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Clinico-morphological spectrum and diagnostic efficacy of fine needle aspiration cytology in enlarged lymph nodes: A hospital based study of 1053 cases

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Abstract

Introduction: Fine Needle Aspiration Cytology (FNAC) is simple, cheap, useful and minimally invasive diagnostic tool for enlarged lymph node lesions. The present study has been undertaken to emphasize the Clinico-cytomorphological spectrum and to determine the diagnostic efficacy of FNAC in enlarged lymph nodes.

Material and Methods: A 5 year hospital based cross-sectional observational study of 1053 patients was conducted, with all relevant clinical details and FNAC was performed and dry and wet smears were prepared and stained. Ziehl-Neelsen (ZN) Staining was done wherever required. The cytomorphological features were correlated with the concomitant histopathological findings, wherever available.

Results: A total of 1053 cases were studied, with slight female preponderance of 51.6%. Out of 1053 cases, 972 were non neoplastic cases while 81 were neoplastic. Cervical group of lymph. Nodes was most commonly involved (628/1053 cases). Maximum number of aspirates were reported as Chronic non-specific lymphadenitis 32.9% (346/1053 of total). Among the neoplastic lesions (81/1053), majority of cases were of metastatic squamous cell carcinoma 42/81 (51.85%). In non-neoplastic lesions, chronic non-specific lymphadenitis and reactive lymphadenitis was most frequently seen in first decade of life, 114/346 cases and 59/182 cases respectively. Whereas tubercular lymphadenitis were more common in 21-30 years age group (101/265 cases) followed by 11-20 age group (80/265cases). Among the neoplastic cases, Metastatic squamous cell carcinoma was most commonly seen in 5th decade. Hodgkin's lymphoma was more common in 11-20 years age group (4/11cases), whereas Non-Hodgkin's lymphoma was maximum in 41-50 years age group (5/15cases). Out of 1053 aspirates, histopathological confirmation was available in 20 lymph node lesions. FNAC findings were correlated with histopathological diagnosis in 85% (17/20) cases. The sensitivity, specificity, positive predictive value and negative predictive value of FNAC of lymph nodes were 77.78%, 100%, 100% and 84.62% respectively. The diagnostic accuracy was 90%.

Conclusion: FNAC is an efficient minimally invasive diagnostic method for early diagnosis of enlarged lymph nodes.

Keywords: FNAC, lymph nodes, clinico-morphological spectrum, cytohistopathological correlation

1. Introduction

The lymphatic system was described by Erasistratus in Alexandria more than 2000 years ago [1]. A normal young adult body contains upto 450 lymph nodes, of which 60–70 are found in the head and neck, 100 in the thorax and 250 in abdomen and pelvis [2]. Enlargement of lymph nodes occur due to infections (Abscess or impacted tooth, ear infection, cold flu and other infection, gingivitis, mononucleosis, mouth sores, sexually transmitted disease, tonsillitis, tuberculosis, skin infections), immune and autoimmune disorders (HIV, Rheumatoid arthritis), cancers (Leukemia, Hodgkin's disease, non – Hodgkin's lymphoma etc) and due to medications (Phenytoin, typhoid immunization) [3]. FNAC is a simple, rapid, reliable, safe, cost effective technique with good diagnostic accuracy. It may obviate the need for surgical biopsy [4].

2. Material and Methods

The present study was conducted in the Department of Pathology, Subharti Medical College,

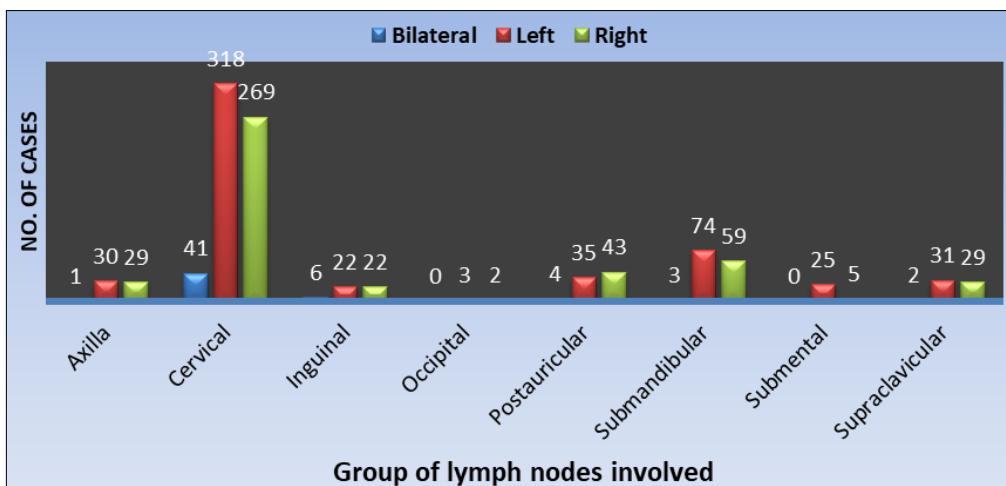
and associated Chhatrapati Shivaji Hospital, Meerut. This is a hospital based cross-sectional observational study from August 2015 to August 2017. FNAC lymph node smears from archives of department of Pathology were also included in present study. Total 1053 cases of lymph nodes were studied, out of which 516 were prospective cases and 537 cases were retrieved from the archives of department of Pathology.

The inadequate samples were excluded from our study. FNAC was performed using a 22 gauge needle by aspiration using the syringe fitted holder or non aspiration (Direct needle puncture) technique. Depending upon the aspirate obtained, both dry and wet slides were prepared. Dry slides were air dried and stained with Leishman Geimsa stain and wet smears were immediately fixed with 95% alcohol & stained by Haematoxylin and Eosin (H&E) and/or Pap stain. Ziehl Neelsen (ZN) staining was done for demonstration of acid fast bacilli wherever required. Slides were studied under the microscope and cytological findings were recorded. For histopathological analysis, formalin fixed paraffin embedded blocks were studied. H & E stained sections were analysed and same were for retrieved cases. The cytomorphological features were correlated with the concomitant histopathological findings, wherever available. Data Analysis was done by Statistical Package for the Social Services (SPSS) version 20. Age, gender and site of FNAC patterns were expressed as frequency and percentage.

Correlation of cytodiagnosis with age and gender was done on the basis of Chi-Square test taking into consideration the gender of freedom (df) relative to each variable. Significance was estimated by p-value; p-value<0.001 showed significant association between the two variables. Diagnostic sensitivity, specificity, Positive predictive value (PPV), Negative predictive value (NPV) and accuracy of FNAC was calculated for lymph node lesions (Non-neoplastic and Neoplastic) by 2 x 2 contingency table by comparing the test diagnosis with the gold standard diagnosis.

3. Results

This study analysed 1053 cases of enlarged lymphadenopathy. The age of patient ranged from 1years to 95 years. Mean age of males and female being 24.42 years and 26.45 years respectively. Majority of the patients were in second decade 26.2% (276/1053) cases, followed by 23.9% & 19.8% in 3rd & 4th decade respectively. There were 51.6% (543/1053.) females and 48.4% (510/1053) males. Female to male ratio was 1.06:1. Out of total 1053 Lymph node lesions, maximum cases, 628/1053 (59.63%), were seen in cervical region followed by submandibular region, 136/1053 (12.91%), postauricular 82/1053 (7.79%) and supraclavicular region, 62/1053 (5.89%). Other groups involved were axilla, inguinal, submental and occipital region. (Figure1).



X2 = 27.262, df = 14, p value (<.018), significant association

Fig 1: Bar diagram showing sidewise distribution of various lymph node groups.

Left sided (51.1%, 538/1053) lymphadenopathy was common than right sided (43.5%, 458/1053). Only 5.4% (57/1053) cases showed bilateral lymph node enlargement. Out of total 1053 Lymph node lesions were included in study, of which 972 (92.31%) were non-neoplastic, and 81/1053 (7.69%) neoplastic. Maximum number of aspirates were reported as Chronic non-specific lymphadenitis 32.9% (346/1053 of total) followed by tubercular lymphadenitis

25.2% (265/1053). Various other non-neoplastic lesions were observed as shown in (Table1). 81 out of 1053 (7.69 %) fine needle aspirates, were diagnosed as malignant lymph node lesions. Majority of cases were metastatic squamous cell carcinoma 42/81 (51.85%). followed by Non-Hodgkin’s Lymphoma 15/81 (18.51%). Rest were metastatic adenocarcinoma and Hodgkins lymphoma as shown in (Table 1).

Table 1: Cytological spectrum of lymph node lesions

Diagnostic category	Cytological diagnosis	No. of cases	Percent
Non-neoplastic (972)	Chronic Non-specific Lymphadenitis	346	32.9%
	Tubercular Lymphadenitis	Granuloma	86/265
		Necrosis	48/265
		Granuloma + Necrosis (Photomicrograph 1)	131/265
	Reactive Lymphadenitis	182	17.3%
Chronic Granulomatous Lymphadenitis	150	14.2%	

	Necrotizing Lymphadenitis	16	1.5%
	Acute Suppurative Lymphadenitis	13	1.2%
Neoplastic (81)	Metastatic Squamous Cell Carcinoma (Photomicrograph 3)	42	4.0%
	Non-Hodgkin's Lymphoma	15	1.4%
	Metastatic Adenocarcinoma	13	1.2%
	Hodgkin's Lymphoma (Photomicrograph 5)	11	1.0%
	Total	1053	100.0%

In tubercular lymphadenitis both necrosis and granulomas were seen in 49.43% cases while 18.11% cases showed only necrosis. 32.45% cases showed granulomas without

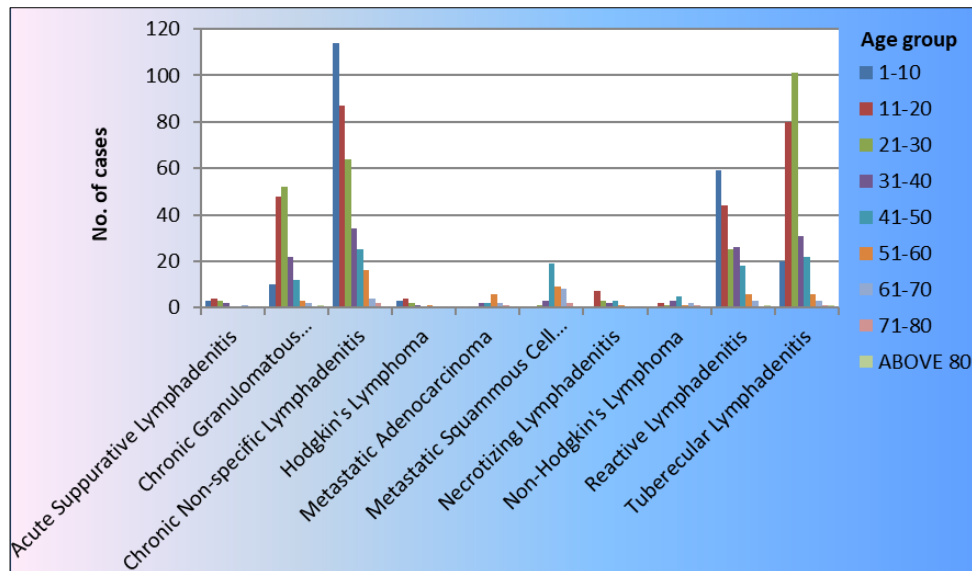
necrosis. Ziehl-Neelsen (ZN) stain for Acid fast bacilli (AFB) was performed on 431 cases. (Table 2).

Table 2: AFB positivity on Zn staining

AFB positivity on Zn staining	No. of cases	Percentage	Cytopathology
AFB Positive	265	61.48%	Tubercular lymphadenitis (Photomicrograph 2)
AFB Negative	166	38.51%	- Chronic Granulomatous lymphadenitis - Necrotizing lymphadenitis
Total	431	100%	

In non-neoplastic lesions, chronic non-specific lymphadenitis (346/1053 cases, 32.85%) constituted the largest disease group with maximum incidence in the 1st decade followed by tubercular lymphadenitis (265/1053 cases, 25.16%) with maximum incidence in 3rd decade. In

malignant lesions, metastatic squamous cell carcinoma constituted the largest disease group (42/1053 cases, 3.98%) with maximum incidence in the 4th decade followed by Non-Hodgkin's Lymphoma (15/1053 cases, 1.42%) with maximum incidence in 4th decade. (Figure 2).



$\chi^2 = 433.043$, $df = 72$, p value ($<.000$), significant association

Fig 2: Bar diagram showing correlation of age group with lymphnode lesions

Male preponderance was noted in Neoplastic lesions of Lymph node as compared to Non-neoplastic lesions which were seen more commonly in females.

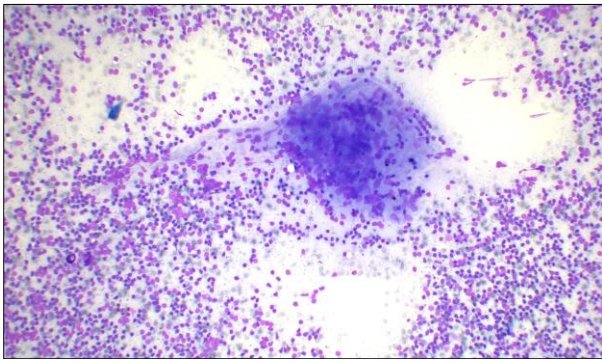
Out of 1053 aspirates, histopathological confirmation was available in 20 lymph node lesions. Histopathology was taken as gold standard. FNAC findings were correlated with histopathological diagnosis in 85% (17/20) cases, However, 3 aspirates showed discrepancy reported on cytopathology, 1 case was diagnosed as chronic non-specific lymphadenitis

while its histopathology showed tubercular lymphadenitis (therefore it remained non-neoplastic).

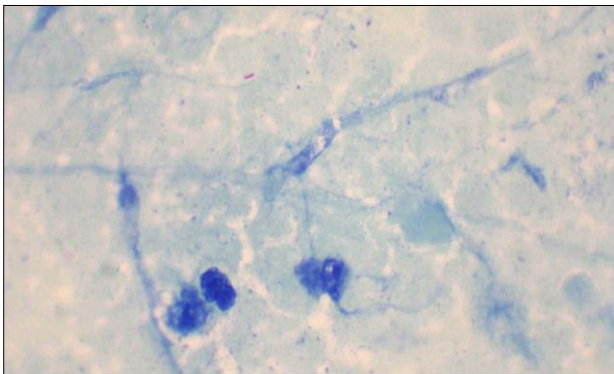
Two cases which were diagnosed non-neoplastic on cytopathology were reported as neoplastic on histopathology. First case was Metastatic Squamous Cell Carcinoma on histopathology diagnosed as Acute Suppurative Lymphadenitis on cytopathology and second case was Hodgkin's lymphoma on histopathology and in cytopathology was reported as reactive lymphadenitis. (False negative cases) (Table 3).

Table 3: Cyto-histopathological correlation

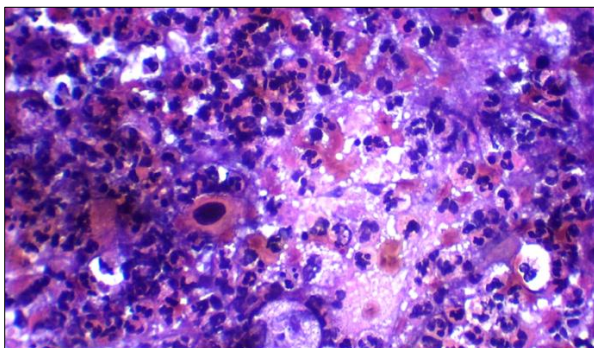
Cytodiagnosis	Histo-pathology Available	Cyto-histo Concurrence	
		Yes	No
Tubercular Lymphadenitis	11	10	1
Metastatic Squamous Cell Carcinoma	2	1 (Photomicrograph 3,4)	1
Non Hodgkins Lymphoma	3	3	-
Hodgkins Lymphoma	4	3 (photomicrograph 5)	1
Total	20	17	3



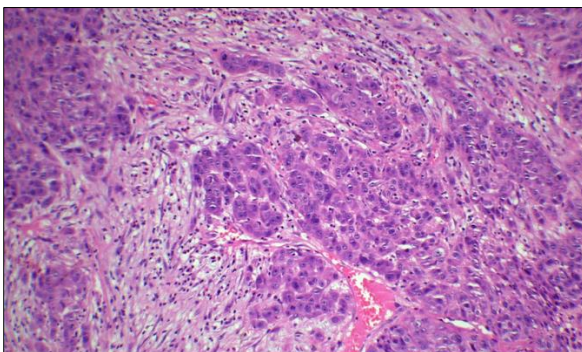
Photomicrograph 1: FNAC lymphnode-Epitheloid cell granuloma in Tubercular lymphadenitis. (Leishman & Giemsa stain, 100 x)



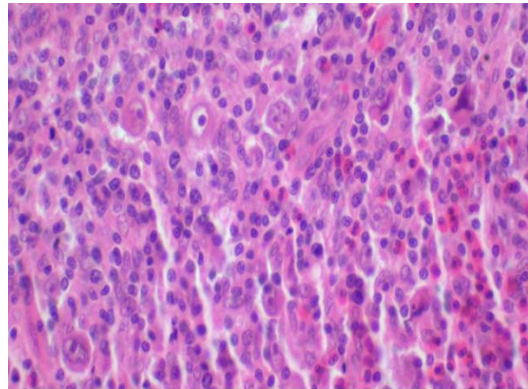
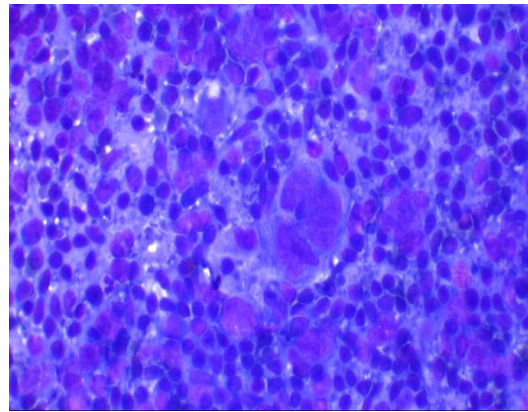
Photomicrograph 2: FNAC lymph node-Tubercular lymphadenitis showing acid fast bacillus (↑) (Ziehl Neelsen stain. 1000x).



Photomicrograph 3: FNAC lymphnode (left) - Metastatic squamous cell carcinoma (Pap Stain, 400 x)



Photomicrograph 4: Histopathology lymphnode- metastatic squamous cell carcinoma (H & E, 400x)



Photomicrograph 5: FNAC lymphnode (left)-(Leishman – Giemsa, 400 x) and Histopathology (right) of Hodgkins lymphoma showing RS cells (H & E, 400x)

Statistical indices of fnac lymph node as a diagnostic test

Considering histopathology as gold standard for diagnosis, the ‘p’ value (chi-square test) for cyto-histomorphological correlation was significant ($p < 0.05$).

The sensitivity, specificity, positive predictive value and negative predictive value of FNAC of lymph nodes were 77.78%, 100%, 100% and 84.62% respectively. The diagnostic accuracy was 90%. (Table 4).

Table 4: Statistical indices of FNAC as a diagnostic test

Cyto-histopathological correlation (Total cases)	20
True positive (TP)	7
False positive (FP)	0
True negative (TN)	11
False negative (FN)	2

4. Discussion

Lymph node lesions are a common clinical problem in India posing a diagnostic dilemma in clinical practice. The causes of lymphadenopathy vary from simple treatable infections to spectrum of malignancies that require highly specialized institutional management. It therefore needs proper and appropriate investigation. In present study 1053 patients of all age group presenting with lymphadenopathy were subjected to FNAC and cytological findings were analyzed. Cytohistological correlation was done wherever it was available and the results were analyzed. In the present study, age of the patient ranged from 1 year to 95 years of age, with the mean age of 25.64 years. Majority of the patients were in 2nd decade 26.2% (276/1053) cases, followed by

23.9 % in 3rd decade, similar to the study done by Buli GA *et al.* [5], Saraswat A *et al.* [6]. Our study was in accordance to the study conducted by Buli G A *et al.* [5] with Female preponderance 51.6% (543/1053) cases and Male to Female ratio of 1:1.06. Lymph node lesions were more common in Left side (51.1%) than right side (43.5%). Bilateral involvement was seen 57 (5.4 %) cases in this study. Similar observations were reported by Buli GA *et al.* [5] Alam K *et al.* [7]. In the present study most common lymph node group involved was cervical, 628/1053 (59.63%) similar to the study by Kochhar A *et al.* [8] Buli GA *et al.* [5] Roy A *et al.* [9] Hirachand S. *et al.* [10], Giri S and Singh K [11], Sharma M *et al.* [12].

Cytomorphological patterns obtained in our study were predominantly non-neoplastic 972 /1053(92.3%) and 81 (7.69%) were neoplastic. Similar results were seen in studies done by Buli GA *et al.* [5], Saraswat A *et al.* [6], Roy A *et al.* [9], Wakely PE Jr, Kardos TF and Frable WJ [13]. In the present study, among the non-neoplastic lesions (972/1053), Chronic non-specific lymphadenitis (346, 35.59% cases) was the most common cytological pattern observed followed by Tubercular lymphadenitis (265, 27.26% cases). Similar cytomorphological patterns were observed by Annam V, Kulkarni MH and Puranik RB [14] and Zohu J *et al.* [15]. In the present study, Tuberculosis was reported in 265cases (25.16%) of lymph node aspirates, out of which 49.43% cases showed both necrosis and granulomas whereas only necrosis and granuloma was seen in 18.12% and 32.45% cases respectively. Special stain for AFB (Ziehl-Neelsen stain) was found to be positive in 61.48% cases. Saraswat *et al.* [6] and Kochhar A *et al.* [8] had found similar findings in their studies. Among neoplastic lesions (81/1053 cases) of lymph nodes, 42/81 (51.8 %) cases were of metastatic squamous cell carcinoma, (16%) 13/81 cases were of metastatic adenocarcinoma, and (32.1%) 26/81 cases were of lymphoma, which was in accordance with the studies by Kochhar A *et al.* [8] and Hirachand S. *et al.* [10] Chachra U *et al.* [16] and Giri S and Singh K [11]. Out of 1053 cases Cytohistopathological correlation was available in 20 cases. Histopathological findings were consistent in 17 cases (Table 3). The sensitivity, specificity, positive predictive value and negative predictive value of FNAC lymph nodes were 77.78%, 100%, 100% and 84.62% respectively in this study. The diagnostic accuracy was 90% (Table 4). This was close to the findings of Alam K *et al.* [7] where 97.9% diagnostic accuracy, 97.9% sensitivity and 100% specificity. Giri S *et al.* [11] reported sensitivity, specificity and diagnostic accuracy 90.32%, 90.90% and 90.56% respectively in their study. Wakely PE Jr, Kardos TF and Frable WJ [13] found that overall sensitivity ranged from 80-97% and specificity was in the range of 85-99%.

5. Conclusion

FNAC in the diagnosis of enlarged lymphadenopathy was sensitive, specific and accurate. It is useful minimally invasive diagnostic tool. The cytomorphological spectrum of enlarged lymph nodes, is required for "On the spot" diagnosis. As it is always urgent requirement of the surgeons and physicians to know whether the lymph node is reactive, tuberculous or malignant for the planning of treatment.

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Conflict of Interest: None

Ethical approval: The study was approved by the institutional ethics committee.

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