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Original Research Article

Cytopathological patterns of tuberculous lymphadenitis: an analysis of 126 cases in a tertiary care hospital

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ABSTRACT

Background: Tuberculous lymphadenitis is one of the most common causes of lymphadenopathy in developing countries. Fine needle aspiration cytology (FNAC) has important role in the diagnosis of tuberculous lymphadenitis. The objective of this study was to evaluate the cytopathological patterns of tuberculous lymphadenitis and to correlate with Ziehl-Neelsen (ZN) staining.
Methods: FNAC of 126 cases diagnosed as tuberculous lymphadenitis over a period of three years were reviewed. FNAC findings were categorized into three patterns: pattern A- epithelioid granuloma without caseous necrosis, pattern B- epithelioid granuloma with caseous necrosis, pattern C- caseous necrosis without epithelioid granuloma. Chi-square test was done to correlate cytopathological pattern and acid fast bacilli (AFB) positivity.
Results: Tuberculous lymphadenitis was most frequent in the age group of 21-30 years (40.5%). Most common lymph node involved was cervical lymph node (82.53%). The most common pattern observed was Pattern B- Epithelioid granuloma with caseous necrosis in 53.17% cases. Overall AFB positivity was seen in 34.92% cases. Maximum AFB positivity was seen in Pattern C- Caseous necrosis without epithelioid granuloma in 81.81% cases. Serum adenosine deaminase (ADA) was elevated in 66.66% patients.
Conclusions: FNAC is safe and cost effective diagnostic tool for the diagnosis of tuberculous lymphadenitis. Ziehl-Neelsen stain for Acid fast bacilli and Serum ADA can be used as an adjunctive tool for the diagnosis of tuberculous lymphadenitis.

Keywords: Acid fast bacilli, Cytopathological patterns, Tuberculous lymphadenitis

INTRODUCTION

Lymphadenitis is the most common clinical appearance of extrapulmonary tuberculosis. Tuberculous lymphadenitis is one of the most common cause of lymph node enlargement in developing countries.[1] Diagnosis of tuberculosis can be done by various diagnostic methods as fine needle aspiration cytology (FNAC), biopsy, Acid fast bacilli (AFB) culture and polymerase chain reaction (PCR). FNAC is a routine cytological technique for diagnosis of tuberculous lymphadenitis as it has sensitivity and specificity of 88-96%. FNAC is economical and rapid compared to other tests as AFB culture and PCR.[2] It prevents unnecessary biopsy of lymph nodes and it can be used for collection of material for cytopathological and bacteriological examination.[3]

For cytological diagnosis of tuberculosis, demonstration of epithelioid cell granulomas with or without caseous necrosis is needed.[4-8] Demonstration of AFB bacilli by Ziehl-Neelsen (ZN) stain provides definitive diagnosis. Other tests as serum adenosine deaminase (ADA)can also

be used as an adjunctive tool for diagnosis. This study was conducted with the following objectives

- To evaluate the cytopathological patterns of tuberculous lymphadenitis
- To correlate the cytopathological patterns with Ziehl-Neelsen stain.

METHODS

This was a retrospective study carried out in the department of Pathology and Biochemistry at KIST Medical College over a period of three years (January 2015 to Jan 2018). One hundred twenty-six patients diagnosed as tuberculous lymphadenitis on FNAC of peripheral lymphadenopathy were included in the study. The data were collected from computer database. Fine needle aspiration slides stained with wright stain and ZN stain were reviewed. All cases were categorized cytologically into three categories as suggested by Das et al.[5] The cytomorphological patterns were: pattern A- epithelioid granuloma without caseous necrosis, pattern B- epithelioid granuloma with caseous necrosis, pattern C- caseous necrosis without epithelioid granuloma with neutrophilic infiltrate. ZN stain in all cases were reviewed. The diagnosis of tuberculous lymphadenitis was based on characteristic cytomorphological features consisting of epithelioid granuloma with or without Langhan giant cells and caseous necrosis and confirmed by ZN stain. Data analysis was done using the Statistical Package for Social Science (SPSS, Version 17) for windows. Chi-square test was done to correlate cytomorphological pattern and AFB positivity. A P value <0.05 was considered as significant.

RESULTS

Out of 126 patients, 59 (46.83%) were males and 67 (53.17%) were females. The age of the patients ranged from 1-71 years with mean age being 28.97±14.4 Years. There was slight female preponderance with male to female ratio of 1:1.13. The disease was more commonly seen in the age group of 21-30 years followed by 11-20 years (Table 1). Most commonly involved lymph node was cervical (82.53%) followed by inguinal lymph node (9.52%).

Table 1: Distribution of tuberculous lymphadenitis in different age groups.

Age group	Male	Female	Total	%
1-10 yrs	8	0	8	6.34
11-20 yrs	9	17	26	20.63
21-30 yrs	19	32	51	40.47
31-40 yrs	10	11	21	16.7
41-50 yrs	4	3	7	5.55
51-60 yrs	5	3	8	6.34
61-70 yrs	2	2	4	3.17
71-80 yrs	1	0	1	0.8

The cytopathological patterns were divided into three groups: pattern A- epithelioid granuloma without caseous necrosis, pattern B- epithelioid granuloma with caseous necrosis, pattern C- caseous necrosis without epithelioid granuloma (Table 2, Figure 1). The most common pattern observed was Pattern B (67 cases, 53.17%). ZN stain for AFB (TB) showed AFB positivity in 44 cases. Thus, overall AFB positivity was 34.92%.

Table 2: Cytopathological patterns of tuberculous lymphadenitis.

Cytopathological pattern	Total No of cases	AFB positive cases	AFB negative cases
Epithelioid granuloma without caseous necrosis	48	1	47
Epithelioid granuloma with caseous necrosis	67	34	33
Caseous necrosis without epithelioid granuloma	11	9	2
Total	126	44	82

AFB positivity in three cytopathological patterns was as follows: A-1/48 (2.08%), B-34/67 (50.74%) and C-9/11 (81.81%). Thus, maximum AFB positivity was seen in pattern C. Distribution of AFB positivity among three groups were statistically significant (P value <0.001 and Chi square 40.8). Out of 126 patients of tuberculous lymphadenitis, serum ADA was done in 28 patients. Elevated serum ADA was found in 18 patients (64.28 %).

DISCUSSION

FNAC is simple, safe and cost effective outpatient procedure. It is used as a first line of investigation for the reliable diagnosis of tuberculous lymphadenitis in patients presenting with lymphadenopathy.[9] Tuberculous lymphadenitis can be seen in any age group. In our study the mean age of presentation was 28.97±14.4 years. Maximum incidence of tuberculous lymphadenitis was seen in the age group of 21-30 years followed by 11-20 years. This finding is in agreement with the study by Hemalatha A et al, and Paliwal N et al.[10,11] Our study showed slight female predominance with male to female ratio of 1:1.13. This is in concordance with other studies.[1,3,11,12] Cervical lymph node was the most common site involved (85.53%) in the present study which was similar to other studies.[1,11,13] Paliwal N et al, and Bezabih M et al noted cervical lymph node involvement in 90% and 74.2% of cases respectively.[11,13]

In the present study the lesions were categorized into three cytomorphological patterns: pattern A- epithelioid granuloma without caseous necrosis, pattern B- epithelioid granuloma with caseous necrosis, pattern C- caseous necrosis without epithelioid granuloma with neutrophilic infiltrate. The most common cytomorphological pattern observed in our study was epithelioid granuloma with necrosis, seen in 53.17% cases. This was also the commonest pattern in the study by Khanna A et al, Bhattacharya S et al and Prasoon D et al.[14-16] They reported this pattern in 50.5%, 69.4% and 44.2% of cases respectively. The presence of caseous necrosis without epithelioid granuloma was the least common pattern in our study, seen in 8.73% cases. Das DK et al and Bhattacharya S et al reported this pattern in 25.3% and 17.7% cases respectively.[5,15] It was the most common pattern in other studies.[11,13] The most important finding for the diagnosis of tuberculosis is the presence of epithelioid cells which was seen in 91.2% of our cases. Giant cells were seen in 17.4% of all cases.

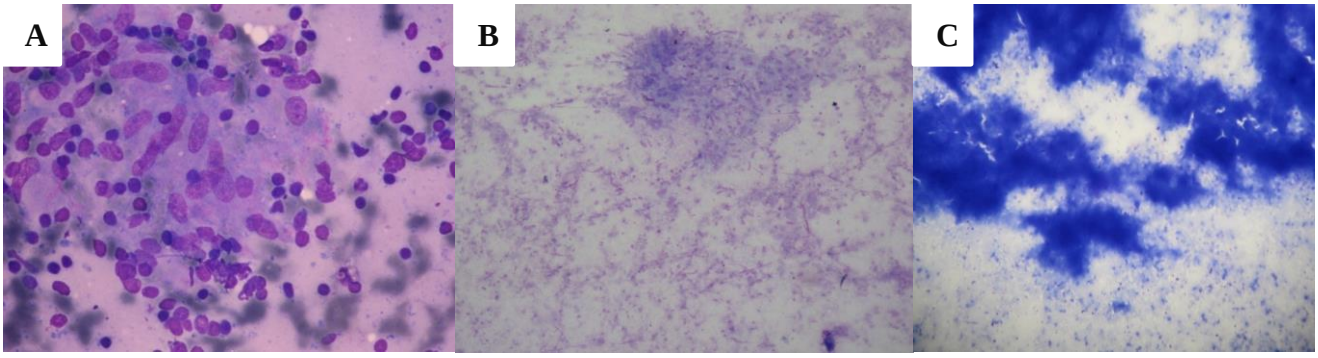

Figure 1. Cytopathological patterns of tuberculous lymphadenitis: A. Epithelioid granuloma without necrosis. B. Epithelioid granuloma with necrosis. C. Only caseous necrosis without epithelioid granuloma.

The overall AFB positivity in the present study was 34.92%. In different studies AFB positivity was seen ranging from 7.4 to 55.2% cases.[5,15-18] In our study, there was inverse relationship between AFB positivity and granuloma. Highest AFB positivity was seen in smears with only necrosis or neutrophilic infiltrate (81.81%), whereas least AFB positivity was seen in smears with only epithelioid granulomas (2.08%). The findings were similar to the study by Paliwal N et al, who demonstrated 85.5 % AFB positivity in cases having caseous necrosis only and 3.2% AFB positivity in smears having epithelioid granuloma without necrosis.[11] Cell mediated immunity of the patient elicits granulomatous response against tubercle bacilli, hence smears containing epithelioid granuloma without necrosis show least AFB positivity. The smears with only necrotic material show maximum AFB positivity due to compromised immune status of the patient and lack of granulomatous response.[15] Paliwal N et al and Bezabih M et al reported 71% and 59.5% overall AFB positivity respectively.[11,13] The low AFB positivity in our study may be due to the presence of epithelioid cell granulomas with or without necrosis in maximum cases (91.2%) in contrast to the study by Paliwal N et al where it was 30.7%.[11] AFB positivity can be increased by doing repeat FNAC.[19] The difference among three cytological patterns and AFB positivity in our study were statistically significant ($p<0.001$).

Diagnostic difficulties arise in smears showing only epithelioid cell granuloma with AFB negativity. Such pattern can be seen in sarcoidosis, brucellosis, Hodgkin lymphoma and metastatic disease. Smears showing only necrosis without epithelioid cell granuloma and AFB negativity can be seen in malignancy, especially squamous cell carcinoma in elderly patients. In such cases clinical correlation along with other investigations as biopsy, AFB culture, ADA and PCR may be useful. PCR has been found to be valuable in cases with absence of granuloma or necrosis with 100% diagnostic accuracy if FNAC is combined with PCR.[20]

In our study, Serum ADA level was elevated in 64.28% patients. The cut off value for serum ADA was taken as 14U/L.[21,22] Mugulkod P et al, found raised serum ADA levels in 83.3% cases in their study.[23] Serum ADA is an indicator of active cellular immunity. It has a role in granuloma formation as it causes proliferation and differentiation of T lymphocytes and maturation of monocytes transforming them to macrophage.[21,22] Raised serum ADA level in the presence of strong clinical suspicion or typical cytological features with negative AFB are valuable for the diagnosis of tuberculosis.

CONCLUSION

FNAC is useful for the diagnosis of tuberculous lymphadenitis. In developing countries with high prevalence of tuberculosis, FNAC coupled with ZN stain should be the first line of investigation in patients presenting with superficial lymphadenopathy. Serum ADA levels are an adjunct to FNAC in the diagnosis of tuberculous lymphadenitis.

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