Original Article

Retrospective study of lymphadenopathy by FNAC in National Institute of Health Islamabad- Pakistan

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Abstract

The objective of the study was to review the pathology of lymph node disorders in adults with peripheral lymphadenopathy. A five year (1998- 2003) retrospective study of lymph node Fine Needle Aspiration Cytology performed at Histopathology department of National Institute of Health Islamabad. Females constitute the major group with 130 cases (64%) in our study. Fifty four percent of cases were below 20 years of age. Benign lesions were found in 91% of the patients, the majority of which were tuberculous lymphadenitis (52%) followed by nonspecific reactive hyperplasia (39%). Frequency of metastatic carcinoma was 9(4%), malignant lymphoma 2(1.0%) and insufficient aspirate in 10 (5%) cases. The commonest site of lymphadenopathy was cervical (71%) followed by sub mandibular (11%), inguinal 8% and axillary 7%. Reactive hyperplasia was more frequent in female (62%) than male patients (38%), similarly tuberculous lymphadenitis was comparatively more frequent in female (64%) than male group (36%) our in study. Tuberculous lymphadenitis was the most common pathological diagnosis in young females (15-25years). It is concluded that the pattern of disease is similar to that of other countries of the region.

Key words: Fine Needle Aspiration Cytology, lymphadenopathy, tuberculous lymphadenitis

Introduction

Lymphadenopathy refers to nodes that are abnormal in size, consistency or number. Chronic lymphadenopathy might be caused by lymphomas and other malignancies. Lymphadenopathy is one of the commonest clinical presentations` of patients, attending the outdoor department. Aetiology varies from an inflammatory process to a malignant condition (Pandit *et al*., 1987). The causes of lymphadenopathy are extensive and include bacterial, viral and fungal infections.

Chronic peripheral lymph node enlargement in adults signifies an underlying disease and has continued to pose a diagnostic dilemma to physicians. Several studies in the developing countries highlight the tuberculosis and other infections as major etiological agents (Mandong *et al.*1999) while malignancies are the predominant cause of lymph node enlargement in developed countries. Primary tumors of the lymphatic tissue are quite common for example in Iraq, it accounts for 8% of the total cancer cases (Iraqi Center, 1993). Moreover, lymph nodes are a common site of metastasis for different cancers. Thus, clinical recognition and urgent diagnosis of palpable lymphadenopathy by FNA is of great importance.

Keeping in view, the plethora of diseases that may cause lymphadenopathy, it is essential to define the pattern of disorders presenting primarily as lymph node enlargement in a particular environment. The pattern of the disease is different in children and adults with non specific reactive hyperplasia as major cause in children with a developing immune system (Afridi *et al*.2005).

This study aims at defining the causes of peripheral lymphadenopathy and the pattern of lymph node distribution in adult patients seen in Histopathology department of National Institute of Health Islamabad.

Patients and Methods

Two hundred and four cases with Lymphadenopathy at various sites were subjected to FNAC technique at National Institute of Health Islamabad from Jan 1998 to Dec 2003. Clinicodemographic data regarding age, sex anatomical site, size, consistency, duration, family history, history of the previous similar lesion, and other relevant lab investigations (if available) were obtained from the departmental history proforma of each patient. The slides of selected cases were retrieved from the archives of the department.

Selection criteria: - Adults with 15 years of age or above suffering from peripheral lymphadenopathy.
Rejection criteria: - Improper fixation, drying artifact, air-dried sample, improperly labeled specimen and metastaic lymph nodes associated with evidence of primaries elsewhere in the body were excluded from the study.

Results

A total of 204 FNAC of lymph nodes were done from adults (15 year old and above) constituting 78% of total number of FNAC lymph nodes done in department during five year period of study (1998 to 2003).

Figure I shows sex distribution in 204 cases. Out of these, one hundred and thirty (64%) were of female while seventy four cases (36%) were of male, giving female to male of 1.7:1.

The cases were divided into five groups. The brief cytological criteria adopted for classification were as follows

1. Reactive hyperplasia: Smears revealed polymorphous population of lymphoid cells with predominance of

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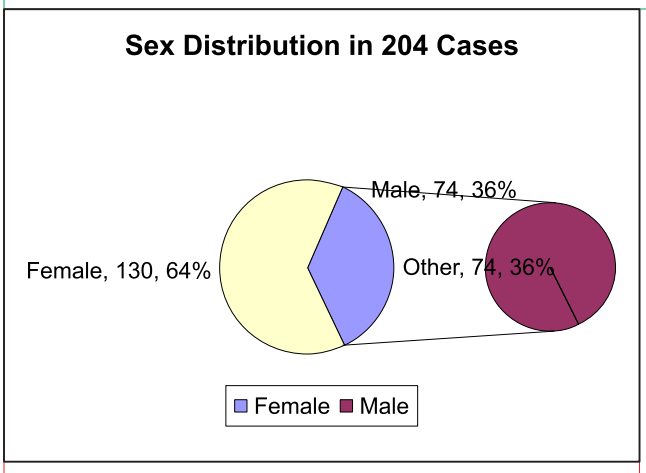

Fig I. Sex Distribution in 204 Cases

mature lymphocytes.

2. Consistent with Tuberculous Lymphadenitis: revealed caseous necrotic material, epitheloid cells, lymphocytes and an occasional giant cell in some cases.
3. Metastatic carcinoma: showed malignant cells, usually arranged in groups or clusters, along with other lymphoid cells.
4. Lymphoma: Non-Hodgkin's lymphoma showed a homogeneous pattern, consisting of atypical lymphoblasts or lymphocytes. Hodgkin's lymphoma showed a mix cell population with the characteristic Reed Sternberg giant cell.
5. Insufficient aspirate: smears revealed mainly hemorrhagic aspirate.

Figure II show the cytological results in 204 cases under study tuberculos lymphadenitis with one hundred and four cases (51%) was the most common pathologic type followed by reactive hyperplasia (39%), metastatic carcinoma (4%) and malignant lymphoma with one case (0.49%). FNA was non-diagnostic in 10 (5%) cases due to insufficient aspirate.

Figure III shows the distribution of cases under study as per their anatomical site. One hundred and forty four lymph nodes (70%) were of the cervical region in our study. Among the remaining cases, 22 (11%) were submandibular, 8 (3.9%) were axillary, 14 (6.9%) were clavicular and 16 (7.8%) were of inguinal region.

Table II shows the diagnosis according to the anatomical site of lymphadenopathy. The cases were divided into five groups. Out of these four were pathological groups while one i.e. insufficient aspirate was to evaluate the level of success of the procedure. Out of 141 cases of cervical region, reactive hyperplasia is in 57 cases while 80 suffered from chronic tuberculosis. Four patients were also suffering from the metastatic carcinoma in this group of our study. Out of 14 cases of axillary lymph node, nine suffered from the tuberculosis.

Table III shows the diagnosis according to the sex distribution in 260 cases under study. Seventy four cases are of male while 130 are of female patients. 18.1% males while 32.8% females were suffering from tuberculous lymphadenitis. Both in males and female group, reactive hyperplasia is the second commonly found pathology with 30 (14.7%) and 50 (32.8%) cases. The pattern of incidence is somewhat similar in female group but here the insufficient aspirate is 6.5% while it is 3.9% in male group. In female group 1.9% cases are also of malignant lymphoma.

Figure IV shows the cytological findings of the cases under study as per their age groups. Reactive hyperplasia was predominant cause of lymphadenopathy in age group 15-25 years while tuberculosis was dominant in age group 25-35 years.

Table I. Age groups and sex distribution in 204 cases under study

S#	Age Groups	Male	Female	Total cases No	%
2	15-25	26	58	84	41 %
3	25-35	27	39	66	32 %
4	35-45	09	24	33	16 %
5	45-55	04	04	08	04 %
6	55-65	06	04	10	05 %
7	65-77	02	01	03	02 %
8	**TOTAL**	**74**	**130**	**204**	**100%**

Discussion

In our study female constitute the major group with 130 (64%) cases while in another study conducted in same area, male preponderance with 54% cases is seen (Sher *et al*., 1996). More frequently involved lymph nodes are that of cervical region with 144 (71%) cases. These results are inline with the results of the study conducted in 2003 by Amin *et al*., with 70% cases of cervical lymph nodes involvement (Amin *et al*., 2003).

The results of our work indicate that benign lymphadenopathy constitutes a significant proportion of findings in aspirates of enlarged lymph nodes with tuberculous lymphadenitis being the main pathological finding followed by the reactive hyperplasia. While in another study, the pattern of incidence of disease was reverse with reactive hyperplasia being the main finding followed by tuberculous lymphadenitis (Pindigo *et al*.

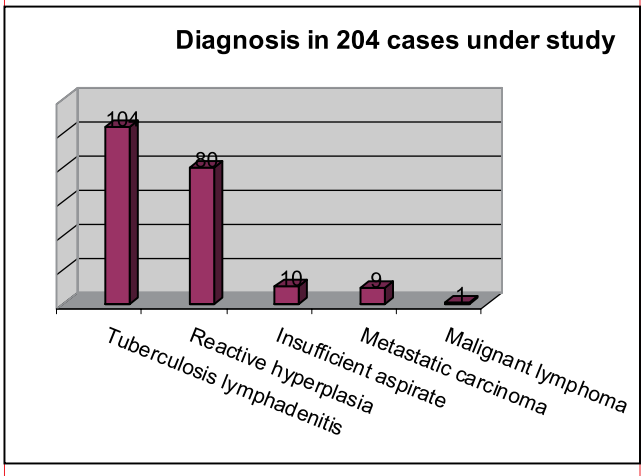

Fig. II. Diagnosis in 204 cases under study

1999). Non-specific reactive lymphadenopathy constituted 80 (39%) cases, which has been documented as a common cause of lymph node enlargement in the tropics (Pindigo *et al.* 1999, Alash *et. al.* 2002). Higher figures have however been observed in children. In this series, cervical lymph nodes (71%) are frequently involved. These figures are in line with reports in the literature (Alash *et al*. 2002)**.**

FNAC was found to be highly effective (94%) in diagnosis and lymph nodes in the posterior triangle of neck were mostly involved (Maharjan *et al*., 2009). Results of our study reveals most commonly involved site is the lymph nodes of cervical region. 71% and 77% cases of reactive hyperplasia and tuberculosis respectively were suffering from cervical lymphadenopathy. Similar findings were published by Abdullah (2000) with 80% involvement of cervical lymph nodes (Abdullah *et al*., 2000).

Total 104 (51%) cases were of tuberculous lymphadenitis in our study. Seventy seven (74%) cases of tuberculous lymphadenitis belong to the age group of 15-35 years, which are the most economically productive age groups of the society**.** In one study the commonest age group affected was 11 – 20 years and constitutional symptoms were not present in most of the patients (Mohapatra and Janmeja , 2009). Tuberculosis has re-emerged as significant public health problem in world and also in Pakistan after an apparent decline in the number of cases some time back. In 2008, globally an estimated 11.1 million people were living with Tuberculosis. Prevalence of tuberculosis in Pakistan is 310/100,000 population while its global prevalence is 170 per 100 000 population. Pakistan is 42 countries with high prevalence of tuberculosis (WHO, 2011)**.** This is an alarming situation as M. tuberculosis which can invades important organs like lungs, bones, intestine, kidney, brain and lymph node affecting their function and quality of patient's life. FNAC of enlarged lymph nodes carries a high diagnostic accuracy. It provides important clues in guiding subsequent clinical management. However, for detailed subtyping of certain disease entities such as lymphoma, surgical biopsy for histological and immunohistochemical studies are required (Sun *et. al.*, 2008)**.** FNAC is a valuable tool and if properly performed and interpreted, than patient can no longer suffer from any delay or misdiagnosis (Ghosh *et al*., 2000). It was observed that the diagnosis of tuberculous lymphadenitis can be made definitely when granulomas composed of epitheloid cells and Langhan's cells are seen. But even in the absence of granulomas, necrosis along with the presence of lymphocytes alone gives an indirect evidence of tuberculous lymphadenitis. However in patients with pyogenic tuberculous lymphadenitis may not necessarily exhibit such a picture. Moreover, FNAC of advanced tuberculous lymphadenitis may frequently display changes that are incompatible with nonspecific-reactive hyperplasia. That is why it is always stressed that in a clinically suspected case, especially if the aspirate contains pus, a bacteriological examination should be tested for acid-fast bacilli and a culture made to improve the diagnostic accuracy. Indeed, the latter was raised to 79% by using the Ziehl Neelsen stain. Same results were found in studies conducted in developing countries (Martelli , 1989). In regions where tuberculosis is endemic, treatment can be instituted without the need for excisional biopsy if the FNA results show characteristic caseating granuloma.

In our study, female were the frequent sufferers of tuberculous lymphadenitis with 67 (64%) cases while 37

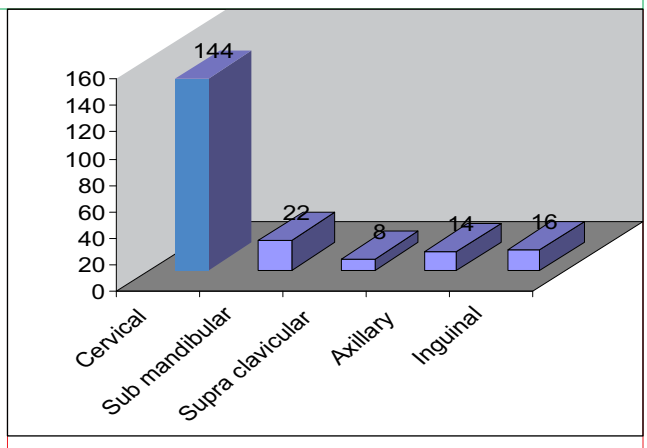

Fig. III. Distribution of the cases under study as per their anatomical site

Table II. Diagnosis according to the anatomical sites of the lymph nodes

Diagnosis	No of Cases	Anatomical Sites of lymph nodes				
		Cervical LN	Sub mandibular LN	Supra Clavicular LN	Axillary LN	Inguinal LN
Insufficient Aspirate	10	03 (1.47)	02 (0.98%)	02(0.98%)	01(0.49%)	02(0.98%)
Reactive hyperplasia	80	57 (27.9%)	14 (6.86%)	02(0.98%)	02(0.98%)	05(2.45%)
Tuberculous lymphadenitis	104	80 (39.2%)	04 (1.96%)	03(1.47%)	09(4.4%)	08 (3.92%)
Metastatic Carcinoma	09	04 (1.96%)	02(0.98%)	01(0.49%)	01(0.49%)	01(0.49%0
Malignant Lymphoma	01	-	-	-	01(0.49%)	0
TOTAL	204	144 (70.5%)	22 (10.8%)	08 (3.9%)	14 (6.9%)	16 (7.9%)

Table III. Lymph node disorders according to age and sex distribution

S #	Diagnosis	Case	%	Male	%	Female	%	M:F	Age range (Years)	Mean age (Years)
1	Insufficient Aspirate	10	4.9	03	1.4	7	3.4	1 : 2.3	15-47	26
2	Reactive hyperplasia	80	39.2	30	14.7	50	24.5	1: 1.6	15-65	32
3	Tuberculous lymphadenitis	104	51.0	37	18.1	67	32.8	1: 1.8	16-85	27
4	Metastatic Carcinoma	09	4.3	04	1.9	05	2.4	1: 1.2	25-45	32
5	Malignant Lymphoma	01	0.5	-	-	01	0.4		15-20	19
6	**Total**	204	100	74	36	130	64	1 :1.7	15-85	27

(36%) male were suffering from this infection. These results have same pattern as that of the study conducted in India in 2009 with 68% female sufferes (Agarwal *et al*., 2009). Same pattern of tuberculous lymphadenitis with these results are in lines with 70% of the female sufferers was found in a study conducted by (Ajmal and Amin, 2003). This sex dependant trend is probably due to the social behavior in Pakistan where female of any age group are more malnourished than male and if they become sick their treatment is not considered the first hand priority as compare to the male member of the family. These discriminative social behaviors can be more frequently observed in the rural population than the urban one.

In our study 3 (1%) cases of malignant lymphoma were also diagnosed on the basis of FNAC. For the diagnosis of lymphoma, FNA provides excellent cytomorphologic material if adequately sampled. The evaluation of FNA in patients with no previously diagnosed malignancy, or in those with suspected lymphoma, should be performed with extreme caution, taking care to obtain a clinical correlation and a confirmatory tissue biopsy, especially in cytologically suspicious cases. However, if malignancy has been previously diagnosed, the legitimate clinical utilization of FNA does not always require follow-up by open biopsy. False-positive results should therefore be reduced to a minimum, since a positive cytologic diagnosis often supports important management decisions (Singh *et al*., 1999). On the other hand, false-negative cases tend to be more common, and are generally based on sampling rather than diagnostic errors, such as the absence of Reed-Sternberg cells, which are important in the diagnosis of Hodgkin disease. However, low-grade (well differentiated) lymphomas with minimal cytomorphologic atypia remained very difficult to evaluate cytologically. Some authors still find it difficult to resolve with certainty the differential diagnosis of lymphoma from reactive hyperplasia or even granulomatous lymphadenitis. Therefore, consultation between cytopathologists and clinicians is mandatory and may result in repeating aspiration or recommending a surgical biopsy. In malignant lymphadenopathies, this inexpensive, relatively painless and rapid technique may not only help in the primary diagnosis of tumors, but remains a useful method of following up patients with known malignancies, and even guiding therapy.

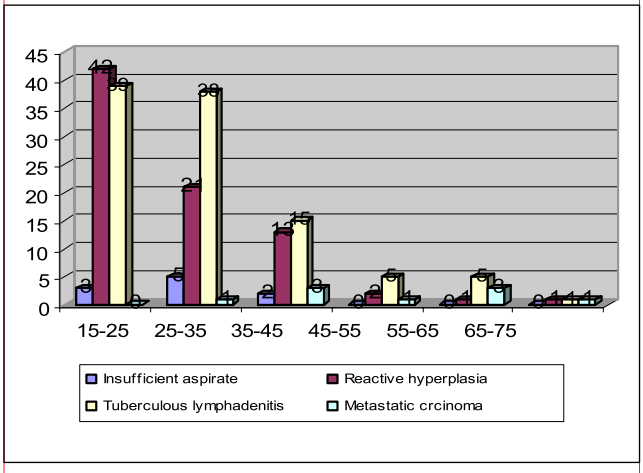

Fig. IV. Age distribution of patients with the four major specific causes of lymphadenopathy

It is concluded that the pattern of disease in this study was similar to other countries of region. Tuberculosis and reactive hyperplasia were the major pathologies and presented mostly with cervical lymphadenopathy. It is also concluded that FNA is the integral tool for the initial diagnosis and management of patients presenting with lymphadenopathy since it offers a high degree of accuracy, lending itself to outpatient diagnosis. Finally this cost-effective and minimally invasive technique can be applied to assess any accessible lesion with existing facilities in Pakistan.

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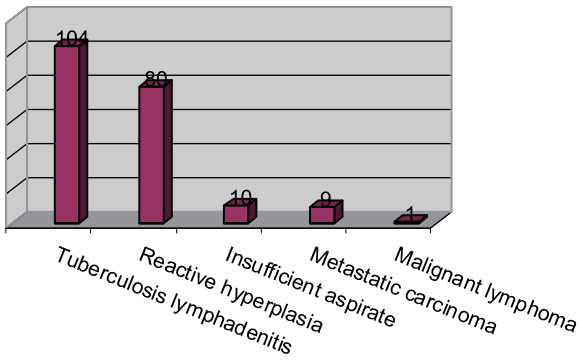

Fig. II. Diagnosis in 204 cases under study

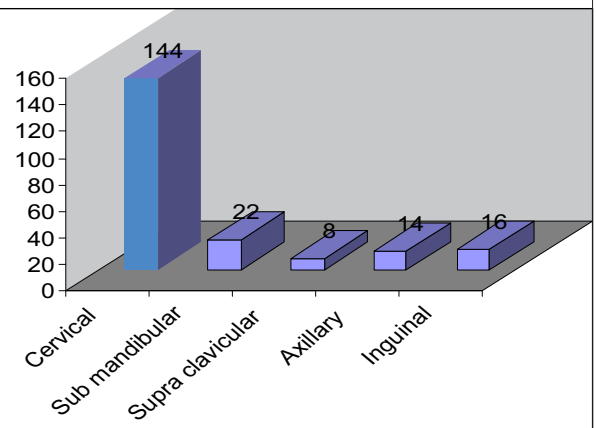

Fig. III. Distribution of the cases under study as per their anatomical site

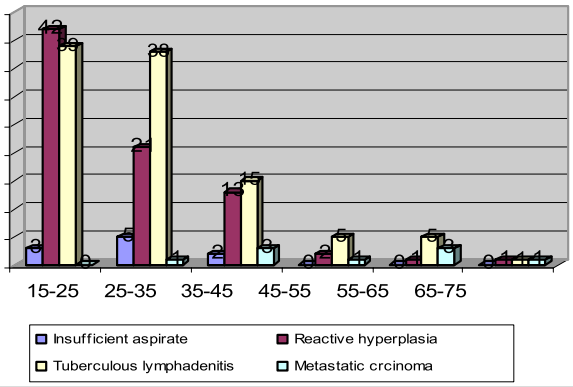

Fig. IV. Age distribution of patients with the four major specific causes of lymphadenopathy

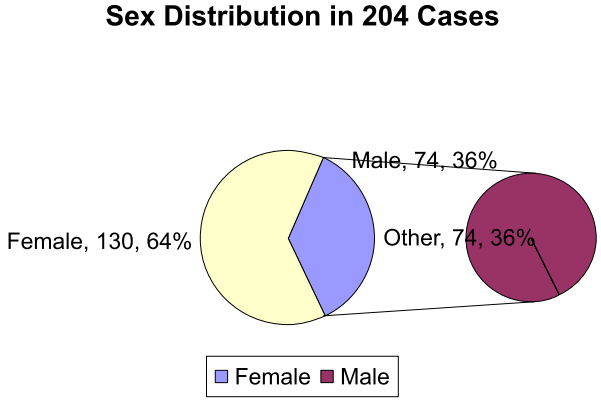

Fig I. Sex Distribution in 204 Cases