

BACKGROUND & OBJECTIVE: The tuberculosis (TB) of the spine is causing permanent deformities since long time. Earliest most possible accurate diagnosis is required to treat either TB or to exclude other lesions to avoid permanent disability.
METHODOLOGY: This is a descriptive study conducted at pathology department of Lahore Medical & Dental College (LM&DC), Lahore from January 2017 to December 2019. All the spine biopsies received in Pathology department were included in the study irrespective of age and sex. Each biopsy was grossly and microscopically examined and reported by a histopathologist.
RESULTS: Out of 386 specimens received, 189 (48.9%) were clinically diagnosed as tuberculosis. Out of these 189 cases, 127 were confirmed on histopathological examination showing clinicopathological correlations in 67.19 % of cases. The rest 62 (32.80%) of the cases were reported as chronic non specific inflammation (38), degenerative changes (11), metastatic tumor (04), and atypical cell infiltrate (02), plasma cell neoplasm (01), Non Hodgkin Lymphoma (01) and other lesions (05) which all were benign. Out of the total 386 spine biopsies, 154 (39.89 %) were histopathologically proven for tuberculosis. From these 154 histologically proven cases, 127 were clinically suspected cases of Tuberculosis. No clinical diagnosis was provided in 02 patients. The rest of 25 patients were clinically labeled as pathological lesion without specific diagnosis.
CONCLUSION: Histopathology should be considered as the most reliable tool for spinal tuberculosis to minimize permanent disability associated with wrong management based on potentially erroneous clinical diagnosis.
KEYWORDS: Spine, Spinal tuberculosis, Histopathology, Diagnosis.

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INTRODUCTION:

Tuberculosis still remains a disease that causes distress and suffering to the patient even in this era of modern medical science and demands that this global issue should be properly addressed [1]. It is a chronic disease which usually presents with low grade fever and weight loss. It is one of the major cause of death in the world. The disease is responsible for about 2 million deaths from approximately 8 million recognized cases worldwide [2]. World Health Organization (WHO) Global Tuberculosis Report of 2016 listed South Africa as having the highest incidence of tuberculosis (TB) per capita in the world, with an estimated incidence of 8-16:100,000, almost 95% of cases diagnosed as tuberculosis, are in developing countries [3].

Once thought to be an endemic disease in underprivileged region/area of developing countries, tuberculosis has now become a problem of international concern spreading all over the world due to easy and frequent cross country travelling. In 1993, WHO declared the TB as a major health problem in developing countries. The history of spinal TB dates back to 1779; and Tuberculous Spondylitis was first reported by Sir Percival Pott [4]. Spinal tuberculosis or spondylitis, is the most common and the most serious form of skeletal tuberculosis [5]. It refers to an infection of the intervertebral disk, the vertebral body itself or the posterior vertebral arch, by Mycobacterium tuberculosis, with or without involvement of the spinal canal [6]. Thoracic region of the spine is usually the most common part which gets involved with the disease [5]. When the body of the spine is involved, instability of the affected spine can occur with anterior or lateral displacement of the vertebra. This results in physical deformity and also carries a risk of cord compression, especially in children and elderly resulting in paraplegia, and pulmonary insufficiency [2,5].

Mycobacterium tuberculosis, the causative organism of TB is a slow-growing, acid-fast aerobic bacillus. This bacillus tends to remain dormant for prolonged periods and multiplies every 15 to 20 hours in aerobic conditions whenever favorable. The primary site of infection can be in the lungs, lymph nodes of the mediastinum, mesentery, gastrointestinal tract, genitourinary system, or any other viscera. Spinal infection is almost always secondary and is caused by the hematogenous spread of this bacillus from a primary site [4].

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Spinal TB is usually insidious in onset. The disease might take from 2 weeks to several years from the onset of symptoms before the diagnosis can be achieved [5].

A patient with spinal tuberculosis seldom presents with symptoms (such as cough, sputum, fever, weight loss, or night sweating), which are common complaints in pulmonary tuberculosis, and this results in a delayed diagnosis. Back pain is usually the most common presenting symptom, followed by night sweats, weight loss, and low-grade fever [7].

Lack of early symptoms and insidious onset make early diagnosis tricky. Physicians and surgeons usually rely on a several modalities for the diagnosis of spinal tuberculosis. These include an examination of clinical signs and symptoms, radiological investigations, microbiological tests, metabolic product detection (interferon-γ [IFN-γ] test), polymerase chain reaction (PCR), and tissue biopsy. Most of these procedures are invasive and complex and diagnosis can take several days. There is currently no single diagnostic method that can detect all tuberculosis types and cases [2].

The Growth of TB bacillus on specific culture media, on inoculation of infected tissue, has been considered as the gold standard for the diagnosis of spinal tuberculosis. However, due to its very poor sensitivity, histopathological studies demonstrating epithelioid granulomas and staining of smears to identify acid-fast bacilli (AFB) are considered as a reference standard for all other diagnostic modalities [4].

Depending only on clinical and radiological features many lesions can be missed resulting in delayed diagnosis thus causing irreversible damage and serious complications. Although plain X-ray, MRI, and CT scans are used for the

detection of spinal pathologies; none of these imaging techniques are reliable with certainty to distinguish between infectious and neoplastic processes. So histopathology is mandatory to confirm the diagnosis of tuberculosis and to rule out other pathologies including malignancies [7].
In developing countries for early detection and differentiation of spine tuberculosis from other similar lesions, clinical features and plain radiographs are the main diagnostic tools for this disease [8,9,10].
Although there is a global consensus about the importance of early identification of spinal tuberculosis but literature is still deficient in guiding the primary health care practitioners to adopt a good clinical approach and use of an appropriate diagnostic tool in resource poor setting for prompt diagnosis and management [3].The literature is also deficient on the frequency of lesions that mimic spinal tuberculosis [2,8].
Taking histopathological biopsy as a reference standard, the study was planned to determine the accuracy of clinical diagnosis of cases of spinal tuberculosis by correlating it with histopathological biopsy report. This study will highlight the importance of histopathological biopsy as an adjunct to clinical signs and symptoms suggestive of TB. It will also differentiate tuberculosis from other malignant and benign lesions that resemble this common and disabling disease on clinical and/or radiological findings. It will also provide the basic knowledge for the future to determine the relative reliability of different diagnostic modalities and to establish a more accurate diagnostic tool in spinal tuberculosis.

METHODOLOGY:

This descriptive cross-sectional study was conducted in the Pathology department of Lahore Medical and Dental College (LM&DC) Lahore for 03 years i.e., from January 2017 to December 2019. After ethical approval from IRB-LM&DC, data was collected.
This study was carried out on 386 biopsies of the spine that were received in the Pathology Department of LM&DC Lahore. All the cases of spine biopsy irrespective of age, sex, and origin were included in this study. Patient particulars, history, clinical information, investigation, and all other information provided on the request form were entered on a separate clinical performa for each biopsy. Most of the biopsy material was received from the spine centre of Ghurki Trust Teaching Hospital (GTTH), one of the largest spine centre, where patients come from all over Pakistan. The specimens received were all fixed in 10 % formalin. The Gross examination was done and representative sections of the lesion were taken, which were processed in an automated tissue processor. Initially, routine staining with Hematoxylin and Eosin was done. Z N staining was done in those cases where tuberculosis was suspected on microscopy. The slides were initially examined by residents and then the concerned consultant examined every case personally for final diagnosis and reporting. Intra-departmental consultation was done where required.
Data was entered in SPSS-22 package. Descriptive statistics was used to analyze the data, which was presented in the form of tables.

RESULTS:

Total 386 cases of spine biopsy received were included in this study. The age of patients ranged from 03 to 72 years with the mean age being 35 years. The majority of patients were of 21-50 years of age. No sex predilection was observed, both the female and the male patients were equally affected by tuberculosis of spine. Almost all of the cases were from thoraco-lumbar spine; thoracic region was involved more than lumbar area. Clinically tuberculosis was suspected in 189 (48.96 %) cases from the total 386 spine biopsies. From these 189 clinically suspected tuberculous biopsies 127(67.19 %) were confirmed on histopathological examination as well showing clinicopathological correlations in 67.19 % of cases. The rest of 62 (32.80%) cases were reported as chronic nonspecific inflammation 38 (20.10%), degenerative changes11 (5.82%), metastatic tumor 04 (2.11%), atypical cell infiltrate 02(1.05%), plasma cell neoplasm 01(0.52%), Non-Hodgkin's Lymphoma 01(0.52%) and other lesions 05(2.64%) all of those were benign (Table-I).

Table-I: Histopathological diagnoses in spine biopsies clinically suspected as tuberculosis.

No	Histopathological Diagnosis (n=189)	No of Cases	%
1	Tuberculosis	127	67.19
2	Chronic Non Specific inflammation	38	20.10
3	Degenerative Changes	11	05.82
4	Metastatic tumor	04	02.11
5	Atypical cell Infiltrate	02	01.05
6	Plasma cell neoplasm	01	00.52
7	Non Hodgkin Lymphoma	01	00.52
8	Others	05	02.64

Of the total 386 cases of spine biopsy, 154 (39.89 %) cases were histopathologically diagnosed as tuberculous. From these 154 histopathologically reported cases of tuberculosis of spine biopsies127 were also clinically suspected cases of tuberculosis. No provisional diagnosis was provided in 02 patients. The rest of the 25 patients were clinically labeled as pathological lesions without any specific provisional diagnosis (Table-II).

Table-II: Clinical diagnoses in histopathologically proven tuberculous spine biopsies:

No	Clinical Diagnoses (n=154)	No of Cases	%
1	Tuberculosis	127	82.46
2	Pathological lesion	25	16.23
3	No diagnosis	02	01.29

DISCUSSION:

Skeletal tuberculosis accounts for 10 % of extrapulmonary tuberculosis and about 50% of Skeletal tuberculosis involves the spine. Predisposing factors include malnutrition, diabetes, drug abuse, alcohol, and other chronic diseases. Symptoms are insidious and can be there for months to years before it is suspected by clinical findings and history of contact with tuberculous patients. The radiological /imaging methods along with laboratory investigations like ESR and Mantoux test are usually reliable for diagnosis [7]. In a study, it was observed that most of their patients were young with a mean age of 34 years [11]. In other studies, most patients were young adults in the 3rd to 5th decades of life [12, 13]. In our study, the mean age was 35 years which coincides with previous studies. Our study revealed that thoraco-lumbar spine was the most commonly affected region of spine by tuberculosis, with a predilection for thoracic than lumbar area. In other studies the thoraco-lumbar involvement was maximum but there were more cases in which the lumbar vertebrae were affected by TB[14,15]. Early diagnosis and management of spinal tuberculosis saves the patient from severe disabling complications requiring prolonged and interventional management and this can only be achieved by a multidisciplinary approach involving radiology and histopathology along with clinical assessment. Laboratory investigations like culture sensitivity and Polymerase chain reaction (PCR) are very helpful in diagnosis but the late and insensitive result of culture sensitivity and low specificity of PCR are major limitations [13,16]. The malignant entities of spine like multiple myeloma and metastatic tumor are also very similar to tuberculosis on clinicoradiological assessment which cannot be

relied upon for definite diagnosis in such cases [13]. Tuberculosis and other nontuberculosis lesions are very frequently encountered in the spine and can be missed, misdiagnosed, or mistaken if a definite diagnosis has relied on clinicoradiological findings only which will result in delayed management of malignant lesions with grave effects[11, 13,17, 18]. The spinal TB is very likely to be misdiagnosed due to lack of specific clinical features. The false-negative results of the laboratory tests and imaging studies further increase the possibility of missing tuberculosis. The early diagnosis and management of Spinal TB by drugs reduce the surgical intervention and economic burden. Active tuberculosis is treated with drugs. The surgical intervention in spinal tuberculosis is done for getting biopsy material, debridement, and halting the deformity. In old healed lesions, surgery is required for reinforcement of stability and correction of disabling deformity of the spine [4,11]. The gold standard for diagnosis should be isolation and culture of Mycobacterium tuberculosis but slow and insensitive results are its limitations [13]. PCR is simple, sensitive, and quick but has poor specificity [13]. A quick and most reliable diagnostic tool for early and most possibly accurate diagnosis was needed to reduce the disability by spinal TB.

Watts and Life so and others have observed that the management of spinal tuberculosis should be based on histopathological diagnosis [4, 11, 13]. The result of our study concurs with previous studies in suggesting that histopathological examination of biopsy should be considered as the most reliable diagnostic tool for spinal tuberculosis.

CONCLUSION:

The study on 386 spine biopsies revealed that tuberculosis is the most common pathological lesion in 154 (39.89 %) cases with a predilection for the thoracic region. From 189 clinically tuberculous cases, clinical-histopathological correlation was found in 127 (67.19 %) cases. The rest of 62 (32.81 %) cases with poor clinical-histopathological correlation were clinically misdiagnosed as tuberculosis which on histopathology turned out to be malignant lesions like plasma cell tumor, lymphoma, and secondaries besides benign entities. So reliance only on clinical diagnosis may lead to grave disability because of inappropriate management based on clinical diagnosis which may be erroneous. Histopathological diagnosis should be considered as the most reliable diagnostic tool in spinal tuberculosis.

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Author's Contribution:

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Majid Zaheer: Proof reading & Reference collection.
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Shazia Nilofer Ibnerasa: Critical review and final approval.

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