

Histopathological Evaluation of Extra-pulmonary Tuberculosis at a Tertiary Care Hospital

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ABSTRACT

Background: The clinical manifestations of tuberculosis (TB) can be categorized into two primary types: pulmonary TB (PTB) and extrapulmonary TB (EPTB), with PTB being the more prevalent form. EPTB is characterized by the involvement of organs outside the pulmonary system, such as the pleura, lymph nodes, abdomen, genitourinary tract, skin, joints, bones, or meninges. Hence; the present study was conducted for histopathologic evaluation of extra-pulmonary tuberculosis patients.

Materials & Methods: A total of 100 patients diagnosed with presence of extra-pulmonary tuberculosis were enrolled. Complete demographic and clinical details of all the patients were obtained. Histopathology specimens for EPTB were evaluated. The variables analyzed were age, gender, site, presence of granuloma, AFB, caseous necrosis. All entries with the histopathology diagnosis of tuberculosis in organs other than lungs were included in the study. All the results were recorded in Microsoft excel sheet and were subjected to statistical analysis using SPSS software.

Results: A total of 100 patients were evaluated. Mean age of the patients was 51.9 years. Majority proportion of patients were males. Epithelioid granuloma was seen in 96 percent of the patients. Among them, 8 patients were positive for ZN

staining. Lymph nodes, Skin, GIT, Urogenital and Bone/joints were involved in 62 percent, 10 percent, 8 percent, 8 percent and 7 percent of the patients respectively. Caseous necrosis was seen in 92 percent of the patients.

Conclusion: Among cases of Extra Pulmonary Tuberculosis, over half of cases exhibited tubercular lymphadenitis, with granulomatous formation observed in the majority of these instances.

Keywords: Extra-pulmonary, Tuberculosis, Histopathologic.

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INTRODUCTION

The clinical manifestations of tuberculosis (TB) can be categorized into two primary types: pulmonary TB (PTB) and extrapulmonary TB (EPTB), with PTB being the more prevalent form. EPTB is characterized by the involvement of organs outside the pulmonary system, such as the pleura, lymph nodes, abdomen, genitourinary tract, skin, joints, bones, or meninges. A patient diagnosed with both PTB and EPTB is classified under PTB. For instance, miliary TB is considered PTB due to the presence of lesions in the lungs. Conversely, conditions such as tuberculous intrathoracic lymphadenitis (mediastinal and/or hilar) or tuberculous pleural effusion, which do not exhibit radiographic lung abnormalities, are classified as EPTB.¹⁻³

In 2013, TB notification data indicated that Korea reported a total of 36,089 TB cases, equating to 71.4 cases per 100,000 individuals. Among these, 7,369 cases were identified as EPTB,

representing 14.6 cases per 100,000 and accounting for 20.4% of all TB cases. The most frequently affected sites for EPTB in Korea included the pleura, followed by lymph nodes, gastrointestinal organs, bones and joints, the central nervous system (CNS), and the genitourinary system. The proportion of EPTB cases among total TB cases was approximately 14% from 2005 to 2007, but this figure rose to over 20% between 2010 and 2013. The reasons behind this increase remain uncertain. Factors such as lower rates of voluntary reporting, the diagnostic challenges associated with EPTB, and the likelihood of undiagnosed cases suggest that the actual incidence of EPTB may be significantly higher than reported. The literature identifies several independent risk factors for EPTB, including younger age, female gender, Asian and African descent, and co-infection with human immunodeficiency virus (HIV).⁴⁻⁶

The diagnosis of EPTB poses a particular challenge for clinician because of the protean ways in which the disease presents. Diagnosis of this condition requires high clinical suspicion and special diagnostic procedures. EPTB diagnosis may not be difficult in a few cases with concomitant pulmonary involvement. However, patients with EPTB are more likely to have negative sputum smear results and many EPTB cases do not have direct lung involvement. EPTB diagnosis is much more lacking in rural health facilities that are used by about 70% of the population in developing countries.⁶⁻⁸ Hence; the present study was conducted for histopathologic evaluation of extra-pulmonary tuberculosis patients.

MATERIALS & METHODS

The present study was conducted for histopathologic evaluation of extra-pulmonary tuberculosis patients. A total of 100 patients diagnosed with presence of extra-pulmonary tuberculosis were enrolled. Complete demographic and clinical details of all the patients were obtained. Histopathology specimens for EPTB were evaluated. The variables analyzed were age, gender, site, presence of granuloma, AFB, caseous necrosis. All entries with the histopathology diagnosis of tuberculosis in organs other than lungs were included in the study. All the results were recorded in Microsoft excel sheet and were subjected to statistical analysis using SPSS software.

Table 1: Histopathologic cases

Epithelioid granuloma	ZN stain	Number	Percentage
Present	Positive	8	8
	Negative	88	88
Absent	Positive	1	1
	Negative	3	3
Total		100	100

Table 2: Organs affected

Organs	Number	Percentage
Lymph nodes	62	62
Skin	10	10
GIT	8	8
Urogenital	8	8
Bone/joints	7	7
Others	5	5
Total	100	100

Table 3: Caseous necrosis

Caseous necrosis	Number	Percentage
Present	92	92
Absent	8	8
Total	100	100

RESULTS

A total of 100 patients were evaluated. Mean age of the patients was 51.9 years. Majority proportion of patients were males. Epithelioid granuloma was seen in 96 percent of the patients. Among them, 8 patients were positive for ZN staining. Lymph nodes, Skin, GIT, Urogenital and Bone/joints were involved in 62 percent, 10 percent, 8 percent, 8 percent and 7 percent of the patients respectively. Caseous necrosis was seen in 92 percent of the patients.

DISCUSSION

Extrapulmonary involvement may manifest either independently or concurrently with pulmonary manifestations, as observed in patients suffering from disseminated tuberculosis (TB). The recent pandemic of human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) has altered the epidemiological landscape, thereby re-emphasizing the significance of extrapulmonary tuberculosis (EPTB). In immunocompetent individuals, EPTB accounts for approximately

15 to 20 percent of all tuberculosis cases, while in those who are HIV-positive, it represents over 50 percent of cases. The lymphatic system is the most frequently affected area, followed by pleural effusions, with virtually any anatomical site being susceptible to infection. Due to the atypical clinical presentation of EPTB, obtaining tissue samples for diagnostic confirmation can be challenging, and traditional diagnostic techniques often yield unsatisfactory results, leading to delays in diagnosis.

The advent of advanced imaging modalities such as computed tomography (CT), magnetic resonance imaging (MRI), laparoscopy, and endoscopy have significantly enhanced the anatomical localization of EPTB. Typically, the disease responds well to standard antituberculosis pharmacotherapy. However, biopsy and/or

surgical intervention may be necessary to obtain tissue samples for accurate diagnosis and to address complications.⁷⁻⁹

Hence; the present study was conducted for histopathologic evaluation of extra-pulmonary tuberculosis patients.

A total of 100 patients were evaluated. Mean age of the patients was 51.9 years. Majority proportion of patients were males. Epithelioid granuloma was seen in 96 percent of the patients. Among them, 8 patients were positive for ZN staining. Lymph nodes, Skin, GIT, Urogenital and Bone/joints were involved in 62 percent, 10 percent, 8 percent, 8 percent and 7 percent of the patients respectively. Caseous necrosis was seen in 92 percent of the patients.

Sunnetcioglu et al compared the demographic and clinical features of pulmonary and extrapulmonary tuberculosis cases in adults. Demographic and clinical characteristics were compared for pulmonary and extrapulmonary tuberculosis cases. Of these 411 cases, 208 (50.6 %) had pulmonary tuberculosis (PTB) and 203 were diagnosed with extrapulmonary tuberculosis (EPTB) (49.4 %). The average ages for PTB and EPTB groups were 33.00-27.00 and 31.00-29.75, respectively ($p = 0.513$). Men were more frequently affected by PTB (59.6 %), while EPTB was more commonly detected in women (52.2 %) ($p = 0.016$). Main diagnostic modalities for PTB were sputum/smear analyses (72.7 %), clinical-radiological data (21.7 %) and biopsy (6.1 %); while biopsy (71.5 %), sputum/fluid analysis (18.8 %) and clinical-radiological data (4.9 %) were used for confirming EPTB ($p < 0.0019$). The most common sites of EPTB involvement were lymph nodes (39.4 %), followed by pleura (23.6 %), peritoneum (9.9 %) and bone (7.4 %). Extrapulmonary involvement of tuberculosis is common and females are more likely to be affected.¹⁰

Chakravorty S et al developed universal sample processing (USP) technology for detecting mycobacteria in clinical specimens. In their study, this technology was evaluated blindly on 99 extrapulmonary specimens collected from 87 patients. USP-processed specimens were submitted to smear microscopy for detection of acid-fast bacilli (AFB), culture, and two PCR tests targeting *devR* (Rv3133c) and *IS6110* gene sequences. On the basis of clinical characteristics, histology and cytology, conventional microbiology results, and response to antitubercular therapy, 68 patients were diagnosed with tuberculosis. Although USP smear and culture were significantly superior to conventional microbiology, which was not optimized ($P < 0.0001$), these approaches fell short of PCR tests ($P < 0.0001$). The low yields by smear and culture are attributed to the paucibacillary load in the

specimens. The highest sensitivity in PCR was achieved when *devR* and *IS6110* test results were combined; the sensitivity and specificity values were 83 and 93.8%, 87.5 and 100%, and 66.7 and 75%, respectively, in pleural fluid, needle-biopsied pleural tissue, and lymph node specimens.¹¹

Ahmed HG et al investigated the morphological pattern of tuberculous lymphadenitis, as well as to assess the reliability measures of (ZN) Ziehl-Neelsen and fluorescent methods in identification of *Mycobacterium tuberculosis*. One hundred lymph nodes tissue biopsies that were previously diagnosed by conventional histopathology as having tuberculous lymphadenitis were reinvestigated. Five micron in thickness sections were obtained from formalin-fixed paraffin wax processed tissues. The sections were stained using Haematoxylin and eosin (H & E), ZN, and fluorescent methods. All of the 100 specimens were proved as having histopathological pattern of tuberculosis lymphadenitis. The most major histological features were giant cell (88%), caseation (84%), epithelioid cells (80%), granuloma and caseation (68%), lymphocytes (31%), and histiocytes (4%). After staining the specimens with ZN and fluorescent, of the 100 specimens only 3 (3%) and 9 (9%) specimens were found positive, by ZN and fluorescent methods, respectively.¹²

CONCLUSION

Among cases of Extra Pulmonary Tuberculosis, over half of cases exhibited tubercular lymphadenitis, with granulomatous formation observed in the majority of these instances.

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