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Original Research Article

Study of Cytomorphological Patterns of Tuberculous Lymphadenitis on Fine Needle Aspiration Cytology

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Abstract

Background: Lymphadenitis is one of the most common extrapulmonary manifestations of tuberculosis. Fine Needle Aspiration Cytology (FNAC) of tuberculous lymph node when combined with Ziehl–Neelsen (ZN) staining for acid-fast bacilli (AFB) has a paramount value in the diagnosis of tuberculosis. *Objectives:* To describe the cytomorphological patterns of tuberculous lymphadenitis and their correlation with AFB positivity and to describe spectrum of morphological features seen on cytological smears of tuberculous lymphadenitis. *Materials and methods:* A total of 100 cases of tuberculous lymphadenitis in a tertiary hospital were studied from 2016 to 2017. Fine Needle Aspiration was performed on enlarged lymph nodes and slides were looked for various cytomorphological patterns such as pattern A— epithelioid granulomas without necrosis, pattern B— epithelioid granulomas with necrosis and pattern C— caseaous necrosis without granulomas. Ziehl–Neelsen staining was done for AFB. Cytomorphological patterns of tuberculous lymphadenitis were correlated with AFB positivity. Fisher's exact test was applied to analyze the significance of correlation between cytomorphological patterns and AFB positivity. The p value of <0.05 was considered as significant. *Results:* The most common cytomorphological pattern observed was Pattern B, i.e. epithelioid granuloma with necrosis. AFB positivity was seen in 18% cases and maximum was observed in pattern C smears which was statistically significant ($p = 0.0422$). *Conclusion:* Fine needle aspiration cytology of tubercular lymph node when combined with ZN staining for AFB is one of the useful and economical investigations to understand the different cytomorphological patterns and in the diagnosis of tuberculosis.

Keywords: Tuberculous lymphadenitis; Ziehl–Neelsen stain; Acid-fast bacilli; Epithelioid granuloma; FNAC lymph node; Extrapulmonary tuberculosis.

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Introduction

Tuberculosis is one of the most ubiquitous infections in the developing and underdeveloped countries. India being one of the most populous countries, accounts for one-fifth of the global incidence of tuberculosis. In 2015, 2.8 million cases were reported from India out of 10.4 million cases worldwide.[1] Of which, lymphadenitis is one of the most common extrapulmonary manifestations which is seen in nearly 35% of extrapulmonary tuberculosis.[1] Fine Needle Aspiration Cytology is a routinely done technique in diagnosing tuberculous lymphadenitis. Although, culture studies are considered to be gold standard in the diagnosis, they are time devouring and demand skills. Other techniques like auramine rhodamine staining and polymerase chain reaction for tubercle bacilli DNA demands resources.[2] Hence, FNAC has been considered as one of the useful, economical, rapid technique and also less invasive compared to core needle and excision biopsy in diagnosing granulomatous inflammation in lymph nodes.[3] It has been considered as highly reliable investigation when combined with Ziehl–Neelsen staining for acid-fast bacilli in the resource limited countries like India.

Objectives

The objective of the study is to describe the cytomorphological patterns of tuberculous lymphadenitis and their correlation with AFB positivity and also to describe spectrum of morphological features seen on cytological smears of tuberculous lymphadenitis.

Materials and Methods

A prospective study of hundred cases of clinically diagnosed tuberculous lymphadenitis with supportive clinical history and laboratory investigations were aspirated for cytological examination in Department of Pathology, JJM Medical College Davangere from 2016 to 2017. All aspirations were performed using 23 gauge needle with aseptic precautions. Smears were stained with hematoxylin and eosin (H&E), Giemsa, Papanicolaou (PAP) and Ziehl–Neelsen (ZN) stains. Cytological criteria for the diagnosis of tuberculosis are epithelioid cell granulomas and caseating necrosis with or without giant cells. Cytomorphologically, all cases were categorized into three patterns as suggested by Das et al. The three cytomorphological patterns were: Pattern A— Epithelioid granulomas without necrosis; Pattern B— Epithelioid granulomas with necrosis; Pattern C— Caseous necrosis without epithelioid granuloma.[4] These patterns were then correlated with AFB positivity on ZN stained smears.

Results

Among 100 cases studied patients age ranged from six years to seventy-eight years. The distribution of cases in various age groups and gender is represented in Table 1. Maximum numbers of cases were seen in the age group of 21–30 years followed by 11–20 years and 31–40 years. Male to female ratio was 0.82.

Table 1: Distribution of tuberculous lymphadenitis in relation to age groups and gender

Age group	Male	Female	Total
0–10 yr	2	3	5
11–20 yr	8	11	19
21–30 yr	15	24	39
31–40 yr	8	7	15
41–50 yr	6	4	10
51–60 yr	3	2	5
>60 yr	4	3	7
Total	46	54	100

Patients with tuberculous lymphadenopathy also had associated other clinical symptoms (Table 2). Of which, 69 patients had associated fever, 53 of them had history of tuberculosis, 32 patients had associated cough and 19 of them had loss of appetite and weight. Twenty patients showed features of pulmonary tuberculosis on chest X-ray and 7 patients were HIV positive and were on Anti Retroviral Treatment (ART). Four patients had associated dyspnea and 2 were having pleural effusion. Most common involved lymph node group was cervical followed by axillary and inguinal group (Table 3).

Table 2: Clinical presentation of patients with tuberculosis

Clinical Features	Percentage of Cases
Lymphadenopathy	100
Fever	69
Cough	32
Loss of appetite and weight	19
History of tuberculosis. Defaulters, ATT	53
Dyspnoea	4
Pleural effusion	2
Features of pulmonary tuberculosis	20
HIV positive/ART	7

Table 3: Distribution of lymph node group involvement

Lymph Node Group Involved	No. of Cases
Cervical	85
Axillary	12
Inguinal	3

Aspirate was blood tinged in 45 cases while it was grey white in 31 cases and purulent to cheesy in 24 cases. Blood tinged aspirate was predominantly seen in Pattern A and B. Purulent to cheesy aspirate were seen predominantly in Pattern C. Out of 100 cases showing cytological features of tuberculous lymphadenitis, 22% of cases showed epithelioid granulomas without necrosis (Pattern A), 49% showed epithelioid granulomas with necrosis (Pattern B) and 29% showed caseous necrosis without epithelioid granulomas (Pattern C) (Table 4). Seven cases were HIV positive and the smears of those patients showed pattern C- Caseous necrosis without granuloma.

Table 4: Correlation between cytological pattern and AFB positivity

Type of pattern	No of cases	AFB positive cases	%
A— Epithelioid granulomas without necrosis	22	1	4.5%
B— Epithelioid granulomas with necrosis	49	7	14.2%
C— caseous necrosis without epithelioid granulomas	29	10	34.5%

Correlation of AFB Positivity With Cytomorphological Pattern

Acid -fast Bacilli was found in 34.5% of cases with caseating necrosis without epithelioid granulomas (pattern C), 14.2% of cases with epithelioid granulomas with necrosis (pattern B) and lowest i.e., 4.5% in epithelioid granulomas without necrosis (pattern A). Overall AFB positivity was seen in 18/100 (18%) cases (Table 4). By comparing pattern A smears with that of pattern C smears using Fisher's exact test, the difference in AFB positivity between the smears was statistically found significant with two-tailed *p* value of 0.0422. We also studied the spectrum of morphological features in cytological smears of all cases. The morphological features observed were presence of caseous necrosis, neutrophils, epithelioid cells, granulomas, lymphocytes, plasma cells and multinucleated giant cells. The distribution of these features in hundred cases is given in the (Table 5 and Figs. 1–7).

Table 5: Distribution of morphological features in cytological smears of tuberculous lymphadenitis

Caseous necrosis	Nil 22	Foci 17	Background 34	Extensive 27
Neutrophils	Nil 24	Few 58	Moderate 7	Marked 11
Epithelioid cells	Few 57	Moderate 33	Marked 10	
Lymphocytes	Nil 5	Few 42	Moderate 26	Marked 28
Plasma cells	Nil 72	Few 27	Moderate 1	Marked 0
Granulomas	Ill-defined 65	Well-defined 35		
Multinucleated giant cells	Nil 79	Present 21		

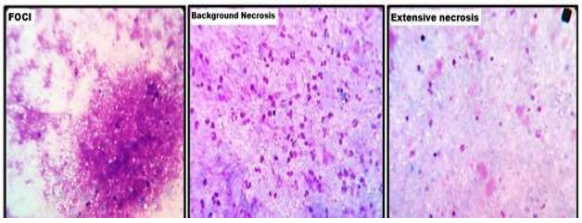

Fig. 1: FNA smears of tuberculous lymphadenitis showing focal, background and extensive necrosis.

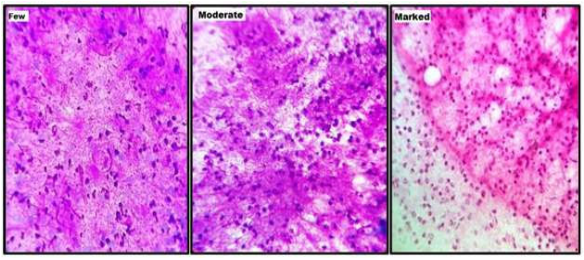

Fig. 2: FNA smears of tuberculous lymphadenitis showing few neutrophils, moderate and marked neutrophilic infiltration.

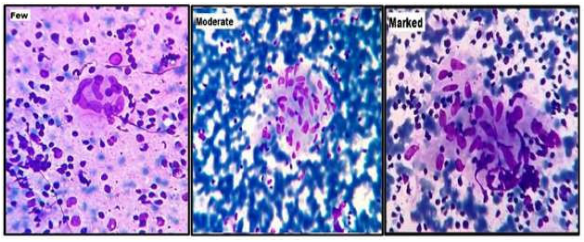

Fig. 3: FNA smears of tuberculous lymphadenitis showing few epithelioid cells in a cluster, moderate number of epithelioid cells and numerous epithelioid cells.

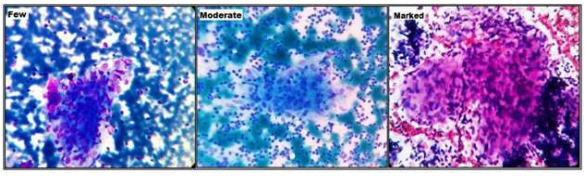

Fig 4: Microphotograph of FNA of tuberculous lymphadenitis showing epithelioid granulomas with sparse lymphocytes, moderate lymphocytes and extensive lymphocytes.

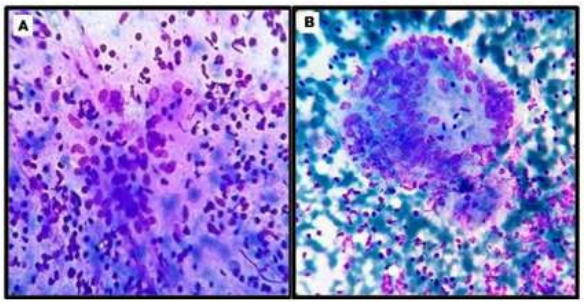

Fig 5: Microphotograph of FNA of tuberculous lymphadenitis showing (A) ill formed granuloma; (B) well formed granuloma.

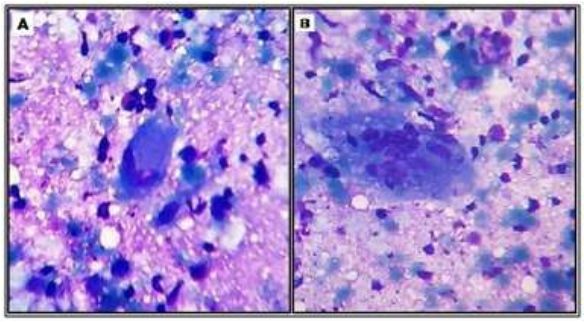

Fig 6: Multinucleated giant cells (A) Langhan giant cell (B) Foreign body type giant cell.

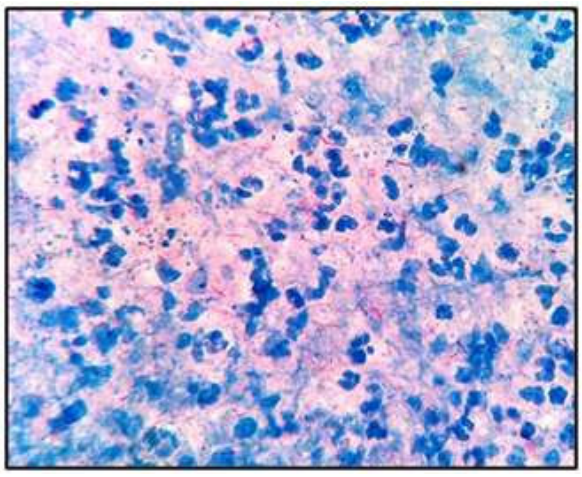

Fig 7: Ziehl Neelsen stained smear showing acid fast bacilli positivity.

Discussion

Tuberculosis is one of the most common diseases worldwide. In 2015, it is estimated that 10.4 million new TB cases globally and 1.8 million deaths due to TB. There were an estimated 2.8 million new cases in India and 0.48 million TB deaths in 2015.[1] Lymphadenitis is the most common extrapulmonary manifestions in tuberculosis and in order to manage this huge disease burden with limited resources, FNAC is considered as one of the safe and economical investigations in the diagnosis of tuberculosis.

Tuberculosis caused by low virulent acid fast bacilli, *Mycobacterium tuberculosis* tend to activate the cell mediated immunity and produces a delayed hypersensitivity reaction. As a result, activated macrophages and T lymphocytes form the aggregates called as granulomas with or without caseating necrosis in the center. Thus, cytological evaluation of tuberculous lymphadenitis could yield epithelioid granulomas without necrosis (Pattern A), epithelioid granulomas with necrosis (Pattern B) or caseating necrosis without granulomas (Pattern C).[2] Although similar pattern of epithelioid granulomas can be seen in various clinical conditions like sarcoidosis, leprosy, cat scratch disease, foreign body granuloma, foci of caseous necrosis and demonstration of AFB using ZN stain confirms tuberculosis.

The most frequent cytological pattern in our study is "Pattern B" seen in 49% of cases which is similar to the study done by Khanna et al. (50.5%).[6] Least common pattern in our study was "Pattern A" (22%) which was consistent with study done by Das et al., Khanna et al. and LlatJos et al. (Table 6).[4,6,7]

Table 6: Comparison of cytological patterns of tuberculous lymphadenitis with other studies

Study	Pattern A	Pattern B	Pattern C
Das et al.[4]	25.3%	39.1%	35.6%
Khanna et al.[6]	21.8%	50.5%	27.7%
Llat Jos et al.[7]	17.29%	30.43%	52.17%
Present study	22%	49%	29%

Overall AFB positivity was seen in 18/100 cases. Maximum AFB positivity was observed in "Pattern C" smears (34.5%) i.e., smears containing only caseating necrosis without granulomas followed by Pattern B (14.2%) and lowest in Pattern A smears (4.5%) and is similar to study done by Hemalatha et al., Paliwal Nidhi et al. and Khanna et al. (Table 7).[2,5,6]

Table 7: Comparison of AFB positivity with respect to cytological patterns of tuberculous lymphadenitis in different studies

Study	AFB Positivity		
	Pattern A	Pattern B	Pattern C
Hemalatha et al.[2]	6/29 (21%)	46/84 (55%)	25/34 (73.5%)
Paliwal Nidhi et al.[5]	4/25 (3.2%)	20/29 (69.5%)	59/69 (85.5%)
Khanna et al.[6]	2/26 (7.6%)	11/60 (18.3%)	10/33 (30.3%)
Present study	1/22 (4.5%)	7/49 (14.2%)	10/29 (34.5%)

The AFB positivity in necrotic smears (Pattern C) was compared to AFB positivity in smears with granulomas without necrosis (Pattern A) using

Fischer-exact test and was found statistically significant (p = 0.0422) and this was consistent with the literature that whenever macrophage activation is minimal it lead on to exuberant tissue destruction with liquefaction containing the bacilli resulting in maximum AFB positivity.

Present study showed that no age group was exempted from the disease and tuberculous lymphadenitis also involved inguinal and axillary groups of lymph nodes which is similar to the studies done by Hemalatha et al., Paliwal Nidhi et al. and Khanna et al.[2,7,8] Cytological smear patterns from early stages usually yeilded inflammatory cells similar to reactive lymph node. Presence of neutrophils does not rule out tuberculous lymphadenitis in our study.

Present study shows that tuberculous lymphadenitis follows a spectrum as the disease progresses from early to late stages. Early stages show suppuration, necrosis without granulomas. As immune response is mounted, ill defined granulomas with scattered and few epithelioid cells are seen. In later stages, well defined granulomas are seen and caseous necrosis disappeared with immunoreaction to the infection. These findings were consistent with the studies done by Das et al., Hemalatha et al. and Khanna et al.[2,4,8]

Conclusion

Tuberculous infection of lymph nodes follows a spectrum as the disease progresses. All patterns must be kept in mind while reporting when tuberculosis is suspected. Fine Needle Aspiration Cytology is quick, reliable as well as conclusive for diagnosing tuberculous lymphadenitis when done along with ZN staining for AFB.

Conflicts of Interest: None

Sources of support: None

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