Original Article

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Pathology Section

An Insight on Cytomorphological Patterns of Tuberculous Lymphadenopathy in Paediatric Age Group

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ABSTRACT

Introduction: The incidence of Tuberculosis (TB) in a developing country like India is very high. Lymphadenopathy is the commonest extrapulmonary manifestation of the disease. In rural and remote areas of India where adequate infrastructure is not available, many cases remain undiagnosed for a long time. Fine Needle Aspiration Cytology (FNAC) may be used as an important diagnostic tool in these cases.

Aim: To provide an insight in the cytomorphological patterns of tuberculous lymphadenopathy complemented with Acid Fast Bacilli (AFB) staining in patients of paediatric age group.

Materials and Methods: It was an observational study involving 175 patients of 0-18 years of age, presenting with peripheral lymphadenopathy in the Out Patient Department/In Patient Department (OPD/IPD) of different departments of Silchar Medical College and Hospital, Silchar, Assam. The duration of the study was one and half years from June 2013 to December 2015. FNAC was done from the enlarged lymph nodes and smears were stained with Giemsa, Papanicolaou, and Ziehl-Neelsen (ZN) staining. Cytomorphological analysis was made for the cases diagnosed with tuberculous lymphadenopathy. Simple statistical analysis was done using Microsoft (MS) EXCEL 2013.

Results: Out of 175 cases, 58 (33.14%) cases were diagnosed with tuberculous lymphadenopathy. Cervical lymph nodes were most commonly involved (42 cases, 72%), followed by axillary lymph nodes, and then generalised lymphadenopathy followed by inguinal lymph node involvement. Cytomorphological analysis showed 33 (56.89%) cases of epithelioid granulomas with caseous necrosis; 14 (24.14%) cases of epithelioid granulomas without caseous necrosis and 11 (18.97%) cases of caseous necrosis without epithelioid granulomas. Overall AFB positivity was 34.48%. Necrosis was found to be associated with highest AFB positivity (81.82%).

Conclusion: The incidence of tuberculous lymphadenopathy in the current study was significantly high. In a resource poor setting, FNAC is useful in diagnosing tuberculous lymphadenopathy where cytomorphology can be complemented with AFB staining to improve diagnostic accuracy.

Keywords: Acid fast bacilli, Extrapulmonary tuberculosis, Fine needle aspiration cytology

INTRODUCTION

According to India TB report 2019, a total number of notified TB cases in India was 2.15 million in 2018 and among them 34.1% cases belong to under 19 years of age group [1]. The burden of Extrapulmonary Tuberculosis (EPTB) is high ranging from 15-20% of all TB cases in HIV-negative patients, while in Human Immunodeficiency Virus (HIV) positive people, it accounts for 40-50% of new TB cases [2]. Lymphadenopathy is the most common clinical presentation of EPTB [3,4]. Tuberculous lymphadenopathy is encountered in nearly 35% of EPTB cases [5,6].

FNAC is one of the most important diagnostic investigations in the evaluation of tuberculous lymphadenopathy. It is a safe, easy, cost effective as well as less time-consuming process which minimises the requirement of an invasive excisional biopsy in majority of cases [6,7].

Since the burden of TB is high in India and use of expensive diagnostic techniques is restricted due to limited logistics in most cases, presence of epithelioid cell granulomas with or without necrotic material is considered to be an evidence of tuberculous lymphadenopathy, even there is absence of AFB in ZN stained smears [3,4]. There are very few studies in paediatric age group with FNAC in India. Therefore authors have tried to highlight the role of FNAC, which is a simple diagnostic tool, yet underused. The aim of the present study was to analyse cytomorphological profile of tuberculous lymphadenopathy complemented by AFB staining. The objective was to emphasise the importance of FNAC, which is a comparatively undervalued diagnostic tool even in resource poor setting in India.

MATERIALS AND METHODS

This was a prospective, observational study undertaken in Department of Pathology, Silchar Medical College and Hospital, Silchar, Assam, India for a period of one and half years from June 2013 to December 2015. The study was approved by the institutional ethical committee. The study group included 175 patients of paediatric age group (0-18 years) presenting with significant superficial lymphadenopathy in the Department of Paediatrics, Medicine, Otorhinolaryngology, Ophthalmology and Surgery, Silchar Medical College and Hospital.

Significant lymphadenopathy was defined in the following manner [8]:

i. Enlargement of cervical lymph node >1 cm.

ii. Palpable axillary lymph node of any size

iii. Palpable inguinal lymph node > 1.5 cm.

iv. Palpable epitrochlear lymph node of any size

(All the measurements were taken in the largest diameter of the affected lymph node)

Relevant history regarding duration of lymph node enlargement, presence or absence of fever, weight loss, cough, night sweats, drug intake, history of contact etc. was obtained. All patients were screened for hepatitis B, hepatitis C and HIV infections.

Inclusion criteria: Patients of paediatric age group between 0 to 18 years with palpable lymphadenopathy as defined above, and FNAC diagnosis with tuberculous lymphadenopathy were included in the study.

Exclusion criteria: All cases with FNAC diagnosis other than tuberculous lymphadenopathy and cases in which lymphadenopathy was resolved after taking a course of antibiotics were excluded from the study.

FNAC was done from enlarged lymph nodes using a 10 mL disposable syringe and 22G needle. 4-5 air dried smears were prepared in each case and stained with Giemsa, Papanicolau and ZN stain. Cytomorphological evaluation was done.

It was an observational study, therefore all the patients presenting with lymphadenopathy and meeting the inclusion criteria were enrolled (no pre-calculated sample size was targeted for the study); all paediatric patients diagnosed with tuberculous lymphadenopathy within the study duration were included in the study group. And cytomorphological patterns were analysed together with frequency of AFB positivity.

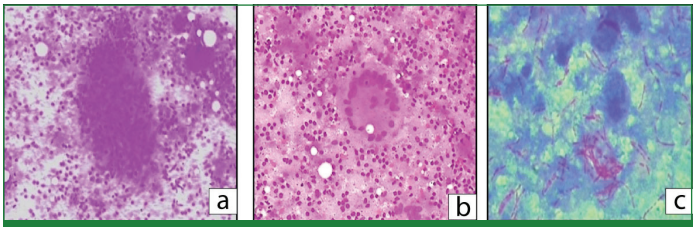
STATISTICAL ANALYSIS

Simple statistical analysis done with the help of MS Excel 2013. Percentages and descriptive statistics were used to analyse the data.

RESULTS

The diagnosis of TB lymphadenopathy was made if the aspirate from FNAC showed ZN stain positive for AFB, and/or granulomatous changes with or without necrosis.

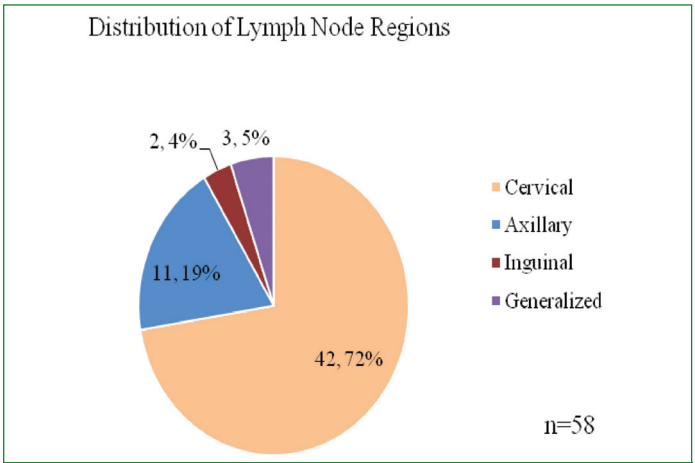
[Table/Fig-1] is showing cytomorphological findings of lymph node of a case of tubercular lymphadenopathy in the present study including a granuloma, a Langhans Giant Cell and Acid Fast Bacilli.



[Table/Fig-1]: FNAC lymph node of a case of tubercular lymphadenopathy. {a. Granuloma (MGG stain x100), b. Langhans Giant Cell (MGG stain, x400), C. Acid Fast Bacilli (ZN Stain, x1000)}

Among 175 cases, 58 (33.14%) cases were of tuberculous lymphadenopathy. In the study population, 31 patients (53.44%) were male. The male:female ratio was 1.15:1. Among total 58 cases, only 5 (8%) cases were found to have contact history.

Cervical lymph nodes were most commonly involved, followed by axillary lymph nodes, and generalised lymphadenopathy followed by inguinal lymph nodes. As shown in [Table/Fig-2], cervical 42 (72%) followed by axillary 11 (19%) were the commoner group of lymph nodes involved. Presenting features other than lymph node enlargement are given in the [Table/Fig-3].



[Table/Fig-2]: Distribution of lymph node regions.

Clinical features	Number of patients (n)	Percentage (%)
Fever and Cough	38	65.52%
Weakness	5	8.62%
Weight loss	6	10.35%
Haemoptysis	1	1.72%
Asymptomatic	5	8.62%
Others (malaise, anorexia etc.)	3	5.17%

[Table/Fig-3]: Clinical features of the patients evaluated for lymphadenopathy.

Chest X-ray findings: Among 58 cases, lung involvement was found in 10 cases (17.24%).

Cytomorphological pattern: On the basis of cytomorphological analysis, cases of TB lymphadenopathy were categorised into three patterns:

1. Epithelioid granulomas with caseous necrosis
2. Epithelioid granulomas without caseous necrosis
3. Caseous necrosis without epithelioid granulomas

As shown in [Table/Fig-4], typical epithelioid granuloma with caseous necrosis was found in 33 cases (56.89%). Percentage of AFB positivity varied in different cytomorphological patterns of tuberculous lymphadenopathy. Total 20 cases (34.48%) were AFB positive. Caseous necrosis without epithelioid granuloma pattern was found to be associated with highest AFB positivity (81.82%).

Cytomorphological pattern	Number of cases, n (%)	AFB positivity, n (%)
Epithelioid granuloma with caseous necrosis	33 (56.89)	10 (30.30)
Epithelioid granuloma without caseous necrosis	14 (24.14)	01 (7.14)
Caseous necrosis without epithelioid granuloma	11 (18.97)	09 (81.82)

[Table/Fig-4]: AFB positivity in different cytomorphological pattern.

DISCUSSION

The burden of TB is high in India and use of expensive diagnostic techniques is not always possible in resource poor settings, presence of epithelioid cell granulomas with or without necrotic material even in the absence of AFB in ZN stained smears is considered as evidence of tuberculous lymphadenopathy [3,4].

With this background, this study was performed to analyse cytomorphological profile of tuberculous lymphadenopathy complemented by AFB staining to aid in timely diagnosis of this commonest presentation of the EPTB which can lead to the definitive management of these cases.

Among the total 175 cases, 58 (33.14%) cases were of tuberculous lymphadenopathy. In similar studies done by, Dhingra V et al., Handa U et al., and Sharma M et al., the percent of tuberculosis lymphadenopathy was 28.1%, 25.2% and 16% respectively [9,10,11].

In the present study, most commonly affected age group was of 10-18 years, whereas it was 11-20 years and 7-14 years in the studies done by Jha BC et al., and Ahmed S et al., respectively [12,13]. Male patients slightly outnumbered female patients with a male: female ratio of 1.15:1. The study by Seth V et al [14] also revealed male predominance with an M:F ratio 1.15:1, which was in concordance with studies done by Seth V et al. (M:F =1.5:1) and Giri S et al. (M:F=2:1) [14,15]. Cervical lymph nodes were most commonly involved region, followed by axillary lymph nodes, same as in studies done by Dhingra V et al., Sen R et al. and Narang P et al. [9,16,17]. Bezabih M et al., also found highest incidence in cervical lymph nodes, followed by involvement of axillary lymph nodes and inguinal lymph nodes [18]. The recent analysis done by Masilamani S et al., also reflects the similar findings [19].

In this study, 60% of all matted lymph nodes and 25% of all discrete lymph nodes were due to tuberculous lymphadenopathy. This finding matches well with that of Narang P et al., who had done their study on Indian children and found that 66.7% of matted lymph nodes and 26.7% of all discrete lymph nodes were due to tuberculous lymphadenopathy [17].

Among 58 cases, only 8% cases were found to have contact history, in the current study. Narang P et al., found 6.316% cases with positive contact history [17]. In the present study, other than lymph node enlargement, patient presented with fever and cough, weight loss, and weakness. One patient presented with haemoptysis. Five patients (8.68%) patients had asymptomatic lymph node enlargement only. Handa U et al., stated that patients usually presented with slowly enlarging lymph nodes which might otherwise be asymptomatic [20]. Some patients might manifest systemic symptoms such as fever, weight loss and fatigue. Jha BC et al., found that other than lymph node swelling, patients presented with malaise, weight loss, fever, cough and haemoptysis [12].

Among the 58 cases, lung involvement was found in 10 cases (17.24%). In a review study done by Mohapatra PR and Janmeja AK, it was mentioned as, associated chest lesions as seen on chest radiography were very common in children but less common in adults, evident nearly in 15% cases [3]. This finding was also supported by the result of the studies done by Dandapat MC et al., and Kanlikama M et al., [21,22]. Jha BC et al., found in their study that associated lung involvement was 16% as detected by chest radiography [12].

In the present study, overall AFB positivity was 34.48%. previous studies, such as, studies by Dasgupta S et al., Dhingra V et al., Lau SK et al., Das DK et al., Llatjos M et al., Vignesh R et al., Sethuraman G et al., show that AFB positivity in tuberculous lymphadenopathy ranges from 7% to 70% [6,9,23-27]. As previously discussed, three types of cytomorphological patterns of tuberculous lymphadenopathy were found. Their distribution in the study population in the present study and previous studies were compared and summarised in the following table [Table/Fig-5] [6,9,10,24,25].

Study	Cytomorphological patterns		
	Epithelioid granuloma with caseous necrosis	Epithelioid granuloma without caseous necrosis	Caseous necrosis without epithelioid granuloma
Present study	56.89%	24.13%	18.96%
Dasgupta S et al., 2017 [6]	26%	21%	53%
Dhingra V et al., 2010 [9]	67.10%	32.89%	0%
Handa U et al., 2003 [10]	46.85%	31.43%	21.71%
Das DK et al., 1990 [24]	39.1%	25.3%	35.6%
Llatjos M et al., 1988 [25]	30.43%	17.29%	52.17%

[Table/Fig-5]: Comparison of distribution of cytomorphological patterns with relevant published literature [6,9,10,24,25].

Das DK et al., found in a multivariate regression analysis that necrosis was the only independent contributing factor in AFB positivity [24]. Low AFB positivity can be explained by the facts that many cases of EPTB are pauci-bacillary and early stage of the disease and variable immunologic status of the patients. Number of AFB has to be 103 to 106/mL of the material to be detected by light microscopy. Necrosis was found to be associated with highest AFB positivity in the present study. This finding also matches with that of Dasgupta S et al., and Giri S et al., [6,15]. Chandanwale S et al., found in a multivariate regression analysis that necrosis was the only independent contributing factor in AFB positivity [28]. Llatjos M et al., studied cytologic pattern for diagnosing tuberculous lymphadenitis in AIDS and concluded that FNAB is a useful, inexpensive, and safe technique in HIV-infected patients and stated that the finding of a necrotising lymphadenitis pattern is suggestive enough to start anti-tuberculous treatment [25].

Limitation(s)

The impact of the result of the study was limited by less number of cases, short duration of the study and limitation of resources which prevented inclusion of culture and molecular techniques in the methods. In a resource constraint set up like in our cases where facilities for culture and molecular study of these cases were not available and could not be done as part of the study, an insight into the cytomorphological patterns complemented with AFB staining is still an important and essential tool for not to miss the cases of tuberculous lymphadenopathy in children.

CONCLUSION(S)

The present study was an effort to throw a light on the cytomorphological pattern of tuberculous lymphadenopathy in the paediatric population in the resource poor setting. The study corroborated with the fact that, in this geographic region, the disease continues to be one of the leading causes of lymphadenopathy in paediatric age group. As many cases of TB lymphadenopathy did not reveal AFB positivity, a meticulous interpretation of different morphological patterns of TB lymphadenopathy is essential for early and appropriate cytological diagnosis.

Future studies are needed with longer duration, larger study population and improved laboratory facility for correlation with culture and molecular studies to evaluate different clinico-pathologic aspects of tuberculous lymphadenopathy in children.

Authors' contributions: BD, SKB and SC contributed in concept, design, literature search, clinical studies, acquisition, analysis or interpretation of data and statistical analysis. BD and PKM contributed in manuscript preparation and manuscript editing. All the authors critically reviewed the manuscript and approved it. All the authors will act as guarantor(s) of this manuscript.

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