Tuberculous lymphadenopathy in cervical and axillary lymph nodes as determined by fine needle aspiration cytology

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Author Contributions

MW conceived idea, MW MYK planned the study MW MYK NI drafted the manuscript, MW NI collected data, did statical analysis and interpretation, MW MYK critical reviewed manuscript MYK approved the final version to be published.

Declaration of conflicting interests

The Authors declares that there is no conflict of interest.

ABSTRACT

Background: The extent of workup in patients with cervical lymphadeponpathy has always been controversial. Extensive workup in the absence of a histologic diagnosis indicative of a malignant process is unwarranted. Although open byopsy maybe necessary for certain benign conditions, its routine application for metastatic nodes is not advised.

Objective: To determine the histological pattern of Fine needle aspiration cytology (FNAC) in patients of tuberculous cervical and axillary lymphadenopathy.

Materials and methods: This was a correctional descriptive study conducted at advance medical laboratory, Peshawar - Pakistan from September 2016 - October 2017. Fifty Four patients presenting with enlarged cervical and axillary lymph nodes of all ages and both sexes referred to Advanced Medical Laboratory, Peshawar were included in the study. All the patients underwent FNAC. The slides were prepared and examined by the histopathologist. The diagnoses were recorded in predesigned proforma and results were drawn accordingly.

Results: A total of 54 patients with cervical and axillary lymphadenopathy were included in the study. Age of the study sample ranged from 3-35 years, with mean age of 24 years ± 3 SD. Out of 54 patients, 40 (74%) patients were males and 14 (26%) patients were females. Male to female ratio was 2.8:1. FNAC findings showed that the commonest cause of lymphadenopathy was chronic granulomatous lesion, which was seen in about 43 (79%) cases, followed by 8 (15%) cases of reactive lymphoid hyperplasia, and 1 (2%) case each of lymphoproliferative disorder and metastatic disease .Out of 43 cases of granulomatous lesion, about 30 (56.5%) cases had well formed granuloma suggestive of tuberculosis, while remaining 13 (24.5%) cases showed ill-formed granuloma. Evaluation of these 13 cases with sputum AFB, Montoux test and chest radiograph confirmed the diagnosis of tuberculosis in 6 (46%) cases only, while the remaining 7 (54%) cases could not be proved to have tuberculosis and so were labeled as having chronic non specific inflammation. Thus in total 36 (66.6%) patients had tuberculous lymphadenopathy.

Conclusion: Tuberculous granuloma is the commonest cause of cervical lymphadenopathy in our setup, followed by reactive hyperplasia . FNAC is a simple and minimally invasive procedure for the workup of tuberculous lymph nodes. Thus, FNAC should be part of the initial evaluation of patients with cervical lymphadenopathy before determining the treatment plan.

Keywords: Cervical lymph node; Fine needle aspiration cytology; Reactive hyperplasia; Tuberculous lymphadenitis; Tuberculosis

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Introduction

Lymphadenopathy is defined as an abnormal increase in the size of the lymph nodes due to accumulation of inflammatory or neoplastic cells in the lymph nodes.[1,2] Enlarged lymph nodes are encountered by the physicians and surgeons in clinical practice on daily basis.[3,4,5] In certain cases, lymphadenopathy poses a diagnostic challenge, because the laboratory and physical findings in such cases do not give clear final diagnosis.[6] As enlarged lymph nodes are easily accessible for fine needle aspiration, therefore FNAC is done in such cases to find the cause of lymph node enlargement.[1,5-7]

Lymph node enlargement is due to a number of causes, which may range from mild infections to life threatening malignant neoplasms like lymphoma.[8] Various bacterial and viral infections commonly cause lymphadenopathy.[9] Metastatic diseases involving lymph nodes and tuberculosis are also common causes of lymph node enlargement.[5,9,10] Drug reactions rarely lead to lymphadenopathy.[7] Lipid storage disorders, lymphoproliferative disorders and systemic lupus erythematosus are commonly seen disorders that cause lymphadenopathy.[7] So, a lot of differential diagnoses may be made on the basis of history and clinical examination, which can create confusion and diagnostic challenge.[8,11,12]

The evaluation of lymphadenopathy is a common diagnostic challenge for clinicians.[9] A detailed history and physical examination can help identify the cause of lymphadenopathy, but the final diagnosis can only be made by the examination of the lymph node specimen.[9] The various methods available for the examination of lymph nodes are fine needle aspiration cytology (FNAC) and open biopsy.[1,9] FNAC is a simple, cost effective and safe procedure.[1] Open biopsy of the lymph node is costly procedure, which needs anaesthesia and is time consuming.[1] FNAC of the enlarged lymph node is now preferred and thus has become an integral part of the initial investigationfor the patients presenting with lymphadenopathy.[13,14] The minimal invasive nature, early availability of report, and low cost of FNAC makes it preferred alternative to open biopsy for initial workup of lymph nodes enlargement.[8]

Tuberculosis has been reported to be the commonest cause of lymphadenopathy in our setup. The present study was conducted to determine histological pattern of cervical and axillary lymphadenopathy through FNAC in our setup, thus highlighting its diagnostic significance.

Materials and Methods

This was a cross sectional descriptive study conducted at Advanced Medical Laboratory, Peshawar, from September 2016 to October 2017. All patients referred for FNAC, presenting with cervical and axillary lymph node enlargement were included in the study. FNAC was performed. Slides were prepared and examined by the histopathologist. Cytological diagnosis was recorded and results were drawn accordingly.

Inclusion criteria: All patients referred for FNAC, presenting with cervical and axillary lymph node enlargement were included in the study.

Exclusion criteria: All patients with swellings in cervical and axillary region other than lymph nodes were excluded from the study.

Data Analysis

All data was analysed by using SPSS version 18.0. Continuous variables like age were measured in Mean and Standard deviation. Categorical variables like sex and FNAC diagnoses were measured in frequency and percentage

Results

A total of 54 patients were included in the study. Age of the study sample ranged from 3-35 years, with mean age of 24 years ± 3 SD. Out of 54 patients, 40 (74%) patients were male, and 14 (26%) patients were females. Male to female ratio was 2.8:1. FNAC findings showed that the commonest morphological pattern of lymphadenopathy was chronic

Table 1: Pattern of diseases diagnosed through FNAC in cervical and axillary lymphadenopathy

S No.	Pattern of disease	n (%)
1	Granulomatous lesion	44 (81.48)
2	Reactive Hyperplasia	8 (14.82)
3	Lymphoproliferative disorder	1 (1.85)
4	Metastasis to lymph node	1 (1.85)
	Total	54 (100)

Table 2: Morphological types of Granulomatous lesion

S.No	Type of Granulomatous lesion	n(%)
1	Well formed granuloma-tuberculous lymphadenitis	30 (68.2)
2	Ill formed granuloma	14 (31.8)
	Total	44 (100)

Table 3: Etiology of ill-formed granuloma

S. No	Eitiology	n(%)
1	Tuberculous lymphadenitis	6 (46)
2	Chronic non specific inflammation	7 (54)
	Total	13 (100)

granulomatous lesion, which was seen in about 44 (81.48%) cases, followed by 8 (14.82%) cases of reactive lymphoid hyperplasia, and 1 (1.85%) case each of lymphoproliferative disorder and metastatic disease (Table 1). Out of 44 cases of granulomatous lesion, about 30 (68.2%) cases had well formed granuloma suggestive of tuberculosis, while remaining 14 (31.8%) cases showed ill-formed granuloma (Table 2). Evaluation of these 13 cases with sputum AFB, Montoux test and chest radiograph confirmed the diagnosis of tuberculosis in 6 (46%) cases only, while the remaining 7 (54%) cases could not be proved to have tuberculosis and so were labeled as having chronic non specific inflammation (Table 3). Thus in total 36 (66.6%) patients were diagnosed with tuberculous lymphadenopathy.

Discussion

The development of the lymphatic system starts at the fifth week of gestation.[1] About two paired and two unpaired endothelial sacs are formed in fifth week of gestation.[1] These sacs form the lymphatic system in adults.[1] The human body contains about 800 lymph nodes.[1] About 300 lymph nodes are located in the neck which drain lymph nodes from various sites of head and neck .[1,2]

Enlarged lymph nodes are evaluated to find the etiology of the underlying condition.[5] FNAC is commonly used investigation to reach to the final diagnosis of enlarged lymph nodes.[5,7] The main role of FNAC in evaluating cervical and axillary lymph nodes in developed countries is to differentiate between metastatic lesions and reactive lymphoid hyperplasia.[5] If metastatic involvement of the lymph nodes is suspected cytologically, further tests are done to find the primary site of the malignancy.[5] While in developing countries, especially in the Indo-Pak subcontinent, tuberculosis is the commonest cause of cervical and axillary lymphadenopathy. Thus there is a trend among the clinicians to put these patients straightaway on anti-tuberculous drugs. This can sometimes In the present study, the age of study sample ranged from 3 years to 35 years with the mean of 24 years ± 3 years. Male to female ratio was 2.8:1. In a study done by Mabedi in 2014, mean age of study sample was 30 years ± 19 SD.[9] In another study done by Bosch in

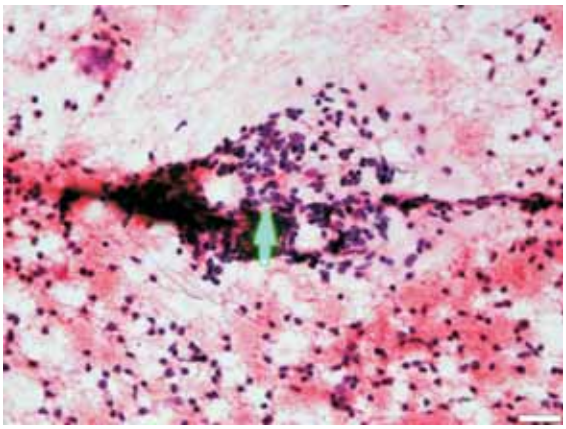

Figure 1: Photomicrograph of well-formed granuloma in cytological smear showing aggregate of epitheloid cells, surrounded by mature to reactive lymphocytes, plasma cells. Multinucleated giant cell is also present. (400x , Hematoxylin and Eosin stain)

2014 in Spain, the mean age of study sample was 45 years ± 14 SD with male to female ratio of 1: 1.3.[11] In another local study done by Fatima S in 2011, the mean age of study sample was 32 years, with male to female ratio of 1:1.5.[8] In all these studies, proportion of females was greater than males.[8,11] This finding is contrary to that in the present study, where males are predominant.

The most common cause of lymphadenopathy in the present study was chronic granulomatous lesion which was seen in 81.48% cases. The lymph node cytology showed well-formed caseating granulomas in about 68.2% cases, suggestive of tuberculosis (Figure 1). Ill-formed granulomas were seen in 31.8% cases (Figure 2). The sputum AFB, chest radiograph and Montoux test confirmed the diagnosis of tuberculosis in 46% of the 13 cases with ill-formed granuloma. While the remaining 54% cases had no evidence of tuberculosis, so they were labeled as chronic non-specific inflammation. Tuberculous lymphadenopathy was seen in 66.6% of cases. Reactive lymphoid hyperplasia was seen in 14.8% of the cases in the present study, and all of them presented with unilateral cervical or axillary lymphadenopathy (Figure 3). About 1.85% cases presented each with lymphoproliferative disorder and metastatic lymph node

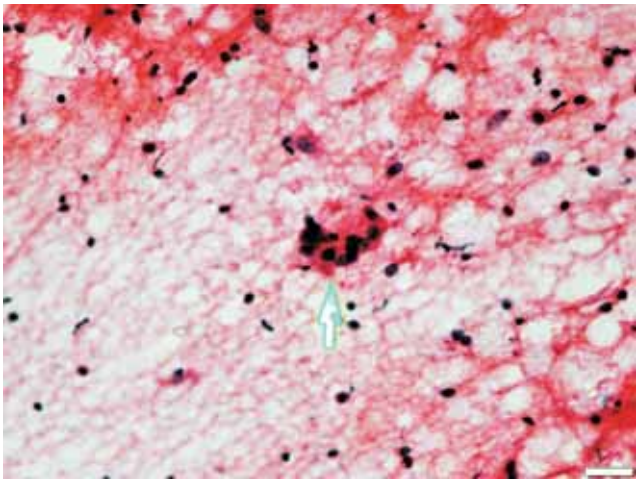

Figure 2: Photomicrograph of ill formed granuloma in cytological smear showing scattered epitheliod cells, Langhan's giant cells. Scattered mature and reactive lymphocytes. Arrow pointing towards giant cell. (400x , Hemotoxylin and Eosin stain)

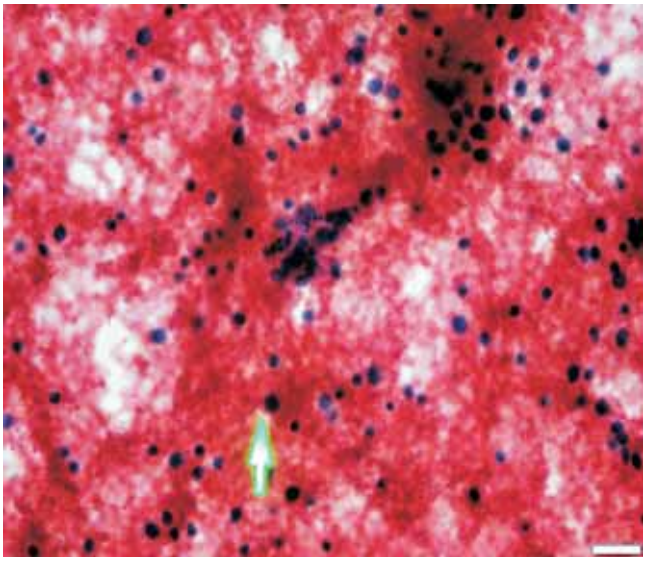

Figure 3: Photomicrograph of reactive hyperplasia in cytological smears showing tangible bodies, immunoblasts, reactive to mature lymphocytes. (400X , eosin and hematoxylin stain)

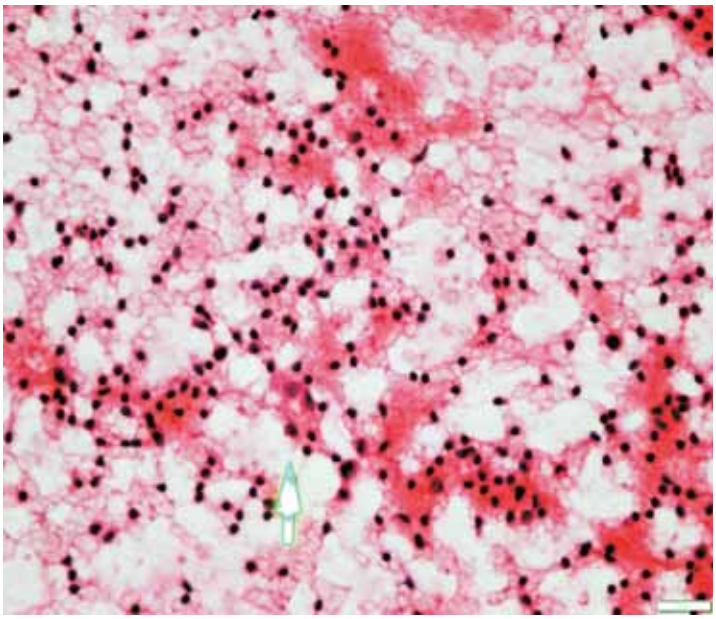

Figure 4: Photomicrograph of normal lymph node in cytological smears showing mature lymphocytes and scattered scanty macrophages. (400x Eosin and hematoxylin stain)

involvement (Table 1). Thus FNAC is very helpful in establishing a diagnosis of Tuberculous lymphadenitis.

In a study done by Bosch in Spain in 2014, the commonest cause of cervical lymphadenopathy was reactive lymphadenitis seen in 30% cases, followed by chronic non-specific inflammation seen in 24% cases, lymphoma in 24% cases, tuberculous lymphadenitis in 7% cases and metastatic carcinoma in 6%.[11] Reactive lymphadenitis was the commonest cause, while the incidence of tuberculous lymphadenitis was very low as compared to the present study. This may be due to better health care services in the Western countries as compared to our setup. Similar data was presented in two different studies done by Mabedi and Khan R.[9,15] Similarly, El Haq from Saudia Arabia showed in his study that reactive hyperplasia was the commonest cause of cervical lymphadenopathy.[16]

In another study done by Pandy V in 2017 in India, the commonest cytological finding was tuberculous lymphadenitis seen in 49%, followed by non specific inflammatory lymphadenitis seen in 27%, metastatic lymph node involvement seen in 16% and lymphoma in 8% cases.[1] So, tuberculosis was common cause of lymphadenopathy in this study.[1] The findings of this study are similar as the present study. Similar findings of high incidence of tuberculous lymphadenitis were presented in different local studies done by Mitra S , Fatima S, Wahid F, Ahmed T and Shahid F.[8,17-20]Gupta K and Agarwal D from India showed that tuberculosis was the commnest cause of lymphadenopathy in their studies.[21,22]

In another study done by Iqbal in 2010, tuberculous lymphadenitis was the commonest cause of cervical lymphadenopathy seen in 70% cases, followed by reactive hyperplasia seen in 14% cases, metastatic lymph nodes in 5% cases, and chronic non specific inflammation seen in 2% cases.[6] These findings are similar to those presented in the present study. 3% of cases of tuberculous lymphadentits had positive family history in study done by Iqbal [6].On the other hand, all patients had positive family history of tuberculosis in the present study. Iqbal showed that most of patients with tuberculous lymphadenitis were males.[6] Similar data is seen in the present study. However, in study done by Wahid F, it was common in females.[18] Reason for male predominance may be due to the fact that females are neglected regarding the heath care in our setup and cannot make it to the clinics and for workup of lymph nodes as compared to males.

The FNAC successfully helps in making final diagnosis of cervical and axillary lymphadenopathy.[18] It is through FNAC that different causes of lymphadenopathy are identified in time. Thus FNAC has proved itself as quick and cost effective procedure in evaluation of cervical and axillary lymph nodes and should be used as early as possible in evaluation of lymph node enlargement.[8,14,23] Moreover, in cases of

ill formed granulomas supplemental investigations like sputum for AFB, chest X-ray and Mantoux test can increase the diagnostic yield of FNAC in tuberculous lymphadenitis.

Conclusion

The commonest etiology of cervical and axillary lymphadenopathy in our setup is tuberculosis, followed by reactive hyperplasia. FNAC, especially if supplemented by sputum AFB, chest X-ray and Montoux test helps reach final diagnosis of lymphadenopathy without patient morbidity, and hence should be part of the initial evaluation of patients with cervical and axillary lymphadenopathy before embarking on costly invasive procedures.

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