

# Study of Fine Needle Aspiration Cytology in Lymphadenopathy with Special Reference to Acid-fast Staining in Cases of Tuberculosis

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## Abstract

The present study was conducted to evaluate the usefulness of FNAC as a diagnostic tool in 1000 patients of lymphadenopathy. Fine needle aspiration was performed in all the patients following through clinical examination and slides were stained with H & E, PAP and Ziehl Neelsen stains. The results of FNAC were further correlated with paraffin embedded sections of tissue blocks. Eight hundred and sixty-four cases (86.4%) were of benign lymphadenopathy; out of which 536 (53.6%) cases were of reactive nature and 328 cases (32.8%) were tubercular. The remaining 136 (13.6%) cases were of malignant lymphadenopathy, consisting 45 (4.5%) cases of primary malignancies i.e. lymphomas and 91 (9.1%) cases of metastasis to lymph nodes. Out of 328 cases, Z-N positivity for AFB was found in 152 cases (46.4%) and Mantoux test was positive in 180 cases (54.9%). On correlation of FNAC findings with histopathology; sensitivity and specificity was found out to be 91.6% and 99%, respectively, with diagnostic accuracy of 97.3% in cases of benign lesions. The same being 97%, 97.5% and 97.4%, respectively in tubercular lesions. The sensitivity, specificity and diagnostic accuracy was 100% each in malignant lesions. FNAC of lymphnodes is an excellent first line method, for investigating the nature of the lesions, as it is economical and convenient alternative to open biopsy.

## Key Words

FNAC, Lymphnodes, Malignant, Tubercular, Reactive.

## Introduction

Superficial lymphadenopathy is a common clinical finding; it may be a sign of inflammation, metastatic malignancy or malignant lymphoma. Fine needle aspiration cytology (FNAC) is a simple and rapid diagnostic technique. Because of early availability of results, simplicity, minimal trauma and complication, the aspiration cytology is now considered as a valuable diagnostic aid and is gaining popularity. The cytomorphological features obtained in needle aspiration, frequently correlate very well with histologic appearance of the same lesion and in some situations has qualities of a micro-biopsy. In conjunction with radiologic studies, it provides ease in following patients with known

malignancy and ready identification of metastasis or recurrence (1). The present study is undertaken to evaluate the usefulness of FNAC as a diagnostic tool in cases of lymphadenopathy and study the different cytomorphological patterns associated with various lymphadenopathies in Pap, H & E and performing acid fast staining in suspected tuberculous cases. This is of particular importance in view of the high prevalence of tuberculosis in our country, atypical presentation of tuberculosis and because of the fact that AFB are seen mostly in purulent aspirate smears which do not show granulomas, necrosis or epithelioid cells and which in absence of Ziehl-Neelsen staining can be dismissed as acute suppurative lymphadenitis (2).

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## Material and Methods

The present study on 1000 patients of lymphadenopathy was conducted in the Department of Pathology J.N. Medical College, AMU, Aligarh from May 2002 to May 2003. FNAC of the enlarged lymphnodes was performed with informed consent of the patient; following thorough clinical examination. Palpable nodes were aspirated in the cytology department and deeply located ones were aspirated by a radiologist using a 23-25 G needle and syringe. In all the cases, alcohol fixed smears were made and stained with H & E and Pap stains; and for each case an additional slide was kept unstained. In all cases where the cytological diagnosis was of a granulomatous disease, Ziehl-Neelsen staining was performed to see for acid fast bacilli. The aspiration smears from the enlarged lymphnodes were studied to arrive at a probable diagnosis. The results of FNAC further correlated with the histological diagnosis, from paraffin embedded sections of tissue blocks, fixed in 10% formal saline.

## Results

The patients were evaluated into two broad categories of benign and malignant disorders. 864 cases (86.4%) were of benign lymphadenopathy, of which 536 cases (53.6%) were of reactive nature and 328 cases (32.8%) were tubercular. The remaining 136 cases (13.6%) were of malignant lymphadenopathy; consisting 45 cases (4.5%) of primary malignancies i.e. lymphomas and 91 (9.1%) cases of metastasis to lymphnodes.

The nodal site sampled most frequently was cervical group in 736 cases (73.5%), followed by axillary groups in 106 cases (10.6%). The peak incidence of benign lesions was seen by us in the first two decades, and of malignant lesions was in the sixth decade. In our study, size of lymph node was found to be less than 1 cm in 80% cases of reactive lymphadenopathy and over 1 cm in 84% and 83% cases of tubercular and malignant lymphadenopathy respectively. Ninety-five percent cases of reactive and 89% of malignant lymphadenopathy showed discrete lymph nodes, whereas 60% cases of tuberculosis had matted lymph nodes.

The criteria by which a diagnosis of reactive lymphadenopathy was established included high cell density; polymorphic patterns of cells without malignant features and a considerable number of tingible bodies.

The aspirates from lymphnodes were diagnosed as tubercular lymphadenopathy based on the presence of either epithelioid cell granuloma with or without langhan's giant cells, with necrosis in a milieu of parent lymphoid cells or epithelioid cells granuloma without necrosis and caseation or only necrotic material consisting of diffuse granular debris. The cytological findings of 328 cases of tubercular lymphadenitis are shown in table-1.

**Table 1. Cytologic findings of 328 cases of tubercular lymphadenitis**

Cytologic findings	Number of cases	Percentage	Z-N positive	
			No.	%age
Granulomas alone	95	28.9	15	15.8
Granuloma+ necrosis	150	45.8	80	53.3
Necrosis alone	83	25.3	57	68.8
<b>Total</b>	<b>328</b>	<b>100</b>	<b>152</b>	<b>-</b>

Out of 328 cases of tuberculosis, 180 cases (54.9%) were Mantoux positive (Mantoux positive was considered when the erythema was present along with induration which was more than or equal to 10 mm in size, 72 hours after intradermal injection of 0.1 ml of PPD in the flexor surface of the forearm). There were 136 (13.6%) cases of malignant lymphadenopathy, which included 45 (4.5%) cases of primary malignancies i.e. lymphomas and 91(9.1%) cases of metastasis to lymphnode. Thus, it was noted that metastatic tumour accounted for 67% cases of malignant lymphadenopathy, Non-Hodgkin's lymphoma for 30(22%) cases and Hodgkin's lymphoma for 15(11%) cases. The ratio of Non-Hodgkin's lymphoma to Hodgkin's lymphoma was found to be 2:1. Out of the total 91(9.1%) cases of metastasis to lymphnode, 49(53.8%) were of metastatic squamous cell carcinoma, 15(16.6%) were of adenocarcinoma, 8(8.8%) were of undifferentiated carcinoma, 13(14.2%) of metastatic ductal carcinoma from breast, 2(2.2%) of metastatic retinoblastoma and 1 each (1.1%) of metastatic malignant melanoma, germ cell tumour, ALL and CML infiltration in lymphnode. Most of the metastatic squamous cell carcinoma had a primary in the oral cavity (49%), followed by occurrence in larynx (16%) and 10% each in nasopharynx and lung. A correlation was done in 115 cases which were diagnosed both by FNAC and histopathology. Out of 115 cases, 47 cases were benign and 68 were malignant. Of the 47 benign lesions, in 3 cases the FNAC diagnosis did not correlate with the histopathological diagnosis. Of the 47 cases, 12 were of reactive lymphadenopathy, 11 of

which were true positive, and 1 was false positive which turned out to be a lymphoma on histopathological examination. The results show 91.6% sensitivity, whereas specificity was found to be 99%, with diagnostic accuracy of 97.3%.

In 35 cases of tubercular lymphadenitis, histological correlation was seen in 33 cases. Two cases which were diagnosed as tuberculous on FNAC were found to be lymphoma on histopathological examination. Sensitivity, specificity and diagnostic accuracy was found to be 97.0%, 97.5% and 97.4% respectively.

Out of the 68 malignant lesions in which cytohistological correlation was done, 28 were of lymphomas and 40 of metastatic carcinoma. Out of the 28 cases of lymphoma, histological correlation was found in 26 cases, one was diagnosed as reactive lymphadenopathy and other one as tuberculosis on histopathology. Sensitivity in cases of lymphoma was thus 89.6%, specificity 97.6% and diagnostic accuracy 45.6%. In cases of metastatic carcinoma to lymphnodes, all 40 cases showed exact correlation in histopathology. Thus sensitivity, specificity and diagnostic accuracy was 100% each (Table 2).

**Table 2. Sensitivity and specificity of cytological diagnosis in various diseases**

Cytological Diagnosis	No. of cases	Histopathology				Sensitivity(%)	Specificity(%)	Diagnosis Accuracy(%)
		Reactive	Tuberculosis	Lymphoma	Metastasis			
Reactive	12	11		01		91.6	99.0	97.3
Tuberculosis	35		33	02		97.0	97.5	97.4
Lymphoma	28	01	01	26		89.6	97.6	95.6
Metastasis	40				40	100	100	100
<b>Total</b>	115	12	34	29	40			
<b>Overall</b>						94.6	98.5	97.6

## Discussion

Fine needle aspiration is a simple and rapid diagnostic technique for evaluation of lymphadenopathy. In the present study, out of a total of 1000 patients, 864 (86.4%) cases were benign and 136(13.6%) cases were of malignant lesions. These findings correlate well with the results reported by Sarda *et al* (3), who found 84.5% cases of benign lesions and 15.5% cases of malignant lesions. Pamra *et al* (4) also quoted a similar incidence of benign lesion as 85.4% and malignant lesions

as 14.6%. However, Steel *et al* (1) reported 59% cases of malignant lesions and 34% cases of benign lesions. This may be attributed to the fact that western countries, where these studies were carried out show predominance of malignant conditions over benign conditions. In our study bulk of diseases are of reactive nature due to infections and of tubercular lesions, which are uncommon in western countries. The lesions arising in the lymphnode can be found in patients ranging from early to advanced age. In our study, the youngest patient was 2 years old and oldest was 95 years of age. These figures come in close comparison to Steel's study (1) of 1,105 patients where the youngest patient was 1 year old and oldest was of 90 years.

In our study the most common site of involvement was cervical lymphnode in 73.6% of cases, which was followed by axillary group of lymphnode (10.8%) and inguinal lymphnode (6.0%). These observations are comparable with the findings of Egea *et al* (5), who reported 67.5% cervical, 9.0% axillary and 6.5% inguinal lymphnode involvement. We observed the peak incidence of benign lesion in the first two decades while the malignant lesions in the sixth decade, which correlated with that of Sarda *et al* (3). Majority of the cases were reactive in nature, 536 (53.6%) cases which correlated well with findings of Egea *et al* (5), who reported 55.1% cases of reactive or non-specific lesions. Reactive glands were mostly less than 1 cm in size in 80% cases whereas tubercular and malignant glands were over 1 cm in size in 84.8% and 83.1% cases respectively. These findings are in accordance with that of Bedi *et al* (6), who reported lymphnodes of over 1 cm size in reactive, tubercular and malignant lesions in 28%, 90% and 80% cases respectively. Matted lymphnodes were seen in tuberculosis (60%), whereas discrete lymphnodes were seen in 95.3% and 89% cases of reactive and malignant lesions. Similar has been reported by Bedi *et al* (6) and Pamra *et al* (4).

Our findings constituted 328 (32.8%) cases of tubercular lymphadenopathy, which is in concordance with those described by Tilak *et al* (7). These observations were slightly higher than that reported by Dev Prasoan (8), who noted a percentage of 27.2% in 783 cases analysed during their study. However few authors have reported a higher incidence of tubercular lymphadenopathy as 77.0%, 65.3% and 62.5% respectively (4,6,9). Acid fast staining in cases of tuberculosis showed a positivity rate

of 46.4%. Highest yield of AFB was seen in cases which showed necrosis and a purulent or pus like aspirate (68.7%) as reported earlier (2,8,9). Pamra *et al* (4), however, reported a lower AFB smear positivity rate as 35.6%. In this study we found that acid fast bacilli was usually found extracellularly, in the areas of microscopic degeneration, within or at the periphery of the granulomas, the morphology of these bacilli being as short and stumpy rods. These findings correlated with those given by Rajsekaran *et al* (9), who reported a similar view in their studies in tuberculous lymphnodes. Mantoux test in our study was found to be positive in only 180 (54.9%) case of tuberculosis. It is probably due to the fact that in the majority of patients with tuberculosis, the cellular immune response may be depressed (10). It means that a negative tuberculin/Mantoux test cannot be relied upon to exclude tuberculosis. Bedi *et al* (6) and Park (10) are also supportive of this view on Mantoux test in tuberculosis. We report 4.5% cases of lymphoma which correlate with findings of Tilak *et al* (7), who reported an incidence of 5.6%, whereas Egea *et al* (5), have reported 9.5% cases of lymphoma in their studies. We reported a lower incidence of lymphoma as compared to other authors, probably due to the fact that our study included mainly children with non-specific infections. The ratio of Non-Hodgkin's to Hodgkin's lymphoma was 2:1. Similar rates (2.5:1) were reported by Talvalkar *et al* (11).

In our study, the majority of the metastatic nodes sampled were squamous cell carcinoma. Hajdu *et al* (12), in their study also noted that the most common type of metastatic carcinoma to lymphnode was squamous cell carcinoma in 68% cases, followed by adenocarcinoma in 25.0% cases. Similar findings were reported by Engzell *et al* (13) and Sarda *et al* (3). Oral cavity was the primary site in maximum number of cases in our study, a finding which correlated well with the study of Shaha *et al* (14). Correlation study was done between cytological and histological diagnosis in 115 cases. We found overall diagnostic accuracy of 97.6% which matches with 96.2% as reported by Frable *et al* (15). The overall sensitivity and specificity of our study was 94.6% and 98.5%, respectively which matches with 94.1% overall sensitivity and 96.9% overall specificity as reported by Egea *et al* (5).

### Conclusion

The present study confirms that FNAC of lymphnodes is an excellent first line method, for investigating the nature of the lesions. Also combination

of fine needle aspiration cytology with acid fast staining is highly valuable for routine diagnosis of tuberculosis. Other ancillary investigations like mycobacterial culture, lymph node biopsies and polymerase chain reaction can be reserved for cases, in which there is a strong clinical suspicion with equivocal result of FNAC and acid-fast staining. It is an economical and convenient alternative to open biopsy of lymphnodes; whose diagnostic accuracy can be further improved manifold when used in collaboration with other special techniques like cytochemistry, bacteriologic culture, immuno-cytochemistry, ultrastructural studies and molecular hybridization.

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