



CYTOMORPHOLOGICAL EVALUATION OF LYMPH NODE LESIONS BY FNAC: A STUDY OF 252 CASES

Dr. Gulhane Sushma R	MD, DNB, Specialist-cum-assistant professor, Department of Pathology, ESIPGIMSR Andheri, Mumbai.
Dr. Ghanghurde Swati B*	MD, Senior resident, Department of Pathology, ESIPGIMSR Andheri, Mumbai. *Corresponding Author
Dr. Gangane Nitin	MD, DNB, Professor & HOD, Department of Pathology, MGIMS, Sewagram, Wardha.

ABSTRACT Lymphadenopathy is an abnormal increase in size of lymph node due to various causes that may range from non-neoplastic and benign to malignant lesions. The easy accessibility of lymph nodes makes fine needle aspiration cytology (FNAC) a first line of investigation in lymphadenopathy. The present study was undertaken to know distribution of various lymph node lesions amongst age groups, anatomical regions and to evaluate their cytomorphological patterns by FNAC. This study was conducted over five years which included 252 cases of lymph node FNAC. Majority of patients were diagnosed with reactive lymphadenopathy 129 (52.02%), followed by tuberculous lymphadenopathy 52 (20.97%), metastatic lymph node 34 (13.70%), primary neoplasm 14 (5.65%) and other acute and non-specific chronic lesions 18 (7.26%) cases. FNAC is a relatively painless and minimally invasive technique which produces fast results, and its accuracy can approach to histopathology in many cases.

KEYWORDS : cytology, lymph node, metastasis, fine needle aspiration cytology

INTRODUCTION

Lymphadenopathy is one of the common clinical presentations in outpatient department. Lymphoid tissue undergoes reactive changes to a wide variety of antigenic stimuli.¹ Tuberculosis, which is very common in India, can also be diagnosed by cytology of affected lymph nodes. Lymph nodes are also affected in primary neoplasm of the node itself and from metastasis of malignant neoplasm from other organs.²

FNAC has very important role in the diagnosis of lymphadenopathies especially in developing country like ours.³ With the advent of FNAC, most of the inflammatory, reactive and neoplastic conditions can be diagnosed without biopsy. This method is applicable both to lesions that are easily palpable and to deeply located lesions under radiological guidance. The results of FNA compare favourably with those of tissue biopsies.⁴

In this study our experience of the diagnostic utility of FNAC in assessment of lymphadenopathy is presented. It also highlights the cytomorphological spectrum of various lymph node lesions.

MATERIALS AND METHODS

This study is an analysis of 252 cases of lymph node FNAC done over a five year period at a tertiary care hospital. The cases included were all clinically diagnosed patients of lymphadenopathies reporting at the cytology section for FNAC. All the cases with palpable lymph node of size 1cm and more were included in our study. A detailed clinical history, physical examination findings and written informed consent for FNAC were recorded. FNAC was conducted with the help of a 22-24 gauge disposable needle attached to 20cc syringe under aseptic conditions. In case of intra-abdominal, intra-thoracic or deep seated lymph nodes, FNAC was done under ultrasound/computerized tomography (USG/CT) guidance. Three to four smears were made from aspirated material. Two smears were fixed in 95% ethyl alcohol and stained with Papanicolaou (PAP) stain. May Grünwald Giemsa (MGG) stain was done on air dried smears. Special stains like Zeihl-Neelsen (ZN), Per-iodic Schiff's stain (PAS) and Gomori's Methenamine Silver (GMS) were done on dry smears whenever required. All the smears were examined and cytological findings were noted. Inadequate and acellular smears were excluded for the purpose of statistical analysis.

RESULTS

Total numbers of 252 cases were analyzed in this study. The age of patients ranged from 2 to 81 years. The largest number of cases were in the third decade (56 patients) followed by second decade (42 patients). Lymphadenopathy was observed to be slightly more in males (136 cases, 53.97%) as compared to females (116 cases, 46.03%) with M:F

ratio 1.2:1. The lymph nodes size ranged from 1x0.8 cm to 8.5x 7 cm and all the nodes involved by malignancy were 2x2 cm or more in size. Table I shows site wise distribution of enlarged lymph nodes in different anatomical groups. Cervical lymph nodes were the most frequently aspirated (46.82%) followed by axillary (19.44%), inguinal (10.71%), submandibular (10.71%) cases each. Generalized lymphadenopathy was present in 03 cases, all diagnosed to be lymphoma.

Table 1-Distribution of various lymph node groups involved

Site	No of cases	Percentage (%)
Cervical	118	46.82
Axillary	49	19.44
Supra-clavicular	23	09.13
Inguinal	27	10.71
Generalized	03	01.19
Submandibular	27	10.71
Hilar	01	0.39
Abdominal	03	01.19
Iliac	01	0.39
Total	252	100

Table 2-Cytological diagnosis of lymphadenopathy cases (Excluding 04 inadequate aspirates)

Cytological diagnosis	No of cases	Percentage (%)
Reactive lymphadenitis	129	52.02
Tuberculous lymphadenitis	52	20.97
Acute suppurative lymphadenitis	12	4.84
Granulomatous lymphadenitis	06	2.42
Lymphoma(Hodgkin's & NHL)	14	5.65
Metastatic lymph node	34	13.70
Kikuchi Fujimoto lymphadenitis	01	0.40
Total	248	100

The breakup of cytological diagnosis is given in Table 2. Adequate material was obtained in 98.41% (248/252) cases with inadequacy rate of 1.59%. Reactive Lymphadenopathy was the most frequent diagnosis making up 52.02% (129/248) of the cases. In these lymph nodes lympho-histiocytic aggregates were present in 20.93% cases (27/129). (Fig1c-d) There was one case of Kikuchi-Fujimoto lymphadenitis showing necrotizing lymphadenitis with phagocytic histiocytes and extracellular debris. Acute Suppurative Lymphadenopathy was observed in 12/248 cases (4.84%) in our study. (Fig1a-b)

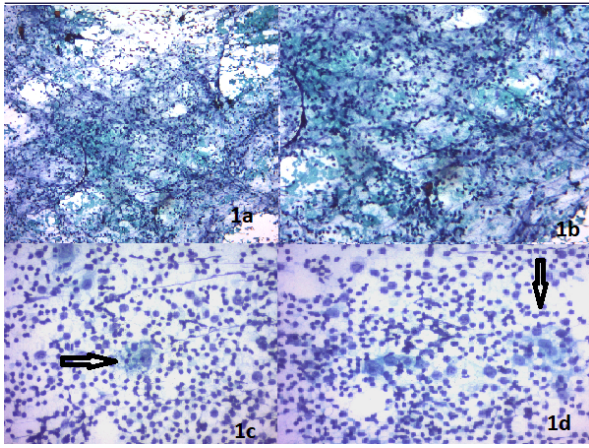


Fig1. 1a: Acute suppurative lymphadenitis (PAP 40x). **1b:** Predominantly neutrophilic infiltrate in acute suppurative lymphadenitis (PAP 100x). **1c:** Tingible body macrophages in reactive lymphadenitis (PAP 400x). **1d:** Lympho-histiocytic aggregates in reactive lymphadenitis (PAP400x).

There were 52 cases (20.97%) of tubercular lymphadenopathy in this series, in which 45 cases (86.53%) showed classical cytological features like presence of epithelioid granulomas, caseation necrosis and Langhans giant cells. However in 06 cases (11.5%) there was only caseation with scattered /degenerating epithelioid cells and secondary acute inflammation. In one case (1.92%) only necrosis was present, but on ZN stain acid fast bacilli (AFB) were seen. The rate of AFB positivity was 15.38% in this series. (Fig 2 a-d)

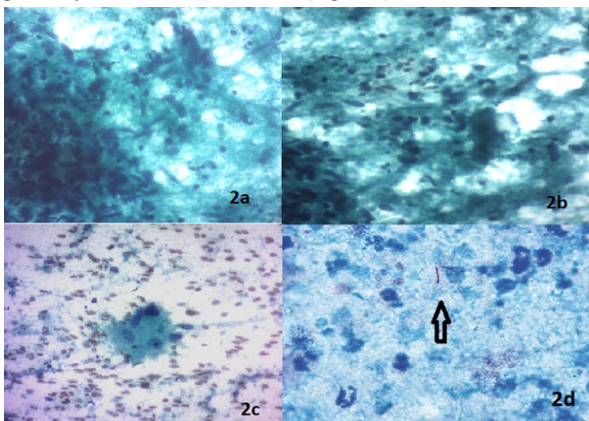


Fig 2. Tuberculous lymphadenitis. **a:** Clusters of loosely cohesive epithelioid histiocytes forming granuloma (PAP 400X). **2b:** Granular material of caseous necrosis (PAP 400X). **2c:** Langhans giant cell (PAP 400x) **2d:** Acid Fast positive bacilli (Zeihl-Neelsen stain 1000x).

Table 3 shows distribution of primary and metastatic malignancies in various lymph node groups. We diagnosed 48/248 (19.35%) neoplastic lesions in the lymph nodes, of which malignancy was clinically unsuspected in 07 cases (14.59%). There were more cases of metastatic involvement 34/48 (70.83%) than lymphoma 14/48 (29.1%). Of the lymphomas, six cases were given as Hodgkin lymphoma on cytology showing RS cells in reactive lymphoid background.(Fig3a-d) Eight cases of Non-Hodgkin lymphoma were diagnosed on cytology by the monomorphic population of cells.(Fig 4a-b) All these cases had were referred to higher cancer centre for further investigations and treatment.

Table 3-Site distribution metastatic tumors in various lymph node groups.

Site	No of cases	Percentage (%)
Cervical	16	47.05
Axillary	6	17.65
Supra-clavicular	3	08.82
Inguinal	5	14.70
Submandibular	4	11.76
Total	34	100

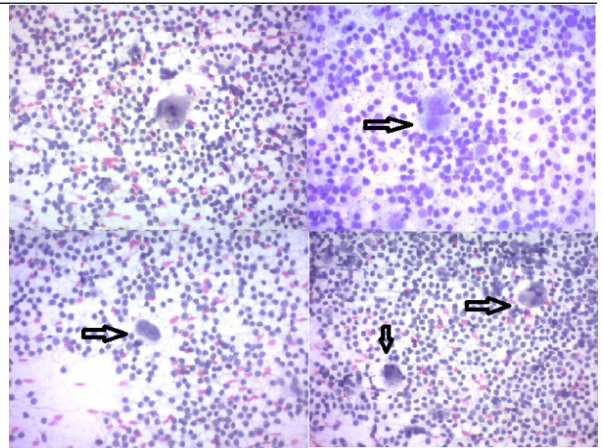


Fig 3.Hodgkin Lymphoma **a:** Reed-Sternberg cell in the background of mainly small lymphocytes (Giemsa 400x). **b:** Classic Reed-Sternberg cell with symmetrically double (mirror) nuclei (Giemsa 400x). **c:** Mononuclear Hodgkin cell with lymphoid background (Giemsa 400x). **d:** Multilobated Reed-Sternberg cell with lymphoid background (Giemsa400x).

Table 4 shows distribution of various types of metastatic malignancies. In metastatic lymph nodes, incidence of squamous cell carcinoma (SCC) was the highest (22 cases, 64.70%), followed by 09 cases (26.47%) of adenocarcinoma. (Fig 4c-d) In these 05 cases were of duct adenocarcinoma from breast metastasizing to axillary lymph nodes. Primary site was unknown (occult) in 04 cases (11.76) at the time of diagnosis.

Table 4-Distribution of various types of metastatic malignancies.

Type of primary malignancy	No of cases	Percentage(%)
Squamous cell carcinoma	22	64.70
Mets of Adenocarcinoma	9	26.47
Melanoma metastasis	2	05.88
Poorly differentiated carcinoma	1	02.94
Total	34	100

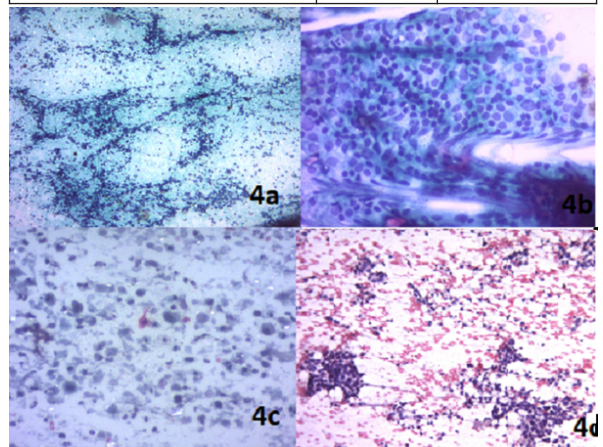


Fig 4: **a:** Non-Hodgkin lymphoma shows monomorphic population of lymphoid cell (PAP 40x). **b:** Non-Hodgkin lymphoma shows monomorphic population of lymphoid cell (PAP 400x). **c:** Metastasis of squamous cell carcinoma in lymph node (PAP 400x). **d:** Metastasis of duct carcinoma in lymph node (Giemsa 100x).

DISCUSSION

Lymphadenopathy has many underlying causes, ranging from self-limiting benign disease to severe neoplastic proliferations. FNAC is a cost-effective and reliable tool for initial investigation of enlarged lymph nodes reducing need of surgical biopsy. The sphere of FNAC has come a long way in conjunction with sophisticated CT and USG guided procedures to become an important diagnostic tool since 1950.⁴ In 1921, Guthrie at the Johns Hopkins Hospital tried to correlate FNA results of lymph node aspirates with various disease processes using Romanowsky staining on air dried films.⁵ It was Dudgeon and Patrick in 1927, who first used FNAC in diagnosis of tubercular lymphadenitis.⁶ In developing countries like India, FNAC plays a

significant role in evaluation of lymphadenopathy as it is a simple economical OPD procedure. Histopathological examination plays a superior role in diagnosis and sub categorizing lymphomas but for metastatic malignancies FNAC plays a very important role as far as diagnosis is concerned.^{7,8}

In the present study, we performed FNAC on 252 cases of lymphadenopathy to study their cytomorphological and epidemiological patterns. Adequate material was obtained in 98.41% of cases which is correlated with study by Hemlatha et al (97%)⁹, Gupta et al (85.2%)¹⁰ and Badge et al (99.38%)². Causes of unsatisfactory smear were scanty cellularity or obscuring blood.

In the study by Badge et al² and Chandanwale et al¹¹ majority of patients were in the age group of 21-30 years and 21-40 years respectively. In our study, the largest number of cases were in the third decade (56 patients) followed by second decade (42 patients) which is correlating well with these studies. Lymphadenopathy was observed to be slightly more in males (136 cases, 53.97%) as compared to females (116 cases, 46.03%) with M : F ratio 1.2:1 in present study whereas Badge et al² found female preponderance with M : F ratio of 1:1.55. The lymph nodes size ranged from 1x0.8 cm to 8.5x 7 cm and all the nodes involved by malignancy were 2x2 cm or more in size.

In the present study, on evaluation of lymph nodes from different anatomical regions or groups, it was seen that the cervical lymph nodes were the most frequently aspirated (46.82% cases) followed by axillary (19.44% cases), inguinal (10.71% cases) and supraclavicular (9.13% cases). Similar observations were made in study by Khajuria et al⁸ and Badge et al².

Other studies showed the pattern of lesions varying from non-neoplastic lesions like reactive lymphadenopathy, tuberculous lymphadenopathy, acute suppurative lymphadenopathy, granulomatous lymphadenopathy, sinus histiocytosis and non-specific lymphadenopathy, to neoplastic lesions like metastatic lymphadenopathy and Lymphomas.^{1,4,8,9} In our study also similar patterns were seen with reactive lymphadenopathy observed to be the most frequent diagnosis in 52.02% cases. It was also the most frequent diagnosis in other studies and its incidence has been seen to range from 18.9% to 42%.^{1,2,4,8,12}

The second most frequent diagnosis in present study was observed to be chronic granulomatous inflammation in cases 23.38%. The incidence of granulomatous inflammation was observed to vary from 9.2% to 25.45% in other studies.^{4,6,7,12,13} In our study 20.97% cases were diagnosed as tubercular lymphadenitis whereas 2.42% cases were of nonspecific granulomatous inflammation. This correlated with the previous studies in which incidence of nonspecific granulomatous inflammation is reported to be 2.30% to 2.63% of all lymph nodes aspirated.^{9,11}

Tuberculosis lymphadenopathy diagnosed by cytology alone in other previous studies showed a range varying from 28% to 52%.^{1,2,4,6,12} Previous studies on tuberculous lymphadenitis have found only necrosis without epithelioid granuloma or giant cells in 35% cases.^{6,9,11}

In such cases Zeihl- Nielson's stain should be done to demonstrate Acid Fast Bacilli. Low incidence of AFB positivity on ZN smears was noted in our study (15.38%) which is in accordance with the study done by Birader et al¹ (15%) and Agarwal et al¹⁴ (19.65%). This could be attributed to the compromised immune status or inadequacy of the cellular immune response.

Acute Suppurative Lymphadenopathy was observed in 4.84% cases in our study which is in accordance with study done by Birader et al (4.37%) and other studies showing range of 4% to 5.8%.^{14,8,12} All 12 cases of suppurative Lymphadenopathy were negative for Acid Fast Bacilli.

We diagnosed 19.35% cases of neoplastic lesions in the lymph nodes by FNAC, of which 70.83% cases showed metastatic involvement rather than lymphoma (18%). This was similar to other Indian studies.^{2,4,8,12} Other studies have found the incidence of neoplastic involvement to vary from 10.1% to 47.8%.^{3,9,11,15}

There were no biopsies done in any of our cases probably because the clinicians were convinced with our cytological diagnosis, correlating with their clinical diagnosis. In cases of primary neoplasm or

metastatic lymphadenopathy all these patients were referred to Super-specialty cancer hospital for further treatment as facilities for radio/chemotherapy are not available in our institute.

In our study the cervical group was the most common to be involved by metastasis (47.05% cases) and the primary was most often from the oral cavity, which was similar to other studies with SCC being the most common histological type.^{5,8,15} Rates for oral cavity, pharynx, oesophagus and male larynx are highest in India, probably due to the use of multiple tobacco products.¹⁵

In present study in 14.59% cases of malignant involvement of lymph nodes were not clinically suspected. Other studies have found this incidence to vary from 5.8% to 25.03%.^{8,13,15} Hence FNAC plays a major role in diagnosing such cases.

The primary sites identified in lymph node groups in our study correlated well with other similar studies.^{1,4,15} A full history, radiological investigations and immunohistochemistry in difficult cases may help to arrive at a definitive diagnosis.¹⁵ However, in 11.76% cases primary site was occult at the time of diagnosis of metastasis by FNAC. SCC was the most common cytological diagnosis followed by adenocarcinoma in our study. Our findings were in accordance with other pioneer workers.^{8,9,15} Breast carcinoma was the second most common primary site to be involved. The primary site of the tumor could not be established in 04 patients in our study. The results were comparable to other data in previous studies.^{1,2,3,15}

Thus FNAC of the lymph nodes can be used as an effective diagnostic tool for lymph node lesions. The diagnosis given on the cytological material is often the only diagnosis accepted and sometimes there is no further correlation with histopathology, especially in cases of advanced malignancies. It also provides clues for occult primaries and sometimes also surprises the clinician who does not suspect a malignancy.

CONCLUSION

Lymphadenopathy is a commonly encountered clinical condition requiring prompt and accurate diagnosis so that a proper treatment protocol can be started earliest possible. FNAC is a simple technique that has gained wide acceptance since it offers several advantages to patients and clinicians also. With its advent, most of the inflammatory, reactive and neoplastic conditions can be diagnosed without biopsy. It may be the only tool in the diagnosis of metastatic lesions in the lymph nodes and can help to detect occult primary malignancies. Hence, the cytopathologist plays a vital role in the diagnosis of various lesions of lymph node. FNAC should be regarded as an essential component of preoperative/pre-treatment diagnosis, when correlated clinical and radiological observations.

Conflicts of interest- There are no conflicts of interest.

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