



CLINICOPATHOLOGICAL SPECTRUM OF EXTRAPULMONARY TUBERCULOSIS IN A TERTIARY CARE CENTRE OF SOUTH INDIA

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ABSTRACT Tuberculosis (TB) is commonly found in developing countries. Lung is predominantly affected and extrapulmonary tuberculosis (EPTB) is rarely encountered. The clinical features of EPTB can be non-specific that mimics other diseases and is usually misdiagnosed. Thus, it is very important to be aware and be highly suspicious of EPTB infection especially in endemic areas. Although extrapulmonary tuberculosis (EPTB) has existed as a disease entity for decades together, it has gained increased importance recently because of the increase in the number of cases. The current study aims at analyzing the various cases of EPTB diagnosed in our hospital in relation to their occurrence at various sites, age and sex predilection and histopathological diagnosis. Thus, it is crucial to always include tuberculosis as part of working diagnosis especially in regions where tuberculosis is endemic until proven otherwise. Hence it is imperative to start treatment early to ensure better response. The diagnosis was made by histopathological examination and positive Acid Fast Bacilli (AFB) smears, and were successfully treated with anti-tuberculosis drugs.

KEYWORDS : *Extra Pulmonary Tuberculosis, Granuloma, Histopathology.*

1. INTRODUCTION

Tuberculosis has been a global health concern since ages especially in a developing country like ours. WHO claims that India has the highest incidence of tuberculosis in the World with 8.6 million new cases diagnosed every year [1]. Tuberculosis (TB) is a common granulomatous disease caused by *Mycobacterium tuberculosis*, which primarily affect lungs in about 80 % of cases [2]. Extrapulmonary TB (EPTB) is defined as TB of organs other than lung.

Mycobacteria may spread to any organ of the body through lymphatics or haematogenous dissemination and lie dormant for years at a particular site before causing symptoms or disease. Manifestations may relate to the system involved, or there may be constitutional symptoms such as prolonged fever, anorexia, weight loss, malaise and fatigue. In these cases, diagnosis may be elusive and is usually delayed. A retrospective study was carried out to identify the cases of extrapulmonary tuberculosis, and later on were analyzed in accordance with various other parameters.

2. MATERIAL AND METHODS

This retrospective study was conducted in the department of pathology, Tirunelveli Medical College, Tamilnadu. The period of study was one year from January 2021 to February 2022. Study material included all the cases diagnosed as Tuberculosis in organs other than lungs by histopathology and special stains. As per WHO guidelines patients with both Pulmonary and extrapulmonary TB were labeled as having Pulmonary TB and therefore excluded from the study [3].

Biopsies received in the department were subjected to routine processing followed by Haematoxylin and Eosin (H& E) staining. Modified Ziehl Neelsen (ZN) staining for Acid Fast Bacilli was done in all the cases. Other investigations such as culture (Lowenstein Jenson media), serology, imaging studies including chest radiographs, sputum examination, PCR etc. were correlated with the histopathological diagnosis. These investigations were also used to rule out involvement of lung parenchyma thereby reaching to the final diagnosis of EPTB.

3. RESULTS

A total of 26 cases of extrapulmonary tuberculosis were included in the present study. A histopathological diagnosis based on gross,

microscopic examination (Figure 1) was made and correlated with other investigations also.

Table 1: Age And Sex Distribution Of The Cases

S.No.	Age Group	Male	Female	Total
1	1-10	2	-	2
2	11-20	1	2	3
3	21-30	3	3	6
4	31-40	2	2	4
5	41-50	5	1	6
6	51-60	-	1	1
7	Above 60	4	-	4
	TOTAL	17	9	26

In our study, age and sex distribution data showed that EPTB was more in males (65.38%) than females (34.61%). It was also observed that the majority of the patients affected were in the age group of 11- 30 years and 41-50 years [Table 1].

Table 2: Site Specific Distribution Of Extra Pulmonary Tuberculosis (eptb)

S.No	Site	No. of cases	Percentage (%)
1	Lymph nodes	6	23.07
2	Cutaneous (Skin)	3	11.54
3	Synovium	5	19.23
4	Abdominal wall	3	11.54
5	Sinonasal Growth	1	3.8
6	Omental Tubercle	2	7.7
7	Adnexal mass	1	3.8
8	Breast	1	3.8
9	Intestine	4	15.38

Table 2 demonstrates the distribution of EPTB cases in terms of the various sites involved. It can be concluded from Table 2 that the highest number of cases of EPTB is 6 cases reported in the lymph nodes (23.07%) followed by 5 cases (19.23%) in the Synovium and four cases (15.38%) of intestinal tuberculosis were reported in our study. Among the four cases, three cases presented as ileal tuberculosis and in one case there was involvement of ileocaecal junction and appendix. Cutaneous involvement and Abdominal wall involvement

were equal (11.54%). Musculoskeletal system and Breast were involved in 3.8% of the cases. One case in our study presented as sinonasal growth and another interesting case of huge adnexal mass was also reported in our study. Here it is also important to highlight those cases where rare sites were involved and clinical signs and symptoms were obscure. Biopsy was sent to our department which revealed well defined epithelioid cell granulomas with caseation necrosis. Modified Ziehl Neelsen (ZN) staining for acid fast bacilli was positive.

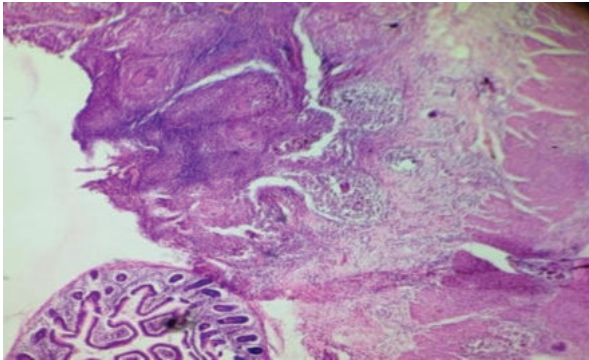


Figure 1: Caseating granuloma: typical epithelioid cell granuloma with central caseation, peripheral lymphocytes and Langhan's type of giant cells. (H and E, 10 X)

4. DISCUSSION

Tuberculosis remains an endemic disease and is the seventh leading cause of death globally [4]. Extrapulmonary Tuberculosis (EPTB) is defined as isolated occurrence of tuberculosis in any part of the body other than lungs. Diagnosis of EPTB is important because it can involve a variety of sites and at times may mimic various disease processes. Types of EPTB that have been reported all over the world are lymphatic, pleural, skeletal, central nervous system, ocular and pancreatic. The other cases of extra pulmonary tuberculosis include genitourinary and cerebral tuberculosis [5]. Extrapulmonary tuberculosis usually presents with a more difficult diagnostic problem. Diagnosis of EPTB is challenging at times. No single test can lead to a correct diagnosis. A variety of direct and indirect methods have to be employed. The bacilli and its products are demonstrated in the direct methods which include Ziehl Neelsen staining, fluorescent microscopy, Lowenstein Jensen culture, BACTEC culture system, Polymerase chain reaction, Antigen based serology, molecular methods, immunohistochemistry and immunocytochemistry. Whereas the indirect methods include histopathology which offers an advantage of differential diagnosis, cytology, antibody based serology, skin tests, interferon release assay, adenosine deaminase assay [6]. Among the indirect methods, histopathology of tissue along with ZN staining and culture for *Mycobacterium Tuberculosis* is considered the method of choice for the diagnosis of EPTB. Precise localisation of the lesion and adequate biopsy has been further made easier with the advent of computerised tomographic scan, magnetic resonance imaging, laparoscopy, endoscopy [7].

In our study, age and sex distribution data showed that EPTB was more in males (65.38%) than females (34.61%). It was also observed that the majority of the patients affected were in the age group of 11-30 years and 41-50 years. This correlates with other similar study conducted by Sreerama reddy et al [8] where the younger age group was more affected. Chandir et al [9] reported maximum number of EPTB cases in 15-29 years age group in Pakistan. These results are comparable with our study. Various determinants including, nutrition, educational status, compliance with treatment, fear and stigma associated with tuberculosis have been found to play an important role.

Amongst the distribution of sites involved by EPTB, the highest number of cases of EPTB is 6 cases reported in the lymph nodes (23.07%) followed by 5 cases (19.23%) in the Synovium and four cases (15.38%) of intestinal tuberculosis were reported in our study. Among the four cases, three cases presented as ileal tuberculosis and in one case there was involvement of ileocaecal junction and appendix. Cutaneous involvement and Abdominal wall were equally involved (11.54%). Musculoskeletal system and Breast were involved in 3.8% of the cases. One case in our study presented as sinonasal growth and another interesting case of huge adnexal mass was also reported in our study.

While comparing the present study with the previous studies, it was observed that, the sites of localization of EPTB can be variable from place to place. In a study conducted by Noertjojo et al, [10] the genitourinary system and the skin were the common sites affected, whereas in a USA based study carried out by Yang et al [29], bones and/or joints were the most common sites. While in the study conducted by Chandir et al [9] the frequency of EPTB cases by site was highest in lymph nodes (35.6%), followed by spine (26.3%). Similarly, in a study conducted by Sreeramareddy et al, [8] the most common site of EPTB was the lymph nodes (42.6%) followed by the peritoneum and/or intestines (14.8%), then bones and/or joints (12.4%).

In the present study, it was also observed that cases of extrapulmonary tuberculosis with unusual presentations presented at rare sites. Such cases were clinically interesting as EPTB was not suspected clinically in any of these cases. Often diagnosis is missed at these sites due to the various differential diagnosis possible. The diagnosis of EPTB in such cases poses a difficult diagnostic challenge and thorough clinical, serological, radiological and histopathological correlation has to be made for a definitive diagnosis. In all the cases of EPTB, patients responded well to the anti-tubercular therapy. Biopsy and histopathology is frequently the saviour in such cases.

5. CONCLUSION

Extrapulmonary TB is rare compared to the pulmonary counterpart. However, the presentation is not unusual that can mimic other entities. Hence, it is very important to have a high index of suspiciousness to rule out TB, as this disease is a curable disease. In a developing country like India extrapulmonary tuberculosis should be kept in the differential diagnosis. Late diagnosis or untreatable TB will lead to high morbidity and mortality. Definitive diagnosis of tuberculosis involves demonstration of *M. tuberculosis* by histopathological, microbiological, cytopathological and molecular methods. Histopathology, in particular assumes great importance when EPTB involves obscure occult sites. It is one of the best methods to diagnose EPTB especially when clubbed with tissue culture and ZN staining. Molecular diagnostic techniques are also used for rapid and accurate detection of tuberculosis. This would ultimately result in overall decreased morbidity and mortality of extrapulmonary tuberculosis (EPTB).

Financial support and sponsorship- Nil

Conflict of interest- There are no conflicts of interest.

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