

Research Article

Evaluation of peripheral lymphadenopathy by fine needle aspiration cytology: a one year study at tertiary centre

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ABSTRACT

Background: Lymphadenopathy is common presenting features in various non-neoplastic and neoplastic lesions. Fine needle aspiration cytology (FNAC) is simple, quick, inexpensive and minimally invasive technique that can be used as an outpatient procedure to diagnose them. The present study was undertaken to assess the various causes of lymphadenopathy through FNAC, and to see the distribution of lesions with respect to age and gender. To assess the diagnostic accuracy of lymph node fine needle aspiration (FNA) cytology in various non-neoplastic and neoplastic conditions.

Methods: Total 555 cases of the lymph node FNAC were studied from January 2014 to December 2014 in Cytopathology department of Government Medical College, Surat. The cytomorphologic features seen in the aspirates were analyzed and correlated with their etiology.

Results: In this study 555 cases of cervical lymphadenopathy were analysed. The age of the patients ranged from 5 months to 90 years of which 60.2% were males and 39.8% were females. Maximum numbers of cases 147(26.4%) were in the age group of 21- 30 years. The most common lesion encountered was tuberculous lymphadenitis 44.8% followed by metastatic tumors 31.3%, reactive lymph node 16.7%, acute lymphadenitis 5.4% and lymphoma 1.8%. Male showed predominance of metastatic carcinoma and lymphoma while chronic reactive hyperplasia and tuberculous lymphadenitis were equally distributed in both male & female.

Conclusions: FNAC is safe, rapid and cost effective method in establishing the diagnosis in large number of cases of lymphadenopathy. It can differentiate a neoplastic from a non-neoplastic process and therefore influence patient management preventing patient from being subjected to unnecessary surgery.

Keywords: Fine Needle Aspiration Cytology, Lymphadenopathy, Lymphoma

INTRODUCTION

Lymphadenopathy is a commonly encountered clinical problem which has a multiple causes.¹ Lymph nodes become secondarily involved in virtually all infectious diseases and in many neoplastic disorders.² Enlarged lymph nodes are easily accessible for fine needle aspiration (FNAC) and hence FNAC is a very simple and important diagnostic tool for lymph node lesions.³ Surgical biopsy is the gold standard for diagnosis. However, it has several drawbacks: costly, time-

consuming and requiring more precautions. FNAC is comparatively less invasive and cost effective than surgical biopsy.⁴ The diagnostic yield of FNAC can be improved by radiological guidance and proper clinical assessment of lesion.^{5,6}

METHODS

Five hundred and fifty five patients presenting with palpable lymphadenopathies, which were referred to cytology section of pathology department from

Government Medical College & New Civil Hospital, Surat over a period of 1 year (January 2014 to December 2014) were included in study. In each cases a brief history, physical examination along with evaluation of relevant investigations if available was carried out. The FNAC was performed by cytopathologist, using a 22-24G needle attached to 10 ml syringe. If needed multiple sites were aspirated. The aspirated material was smeared on slides. Slides were immediately immersed in 95% methanol and remaining air dried. Prepared Slides were stained with May Grunwald Giemsa (dry fixation), Hematoxylin & Eosin (wet fixation) and Papanicolaou's (PAP-wet fixation). Slides were immediately fixed in 95% methanol for wet fixation and after air dried for dry fixation. Whenever required special stain like Ziehl Neelson (Z & N) stain for acid fast bacilli and PAS for mucin or fungal organism were done. If required immunocytochemistry was also used for typing of malignancy. At the end of the study data were analysed. A 42 cases of FNAC was inconclusive because of low cellularity due to deep seated/ small /fibrous swelling/ prominent cystic component, smear shows blood only and repeat FNAC not possible as patients lost in follow up or give negative consent for repeat FNAC. These cases were excluded from study.

RESULTS

This study analysed 555 cases of lymphadenopathy. The range of age of patients was from 5 months to 90 years in which 60.2% were males and 39.8% were females. These cases were divided into 7 groups according to their age: group I (0-10 years) group II (11-20 years), group III (21-30 years), group IV (31-40 years), group V (41-50 years), group VI (51-60 years) and group VII (>60 years).The

maximum numbers of cases were in the age group of 21-30 years 26.4% (n=147).

It was observed that in each of age group causes of lymphadenopathy is different. Chronic reactive hyperplasia were seen most often (69.9%) in first three decades, tuberculous lymphadenitis (73.6%) in second & third decades. Metastatic carcinoma was seen 81.3% after the age of 40 years. Cases of lymphoma were distributed in all age group (Table 1).

Male predominance was noted in acute lymphadenitis, metastatic carcinoma and malignant lymphoma with male: female ratio of 1.1:1, 4:1, 4:1 respectively while in reactive lymphadenitis and tuberculous lymphadenitis there were equal distribution with male: female ratio is 1:1.

Out of 555 cases 372 (66.9%) cases were of infective etiology, 173 cases (31.3%) were of metastatic carcinoma & 10 (1.8%) cases were of lymphoma. In infective etiology maximum number (n=249) of cases were of tuberculous lymphadenitis followed by chronic reactive hyperplasia (n=93). Tuberculous lymphadenitis (n = 249) was found to be the most common pathologic lesion in our study, accounting for 44.8% of cases followed by metastatic malignancy (n = 173) constituting 31.3% of cases (Table 2).

Among the various sites of lymph node involvements maximum numbers were of cervical region 491 (88.5%), followed by axillary region 36 (6.5%) and inguinal region 23 (4.1%). 5 cases (0.9%) show generalized lymphadenopathy (Table 3).

Table 1: Age and sex distribution of patients of lymphadenopathy.

Age (years)	Acute Lymphadenitis		Reactive Hyperplasia		Tuberculous Lymphadenitis		Metastatic Carcinoma		Lymphoma/leukemic Infiltration(LI)*						Total (%)	
	M	F	M	F	M	F	M	F	NHL		HL		LI			
0-10	2	3	11	9	10	9	1	0	0	0	0	0	0	1	0	46(8.3%)
11-20	2	2	10	13	28	44	1	0	0	0	2	0	0	1	0	103(18.6%)
21-30	6	2	9	15	57	51	3	2	1	0	1	0	0	0	0	147(26.4%)
31-40	4	2	9	7	22	12	19	5	1	0	1	0	0	0	0	82(14.8%)
41-50	1	3	1	1	6	3	32	10	0	0	1	0	0	0	0	58(10.5%)
51-60	1	1	1	1	1	4	42	12	0	0	1	0	0	0	0	64(11.5%)
>60	0	1	5	1	1	1	40	6	0	0	0	0	0	0	0	55(9.9%)
	16	14	46	47	125	124	138	35	2	0	6	0	1	1	555	

NHL- Non Hodgkin's lymphoma, HL- Hodgkin's lymphoma LI- Leukemic infiltration

Out of 173 cases of metastatic tumors, maximum cases were of metastatic squamous cell carcinoma 128 (73.9%). other metastatic malignancy noted in present study was poorly differentiated malignancy 18 (10.4%) cases, mammary carcinoma 8 (4.6%) cases, adenocarcinoma 5

(2.8%) cases , Malignant round cell tumor 2 (1.2%) cases, small cell carcinoma 2(1.2%) cases, carcinoma 2 cases (1.2%) and metastasis from papillary carcinoma of thyroid 1 (0.6%) cases, metastasis from Mixed germ cell tumor 1 (0.6%) cases, metastasis from malignant

melanoma 1 (0.6%) cases, metastasis from neuroendocrine carcinoma 1 (0.6%) cases, nasopharyngeal carcinoma 3 (1.7%) cases, pleomorphic carcinoma/sarcoma 1 (0.6%) cases.

Table 2: Cytologic diagnosis of 555 cases of cervical lymphadenopathy.

Cytological diagnosis	No. of case	%age
Acute lymphadenitis	30	5.4%
Chronic reactive hyperplasia	93	16.7%
Tuberculous lymphadenitis	249	44.8%
Metastatic carcinoma	173	31.3%
Lymphoma	10	1.8%
Total	555	100%

In present study diagnosis of lymphoma/leukemia was suggested in 10 cases. Out of which 6 cases were of suspicious/suggestive of Hodgkin's lymphoma, 2 cases were of suspicious/suggestive Non-Hodgkin's lymphoma and 2 cases were known case of leukemia so diagnosis of leukemic infiltration was offered. Further workup for confirmation of diagnosis was advised in all cases. Lymphoid malignancy represents a minority of the cases (1.8%) in our study.

Table 3: Regional distribution of cases.

Site of FNAC of Lymph n	Cases (n=555) (%)
Cervical	491(88.5%)
Axillary	36(6.5%)
Inguinal	23(4.1%)
Generalized*	5(0.9%)

* If two or more groups of lymph nodes were involved it was considered to be generalized lymphadenopathy.

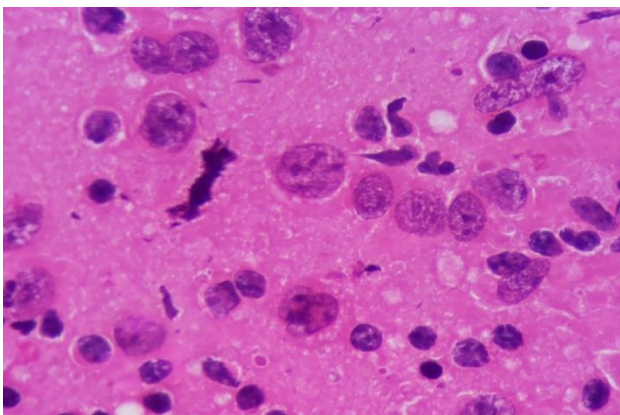


Figure 1: FNAC smear from Hodgkin's lymphoma shows classical/mononuclear variant of Reed Sternberg cell (RS cell) (H & E, 100X).

Reactive hyperplasia-The cytological diagnosis of reactive hyperplasia was established by the presence of high cell density, polymorphous cell population and a considerable number of tingible body macrophages in proper clinical context. The reactive pattern is quite

variable depending on the degree of stimulation, the number and size of germinal centres and site from which the sample is aspirated. If the sample is aspirated from the germinal centre it mainly contains loose tissue fragment of dendritic reticulum cells, centroblast, centrocytes and small lymphocytes whereas paracortical aspirates were found to consist predominantly lymphocytes with variable number of scattered immunoblast, plasma cells, nonspecific histiocytes and endothelial cells (Figure 1).

Tuberculous lymphadenitis-There is two specific pathological criteria for diagnosing tubercular lymphadenitis-caseatious necrosis and granuloma formation along with Ziehl Neelson (Z&N) stain. Granuloma formation less likely to be present in tubercular lymphadenitis associated with advanced HIV disease. This is because T-cell function, which is suppressed in advanced HIV disease, is required for granuloma formation (Figure 2).

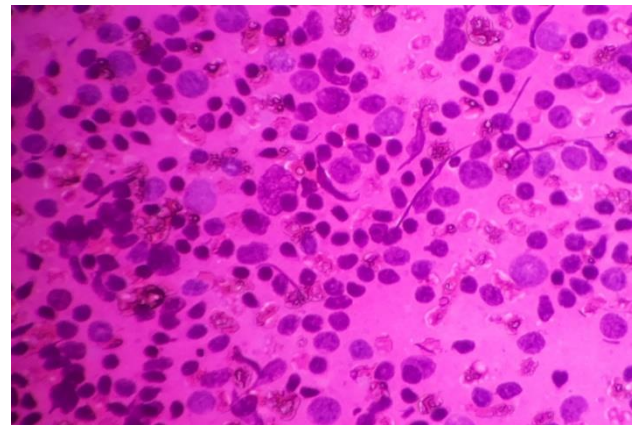


Figure 2: Aspirates from reactive lymphadenitis, showing polymorphous population of lymphoid cells (H & E, 40X).

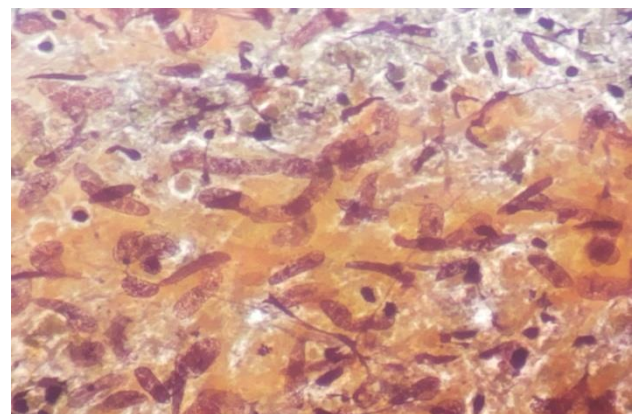


Figure 3: Aspirates from Tuberculous lymphadenitis show well-formed granuloma (PAP, 100X).

Hodgkin's lymphoma-Cytomorphological criteria for Hodgkin's disease include presence of classical Reed Sternberg cell (RS cell) in a background of lymphocytes,

plasma cells, eosinophils and histiocytes. Presence mononuclear variant and lymphohistiocytic variant (popcorn cells) of Reed Sternberg cells in background element should raise the suspicion of Hodgkin's disease even with the absence of classical Reed Sternberg cells (Figure 3).

Non-Hodgkin's lymphoma (NHL) - smears showed an absolute/relative monomorphic lymphoid cell population consisting of small/medium/large sized lymphoid cells being singly scattered (Figure 4).

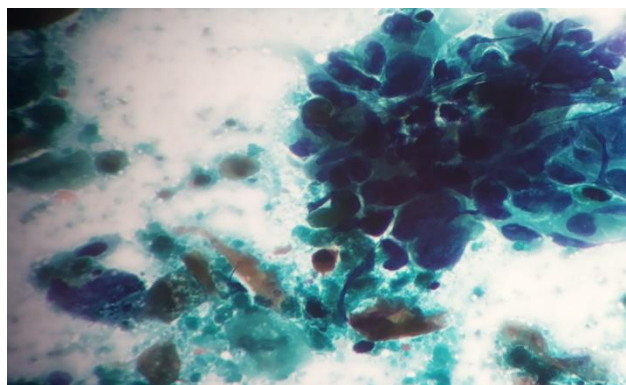


Figure 4: FNAC smear from squamous cell carcinoma shows clusters of malignant squamous epithelium in necrotic background (PAP, 40X).

DISCUSSION

FNA cytology is highly reliable in the identification of benign lesions, metastatic carcinoma and melanoma in lymph nodes, limiting the requirement for diagnostic excision biopsy in many patients. However, the role of aspiration cytology in the assessment of primary lymph proliferative disorders has been less certain. Cytology is often difficult to differentiate Non-Hodgkin's lymphoma from reactive changes and Hodgkin's disease and also typing was not reliable by this method.^[7] Early reports suggested that FNA produced high false negative rates in patients with Hodgkin's disease and low grade non-Hodgkin's lymphoma.⁸

We are presenting our experience with 555 cases of lymphadenopathy gathered over a period of one year. The pattern of benign lesion seen in our study consists of reactive hyperplasia, tuberculous lymphadenitis, acute lymphadenitis and malignant lesion includes metastatic carcinoma and malignant lymphoma/leukemia.

The age group which was studied ranged from 5 months-90 yrs with maximum cases in age group 21-30 yrs which is comparable with those of Shilpa G et al, Patel M M et al and Kumar H et al, however Pandey P et al found maximum no. of cases in the age group 1-10 yrs.^{2,9-11} This variation may be due to different population density or geographic variation.

In present study a male preponderance was noted. Similar male preponderance was noted by Patel M.M. et al, Kumar N et al and Hemalatha A et al.^{4,9,12}

The most frequent site for FNAC was cervical region (88.5%) followed by axillary region (6.5%). Similar findings were also observed by Shilpa G et al, Wilkinson AR et al, Shrivastav A et al Mohanty R et al, Madan Y et al and Paliwal Nidhi et al.^{2-6,13,14}

The most common cytological diagnosis was Tuberculous Lymphadenitis (44.8%) in present study. Similar findings were observed by Shilpa G et al^[2], Kumar N et al^[4] and Wahid F I et al^[15]. Tuberculous Lymphadenitis is one of the most common type of lymphadenopathy in developing countries. The high rate is due to low socio-economic status, illiteracy, incomplete treatment, resistance and increased incidence of HIV infection. However Shrivastav A et al, Mohanty R et al, Pandey P et al found Reactive hyperplasia as the most common cytological diagnosis.^{5,6,11} This difference may be due to different study population and some of the cases were HIV positive coming to our hospital as we have VCTC (voluntary counselling and testing centre).

In present study, second most common cytological diagnosis was Metastatic tumors (31.3%). Similar findings were also observed by Wahid F I et al however Shilpa G et al and Kumar H et al found reactive hyperplasia as the second most common cytological diagnosis.^{2,10,15} It may be due to different study population, genetic factors, environmental factors and habitual factors like smoking and tobacco consumption. Also because our hospital is tertiary care centre and we get number of referred cases. So we get more cases of metastatic malignancy in lymph node.

Squamous cell carcinoma (73.6%) was most common microscopic variant in present study. These findings correlated to study done by K Mamatha et al (56%), Mohan A et al (52.8%), Babu G S et al (70.6%), however Ghartimagar D et al noted most common malignancy was adenocarcinoma seen in 67%.¹⁶⁻¹⁹ In our study adenocarcinoma was seen only in 2.9% cases. This correlates with the high rates of cancers of upper aero digestive tract in India, possibly due to the habit of tobacco chewing in the Indian population.

Lymphoma represents a minority of the tumors (1.8%) in present study. These findings were well correlated with study done by Shrivastav A et al (2.3%) and Shilpa G et al (1.9%), however Dowerah S et al reported higher number of lymphoma cases (10.6%).^{2,6,20}

In present study diagnosis of lymphoma/leukemia was suggested in 10 cases. Out of which 6 cases were of suspicious/suggestive of Hodgkin's lymphoma, 2 cases were of suspicious/suggestive Non-Hodgkin's lymphoma and 2 cases were known case of leukemia so diagnosis of leukemic infiltration was offered. Further workup for

confirmation of diagnosis was advised in all cases. In our study in lymphoma cases Histopathological correlation was possible only in 2 cases. Other cases were lost in follow-up.

In our study in 1 case of diagnosis chronic reactive hyperplasia was offered on cytology however biopsy is advised considering clinical context of these cases. This case was diagnosed as low grade lymphoma on histological examination (1 false negative case).

The diagnosis of low grade lymphomas in cytological preparations is most often based on the presence of a relatively monomorphic lymphoid population, contrasting with the typically polymorphous cell pattern seen in reactive proliferations. Therefore, potential cytological misdiagnoses may occur, either in lymphomas that present an apparently admixed cell pattern (false negative cases), or in reactive proliferations in which atypical cells are identified (false positive cases). For these reasons, excision biopsy is advocated by most authors to confirm a primary cytological diagnosis of lymphoma.⁸

CONCLUSION

FNAC is safe, rapid and cost effective method in establishing the diagnosis in large number of cases of lymphadenopathy. It can differentiate a neoplastic from a non-neoplastic process and therefore influence patient management preventing patient from being subjected to unnecessary surgery. However, the role of aspiration cytology in the assessment of primary lymph proliferative disorders has been less certain. Although FNAC does not replace histological examination in the diagnosis of lymphoma, it is still of value in suspicion/suggested diagnosis lymphoma. Even if aspirate shows polymorphic population to avoid false negative diagnosis biopsy is advisable considering clinical context.

Limitations

In many lymphoma cases typing is not possible on cytology. In many cases of secondary malignant lesions often lead to various secondary changes in the lymph nodes like cystic changes granulomatous reaction and smears with plenty of polymorphs and necrosis which makes their diagnosis on cytology a difficult task. In above mentioned condition histopathological examination is required.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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