Etiological pattern of Lymphadenopathies and Role of Fine Needle Aspiration Cytology (FNAC) in its Diagnosis

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Abstract*—Lymphadenopathy is one of the commonest presentation in inflammatory and neoplastic cases. Pathological diagnosis of enlarged lymph nodes is crucial in further management of patients. Fine Needle Aspiration cytology (FNAC) is quick and cost effective OPD procedure for establishing etiology of enlarged lymph nodes. This study was aimed to observed the pattern of lymphadenopathy as per FNAC and its diagnostic accuracy assuming histopathology as gold standard. This study was conducted on two hundred and thirty one consecutive enlarged lymph nodes attended for FNAC in a secondary care level Government Hospital, Gandhi Nagar, Jammu in a study period of two and a half years. Lymph nodes of these cases were aspirated and subjected to cytomorphological evaluation with Papanicolaou (PAP) and Giemsa stain. After that histopathological examination was done of excised biopsies. Then pattern of lymphadenopathy as per FNAC was observed and its diagnostic accuracy was found out assuming histopathology as gold standard. Maximum number of patients was in the age group of 21-30 years age group with male to female ratio 1.2:1. Out of 231 lymphadenopathy cases 4 remain inconclusisve whereas 200 (88.11%)cases were benign and 27 (11.89%) were malignant including 14 (6.1%) cases of metastatic tumors. Among benign cases, majority had non specific reactive lymphadenitis (42.29%) followed by tubercular lymphadenitis. And among malignant tumors, metastatic tumors (6.1%). were most common. Diagnostic accuracy of FNAC was observed as fairly good i.e. ranging from 100% to 83.3% in various type of lymphadenopathies. So it can be depicted that FNAC is very useful first line investigation in patients presenting with enlarged lymph nodes especially in secondary level health care hospitals/centers where advanced diagnostic modalities are not available. The suspicious cases can always be referred for further evaluation.*

Keywords— Fine Needle Aspiration cytology (FNAC), Lymphadenopathy, Metastatic tumours, Lymphadenitis, Diagnostic Accuracy

I. INTRODUCTION

The era of modern diagnostic cytopathology began with the publication in 1941 and 1943 by Drs G. Papanicolaou and H.Traut of their work on the cytological diagnosis of uterine cancer[1]. The commonest cause of peripheral lymphadenopathy is a reaction to some symptomatic or asymptomatic inflammatory process. Fine needle aspiration cytology (FNAC) of lymph node has become an integral part of the initial diagnosis and management of patients with lymphadenopathy due to early availability of results, simplicity, and minimal trauma with less complication[2].

The clinical utility of FNAC is not limited to neoplastic conditions but also for diagnosis of inflammatory, infectious, immunocompromised and degenerative conditions. At primary level FNAC is used as a primary screening tool to determine whether lymphadenopathy is due to reactive hyperplasia, infection ,metastatic malignancy or malignant lymphoma and can be systematically correlated with surgical histopathology for definitive diagnosis in certain suspicious cases. FNAC has also been advocated as a useful method in comparison to more expensive surgical excision biopsies in developing

countries with limited financial and health care resources[3]. Thus, it can avoid the need for excisional biopsy in most cases and allow rapid onset of therapy[4].
So to observed the pattern of lymphadenopathy as per FNAC and its diagnostic accuracy assuming histopathology as gold standard this study was conducted in Pathology department of Government Hospital Gandhi Nagar, Jammu (J&K) India

II. METHODOLOGY

This hospital based case-series type of descriptive observational study was conducted at Government Hospital Gandhi Nagar, Jammu (Provincial Hospital) over a period of two and a half years from January 2013 to June 2015. All the cases irrespective of patient's age, gender, clinical symptoms, location of lymph nodes were included in this study. Total of 231 patients with consecutive enlarged lymph nodes had attended for FNAC during 1st January 2013 to 30th June 2015. Lymph nodes of these case were aspirated as an OPD procedure and sent for cytological examination. Then histopathological examination of enlarged lymph nodes was also done after excision of biopsy by clinicians. Patient's age, gender, clinical symptoms, location of lymph nodes, gross examination of aspirate and cytomorphological patterns were studied. Detailed history along with clinical examination was elicited in each patient. Lymph node aspiration was done using 22 gauge needle and 10 ml plastic syringe with a detachable syringe holder (Franzen Handle). In each case, three alcohol fixed smears were prepared ,first smear was stained with Papanicolaou stain, second with Giemsa stain and third one was kept unstained for any further required stain. Cytological and histopathological correlation was also observed and diagnostic accuracy of FNAC in various type of etiologies of lymphadenopathy was also assessed.

Statistical analysis was done on Microsoft Excel 2007 and Primer statistical software version 6. Pattern of lymphadenopathy cases was expressed in percentage and proportions. And association was inferred by Chi Square test. P value<0.05 was considered significant.

III. RESULTS

This study was conducted on 231 lymphadenopathy cases attended for FNAC, out of that 200 cases were of benign and 27 (11.89%) were malignant in nature and 4 cases remain inconclusive. (Figure 1) These 27 malignant cases includes 14 (51.85%) cases of metastatic tumor cases of various type, in which majority were of squamous cell carcinoma. (Figure 2)

Figure 1

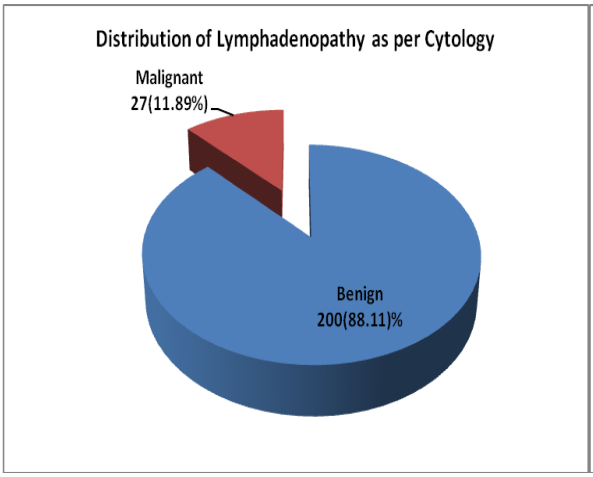
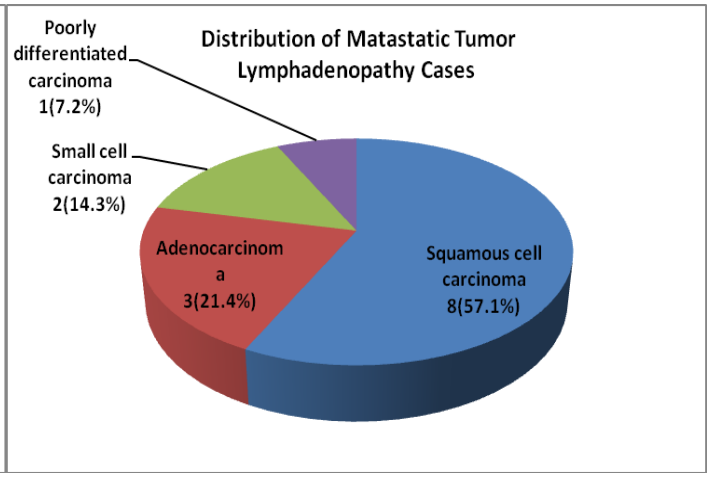


Figure 2



Out of these 227 cases finally taken for study, maximum i.e. 96 (41.6%) cases were of non specific reactive lymphadenopathy followed by Tubercular lymphadenitis, Acute suppurative lymphadenitis etc.

There were 14 (6.17%) cases of metastatic tumors and 5 (2.2%) cases of Hodgkin lymphoma. Even one case of Rosai Dorfman was found. (Figure 3).

Overall, majority of lymph nodes aspirated showed cytological features suggestive of non specific reactive lymphadenitis (41.6%) followed by tubercular lymphadenitis (34.6%). One case of Rosai Dorfman disease (a rare entity) was diagnosed in 18 year old male patient. Among cases of malignant lymphadenitis, metastatic tumours were most commonly observed (6.1%) followed by lymphomas in 5.7% cases. Out of metastatic cases 57.1% were squamous cell carcinomas followed by adenocarcinoma in 21.4% cases with small cell carcinomas in 14.3% and undifferentiated carcinomas in 7.2% cases. There were eight cases of Non Hodgkin lymphoma and five cases of Hodgkin lymphoma among 231 lymph nodes aspirated. Males showed predominance in both benign and malignant lesions except among cases of tubercular lymphadenitis where females had preponderance. Regarding age distribution of benign lesions majority of patients were less than thirty years of age. Malignant lymphadenopathy cases were observed among patients older than thirty years. Maximum cases of Non Hodgkin lymphoma and Hodgkin lymphoma were seen in fifth decade. The cytopathological results were compared with histopathological diagnosis of some excised lymph node cases. (Table 3) .In 44 cases cytology and histopathology correlation was available. The diagnostic accuracy of FNAC in Rosai Dorfman disease, metastatic and Hodgkin lymphoma was 100% and more than 83% in non specific reactive lymphadenitis, acute suppurative lymphadenitis and Non Hodgkin lymphoma cases

Microphotograph of cases of these various type of lymphadenopathies were shown in figure 4 and figure 5A-5D. Microphotograph of a case of Rosai Dorfman Disease in Figure 5 A whereas microphotograph of a case of Metastatic Deposits of Moderately Differentiated Adenocarcinoma in Supraclavicular Lymph Node was seen in figure 5B. Likewise microphotograph of a case of Hodgkins Lymphoma Mixed Cellularity type was seen in figure 5C and microphotograph of a case of Non Hodgkins Lymphoma of Intermediate Grade was seen in figure 5D.

Figure 3

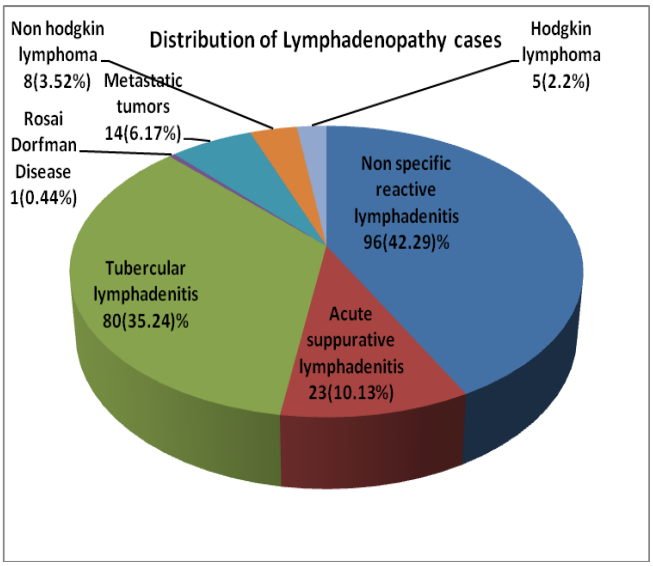


Figure 4:

Microphotograph of a case of Non Specific Reactive Lymphadenitis (20x, PAP stain)

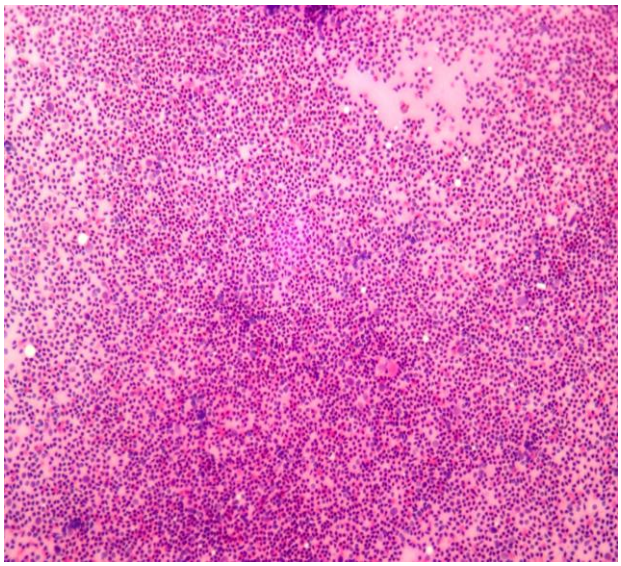


Figure 5

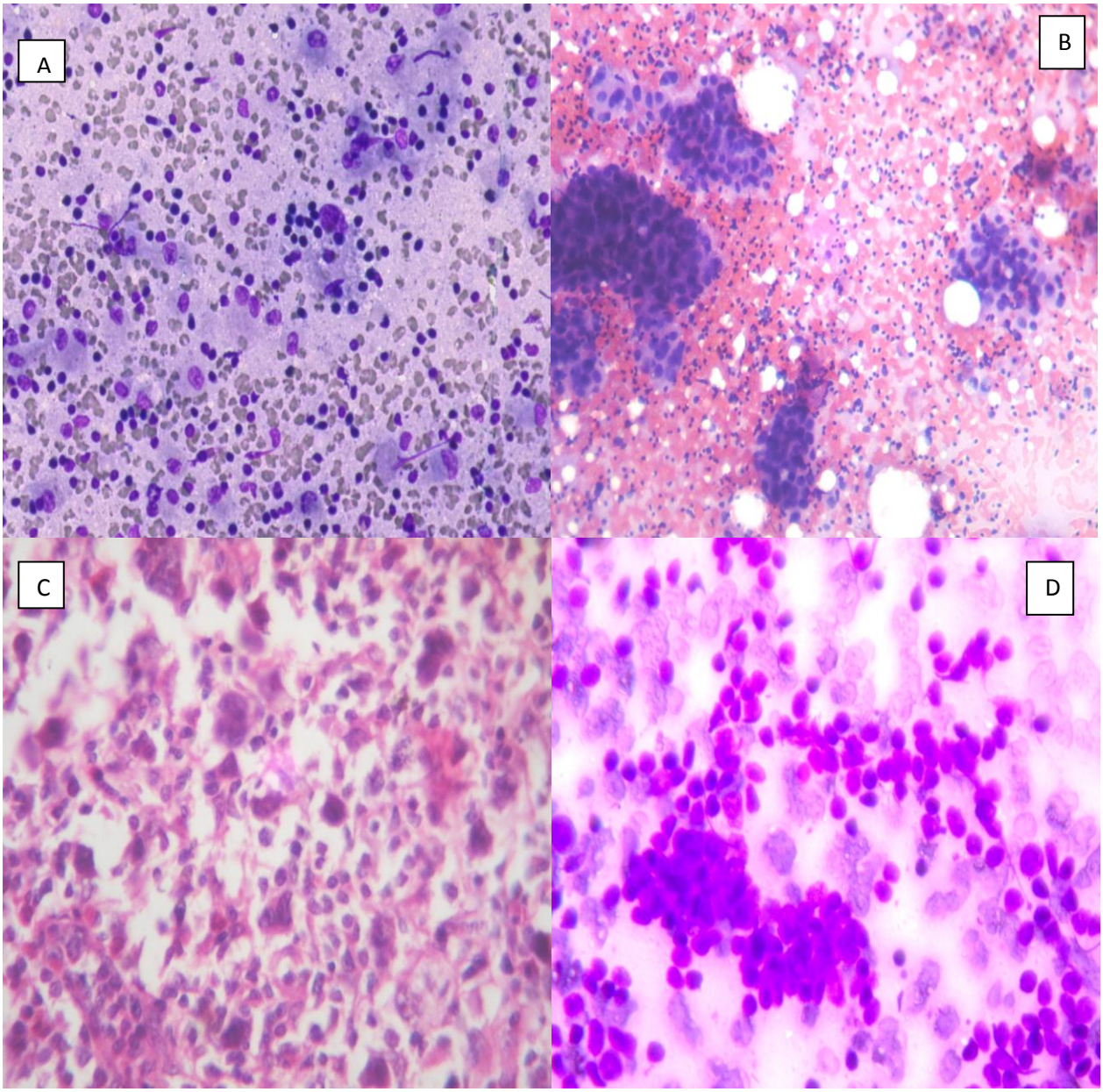


Figure 5A: Microphotograph of a case of Rosai Dorfman Disease (Sinus Histiocytosis with Massive Lymphadenopathy) (40x, Giemsa Stain)

Figure 5B: Microphotograph of a case of Metastatic Deposits of Moderately Differentiated Adenocarcinoma in Supraclavicular Lymph Node (40x, PAP Stain)

Figure 5C: Microphotograph of a case of Hodgkins Lymphoma (Mixed Cellularity)(40x, H&E)

Figure 5D: Microphotograph of a case of Non Hodgkins Lymphoma (Intermediate Grade)

Among these 231 cases studied, 54.5% (n=126) were males and 45.5% (n=105) were females with male to female ratio of 1.2:1. Maximum number of patients (n=55) were in the age group of 21-30 years age group followed by less than 10 years and minimum patients were present in 71-80 years age group (n=6).

When association of biological variables with type of lymphadenopathy tumors cases was evaluated it was found that age was found to have association (p<0.001) with the type of lymphadenopathy cases i.e. benign, malignant and metastasis but sex was found not to have any association (p=0.188) with type of lymphadenopathy cases. (Table 1)

Although sex was not found to be associated in any type of lymphadenopathy cases i.e. benign, malignant and metastasis but age was found to be associated in all the type of tumors i.e. benign, malignant and metastasis. Benign lymphadenopathy cases were significantly more (p<0.001) in younger age (up to 30 years) whereas malignant and metastatic tumors were found significantly more (p<0.001) in older age group (>30 years). When malignant and metastatic tumors were compared as per association with age it was found that metastatic tumors were more common in older age group (>60 years) than malignant tumors. (Table 1)

Table 1

Association of Type of Lymphadenopathies with Biological Variables

Biological Variables		**Benign**		**Metastatic**		**Malignant**		***P Value LS**
		No	**%**	**No**	**%**	**No**	**%**	
Age wise	Upto 30 Years **(N=142)**	142	100	0	0	0	0	P<0.001 S
	31-60 Years **(N=69)**	50	72.46	8	11.59	11	15.94	
	>60 Years **(N=16)**	8	50	6	37.5	2	12.5	
	***P Value LS**	P<0.001 S		P<0.001 S		P<0.001 S		
Sex Wise	Male **(N=123)**	104	84.55	10	8.13	9	7.32	P = 0.188 NS
	Female **(N=104)**	96	92.31	4	3.85	4	3.85	
	***P Value LS**	P = 0.111 NS		P = 0.289 NS		P = 0.404 NS		

Note: 4 FNACs were inconclusive were excluded

***P Value as per Chi-square test and LS is level of significance**

When diagnostic accuracy of FNAC in these lymphadenopathy cases was evaluated assuming histopathology of excised biopsy it was found quite good ranging from 83.3% to 100%. All the cases of matastatic tumors, Hodgkin lymphoma and Rosai Dorfman was diagnosed by FNAC (100% accuracy). Diagnostic accuracy was found 87.5% in Non Hodgkin lymphoma and 84.2% in Non specific reactive lymphadenitis. (Table 2)

As per FNAC 2 cases of Acute suppurative lymphadenitis and one case of Non Hodgkin lymphoma were misdiagnosed as Non specific reactive lymphadenitis. Likewise one case of Acute suppurative lymphadenitis and one case of Non Hodgkin lymphoma was misdiagnosed as Non specific reactive lymphadenitis by FNAC. (Table 2)

Table 2

Correlation of Histological and Cytological Diagnosis

FNAC (No. of Cases as per FNAC Diagnosis)	Histopathological diagnosis						
	Non specific reactive lymphadenitis	Acute suppurative lymphadenitis	Rosai Dorfman Disease	Metastatic tumors	Non Hodgkin lymphoma	Hodgkin lymphoma	Accuracy (%)
Non specific reactive lymphadenitis (N=19)	16	2	0	0	1	0	84.2%
Acute suppurative lymphadenitis (N=6)	1	5	0	0	0	0	83.3%
Rosai Dorfman Disease (N=1)	0	0	1	0	0	0	100%
Metastatic tumors (N=14)	0	0	0	14	0	0	100%
Non hodgkin lymphoma (N=8)	1	0	0	0	7	0	87.5%
Hodgkin lymphoma (N=5)	0	0	0	0	0	5	100%

IV. DISCUSSION

The present study was conducted in secondary care level hospital of Jammu region with the aim to report the pattern of lesions observed on FNAC of lymphnodes. Observations of cytomorphological patterns and AFB positivity of tubercular lymphadenitis cases were same as in previous study of the same author.[5] In this study, maximum patients were present in age group of 21-30 years. However observations made by Bharadwaj K et al, [6] reported maximum number of cases in 0-10 years age group but findings were similar with other studies.[7,8]

Male to female ratio observed in this study was 1.2:1. However M: F ratio of 1.44:1 was also reported in one of the study [9] Also in some other studies [6,10] females outnumbered males. But Chawla N et al [11] also reported well comparable M: F ratio of 1.3:1.

Out of total 231 lymph nodes aspirated 200 cases (86.5%) were benign and 27 cases (11.7%) were malignant. Majority of benign lesions were non-specific reactive lymphadenitis and tuberculous. These findings correlate with studies of various other authors.[12,13,14] The reason may be due to high prevalence of infections and tuberculosis in our country. Out of malignant lymph nodes aspirated maximum were reported as metastatic tumours (6.1%) and most of them were squamous cell carcinoma followed by adenocarcinoma. These findings were in close comparison with Alam etal[15] and others[12,13] Malignant lymphomas were reported in 5.7% cases whereas Ahmad etal[13] reported in 4.5% cases , Egea etal[16] had reported in 9.5% cases. However Hafiz NH[17] and Rakhshan and Rakhshan[14] observed lymphomas in

much higher percentage of cases. The reason may be the study was conducted in cancer institutes where most referral cases are investigated. Hodgkin lymphoma cases were reported in 5 cases (38.5%) and Non Hodgkin lymphoma in eight cases (61.5%) out of 13 primary lymphoma cases. Chawla N[9] reported Hodgkin lymphoma cases in 33.3% cases.

Diagnostic accuracy of FNAC was 100% in Rosai Dorfman disease , metastatic tumours and Hodgkin lymphoma i.e. FNAC of these lesions showed exact corroboration with histopathology. Similar findings were observed by[12,18,19,20] .However in other lesions diagnostic accuracy was reported between 83-87% in our study. Almost similar results were published by other authors as well.[15,17,21].

V. CONCLUSION

Commonest causes of lymphadenopathies in our setting is non-specific reactive lymphadenitis followed by tubercular lymphadenitis, acute suppurative lymphadenitis and metastatic tumors. Although sex was not found to be associated with type of lymphadenopathy but benign lymphadenopathy was more common in younger generation whereas malignant lymphadenopathy was more common in older generation. The diagnostic accuracy of FNAC in all lesions ranged between 83.3% to 100%. So FNAC has proved a good first line method of investigating the cases of lymphadenopathy especially in secondary care centers where advanced diagnostic modalities are not available. The suspicious cases can always be referred for further evaluation.

CONFLICT OF INTEREST

None declared till now.

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