

Original Research Article**Cytomorphological Spectrum of Lymph Node Lesions on FNA with Special Reference to Acid Fast Bacilli Positivity in Tuberculous Lymphadenitis: A 3-Year Study in a Medical College Hospital in Mandya, Karnataka****M.S. Siddegowda^a, Tahniyat Ara^b, S. Shivakumar^c**^aAssociate Professor ^bPost Graduate ^cProfessor and Head of Department, Department of Pathology, Mandya Institute of Medical Sciences, Mandya, Karnataka 571401, India.**Abstract**

Background: Evaluation of lymphadenopathy is of clinical significance as the underlying disease may range from a treatable infectious etiology to malignant neoplasm. Peripheral lymphadenopathy is common in all age groups and management of cases depends on lymph node pathology, which can be evaluated by fine-needle aspiration or excision biopsy.

Objectives: The study was undertaken to assess Cytomorphological spectrum of lymph node lesions on FNA with special reference to Acid Fast Bacilli positivity in Tuberculous Lymphadenitis.

Materials and Methods: A 3 years retrospective analysis of the data was carried out on 944 patients of lymphadenopathy in the Department of Pathology, Mandya Institute of Medical Sciences, Mandya from January 2013 to December 2015. Fine needle aspiration cytology (FNAC) was done and smears were stained with Hematoxylin and Eosin, May-Grunwald-Giemsa and Papanicolaou (PAP) stains. Other stains like Ziehl-Neelson (ZN), Periodic Acid Schiff (PAS), etc were done wherever required.

Results: The spectrum of various lymph node lesions on cytomorphological findings in this study showed 560 cases (59.32%) of reactive nature, 178 cases (18.85%) were tubercular, 34 cases (3.6%) were of acute lymphadenitis and 8 cases (1%) were of chronic lymphadenitis. AFB positivity was found in 39.8% of tuberculous lymphadenitis patients. The remaining 164 cases (17.37%) were of malignant lymphadenopathy, consisting 15 cases (1.58%) of primary malignancies i.e. lymphomas and 149 cases (15.78%) of metastasis to lymph nodes. On correlation of FNAC findings with histopathology overall sensitivity, specificity and diagnostic accuracy as 97.9%, 99.7% and 99.3% respectively.

Conclusion: Fine needle aspiration study is an important tool for evaluation and management of various lymphoid disorders. It is a safe, simple, cost effective and reliable technique for establishing the diagnosis. Demonstration of AFB helps to establish the diagnosis of tuberculous lymphadenitis

Keywords: FNAC; Tuberculosis; AFB; Ziehl Neelson Stain.

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Introduction

Lymphadenopathy is one of the most common clinical finding in outpatient department [1]. It may be due to

infections, autoimmune diseases, metabolic disorders, malignancy etc [2]. Most often it may be the only manifestation of underlying occult malignancy [2].

Fine needle aspiration cytology is a simple, rapid, safe, cost effective procedure and unlike a surgical biopsy, it does not produce any residual scar [3]. It generally does not require anaesthesia or hospitalization, and can be used as an alternative investigation technique to excision biopsy [4]. It can be used for superficial lymphadenopathies as well as deep seated lymphadenopathies in abdominal cavity and thorax with the help of CT scan and ultrasonography [1]. It is used as diagnostic tool in the management of patients presenting with lymphadenopathy and should be considered before more invasive and costly procedures particularly in developing countries [5].

Tuberculous involvement of lymph node is the most common manifestation of extrapulmonary tuberculosis [6]. The incidence of mycobacterial lymphadenitis has increased in parallel with the increase in the incidence of mycobacterial infection worldwide [7]. Tuberculous lymphadenitis is seen in nearly 35 per cent of extrapulmonary tuberculosis and constitutes about 15 to 20 per cent of all cases of tuberculosis [7].

Acid fast staining of FNAC smears is highly valuable for routine diagnosis of tuberculosis [8]. In cases of atypical presentation of tuberculosis such as aspiration of purulent material by FNAC, they may be misdiagnosed as acute suppurative lymphadenitis in the absence of granuloma. Demonstration of Acid Fast Bacilli helps to diagnose such cases as Tuberculosis [9].

FNAC of lymph nodes is very helpful to diagnose primary and secondary malignancy. Malignancies in lymph node are predominantly metastatic in nature [10]. A sentinel lymph node may be the first sign of underlying malignancy in the thoracic cavity, abdominal cavity or pelvic region [11].

Materials and Methods

A 3 year retrospective analysis of the data was carried out on 944 patients of lymphadenopathy in the Department of Pathology Mandya Institute of Medical Sciences, Mandya from January 2013 to December 2015. All patients who had presented with palpable lymphadenopathy to the Cytopathology laboratory of the Department of Pathology, MIMS, Mandya during the study period were included in the study irrespective of age and sex.

Data was retrieved from the records of the Department of Pathology. FNAC was performed by a cytopathologist, using a 23 G needle attached to 10ml syringe and Franzen handle.

Smears of FNAC of lymph node done during the study period and stained with Haematoxylin and Eosin and/or Papanicolaou stain, and May- Graunwald Giemsa stain

were retrieved and reviewed under the microscope. In all cases where cytological diagnosis was of tuberculous lymphadenitis, smears stained with Ziehl Neelson stain were reviewed for presence or absence of Acid fast bacilli.

Records of lymph node biopsy specimens received to Histopathology Laboratory during the study period were reviewed and details regarding their gross appearance are recorded. Histopathological sections stained with Hematoxyllin and Eosin stain of all such cases were retrieved and reviewed under the microscope.

Results

A total of 944 FNACs were studied. The age of the patients ranged from <1 year to 80 years with a male to female ratio of 1.4:1. The nodal site sampled most frequently was cervical group in 793 cases (84%), followed by inguinal group in 74 cases (8%), axillary groups in 60 cases (6%), generalized lymphadenopathy in 12 cases (1.27%), epitrochlear in 2 cases and femoral in 1 case (Table 1).

Maximum cases sampled were between 1-10 years (177), while 151 cases were in the group 11-20 years, 172 cases were in the group 21-30 years, 153 cases were in the group 31-40 years, 110 cases were in the group 41-50 years, 81 cases belonged to age group 51-60 years, 72 cases were in the group 61-70 years and 28 cases were in the group 71-80 years. Reactive hyperplasia was most common in age group 1-10 years, tuberculous lymphadenopathy was commonly seen in age group 21-40 years, most of the lymphoma cases was seen in more than 40 years of age and metastatic carcinoma was most commonly seen in the age of more than 60 years (Table 2).

The patients were evaluated into two broad categories of benign and malignant disorders. 780 cases (82.62%) were of benign lymphadenopathy, of which 560 cases (59.32%) were of reactive nature, 178 cases (18.85%) were tubercular, 34 cases were of acute lymphadenitis and 8 cases were of chronic lymphadenitis.

The remaining 164 cases (17.37%) were of malignant lymphadenopathy, consisting 15 cases (1.58%) of primary malignancies i.e. lymphomas and 149 cases (15.78%) of metastasis to lymph nodes. Thus, it was noted that metastatic tumour accounted for 91% cases of malignant lymphadenopathy, Non-Hodgkin's lymphoma for 11 cases (6.57%) and Hodgkin's lymphoma for 4 cases (2.43%). Out of total 149 cases (15.78%) of metastasis to lymph node, 97 (65%) were of metastatic squamous cell carcinoma, 14 (9.4%) were of metastatic ductal carcinoma from breast, 5 (3.35%) were of metastatic malignant melanoma, 4 (2.68%) were of metastatic adenocarcinoma, 4 (2.68%) were suspicious of malignancy, 3 (2%) were of metastatic papillary carcinoma of thyroid and 22 (14.7%) were of metastatic poorly differentiated carcinoma.

Table 1: Site wise distribution of lymph node lesions

Cytological diagnosis	Total cases	Cervical	Axillary	Inguinal	Femoral	Epitrochlear	Generalised
Benign Lymphadenopathies							
Reactive hyperplasia	560	468	26	52	01	02	11
Acute lymphadenitis	34	27	01	06	-	-	-
Chronic lymphadenitis	08	07	-	01	-	-	-
Tuberculous lymphadenitis	178	158	18	02			
Malignant Lymphadenopathies							
1. Lymphoma							
Hodgkin	04	03	-	01	-	-	-
Non Hodgkin	11	07	01	02	-	-	01
2. Metastatic tumor							
Squamous Cell Carcinoma	149	123	14	12	-	-	-
Infiltrating Ductal Carcinoma	97	92	05				
Poorly differentiated carcinoma	14	03	11				
Adenocarcinoma	22	15	02	02			
Malignant melanoma	04	04					
Papillary carcinoma Thyroid	05	01		04			
Suspicious of malignancy	03	03					
	04						
Total	944	793	60	74	01	02	12

Table 2: Distribution of lymph node lesions in relation to Age

Age (yrs)	Reactive hyperplasia	Acute lymphadenitis	Chronic lymphadenitis	TB lymphadenitis	Lymphoma	Metastatic carcinoma	Total cases (%)
1-10	152	08	01	14	01	01	177(18.75)
11-20	120	06	01	22	01	01	151(16)
21-30	110	05	02	53	02	-	172(18.22)
31-40	88	03	02	53	01	06	153(16.20)
41-50	54	03	-	17	04	32	110(11.65)
51-60	26	03	01	10	03	38	81(8.58)
61-70	08	06	01	05	03	49	72(7.62)
>70	02	-	-	04	-	22	28(2.96)
Total	560	34	08	178	15	149	944(100)

Table 3: Distribution of various lymph node lesions

Sl. No	Cytological diagnosis	No. of cases	Percentage (%)
1.	Reactive hyperplasia	560	59
2.	Acute lymphadenitis	34	3.6
3.	Chronic non specific lymphadenitis	08	1
4.	Tuberculous lymphadenitis	178	19
5.	Lymphoma	15	1.5
6.	Metastatic tumor	149	16

Table 4: Cytomorphological features in tuberculous lymphadenitis with AFB positivity

Cytomorphological features	Cases (%)	AFB Positive (%)
Epithelioid granuloma without caseous necrosis	51(28.65%)	06(11.76%)
Epithelioid granuloma with caseous necrosis	72(40.44%)	52(72.22%)
Caseous necrosis without granuloma	55(30.89%)	13(23.63%)
Total	178	71(39.88%)

Table 5: cytohistopathological correlation of lymph node lesions

Cytological Diagnosis	Histopathological Diagnosis					
	No. of cases	Reactive hyperplasia	Tuberculous lymphadenitis	Hodgkin lymphoma	Non Hodgkin lymphoma	Metastatic carcinoma
Reactive hyperplasia	12	11	01	-	-	-
Tuberculous lymphadenitis	08	-	08	-	-	-
Hodgkin lymphoma	03	-	-	03	-	-
NonHodgkin lymphoma	08	-	-	-	08	-
Metastatic carcinoma	23	-	-	-	-	23

Most of the squamous cell carcinoma metastasized to cervical lymph node, ductal carcinoma of breast to axillary lymph node, malignant melanoma to inguinal lymph node and metastatic carcinoma, metastatic adenocarcinoma, metastatic papillary carcinoma thyroid, metastatic poorly differentiated metastasized to cervical lymph nodes (Table 3).

The criteria by which a diagnosis of reactive lymphadenopathy was established included high cellularity, polymorphous pattern of cells without malignant features, mitotic activity and a significant number of tingible bodies (Figure 1a & 1b).

Acute suppurative lymphadenitis cases showed predominantly polymorphonuclear leukocytes, necrotic debris and other lymphoid cells.

The aspirates from lymph nodes were diagnosed as tubercular lymphadenopathy based on the presence of epithelioid cell granuloma and caseous necrosis with or without Langhan's giant cells in a background of lymphoid cells or epithelioid cell granuloma without caseation or only necrotic material consisting of diffuse granular debris. All cases were stained with Ziehl Neelson staining, among these only 39.88% cases were positive for acid fast bacilli (Figure 2a, 2b, 2c, 2d). Predominant cytomorphological

pattern was epithelioid cell granuloma with caseous necrosis (40.44%). AFB positivity was seen in 71 cases (39.8%) and was maximum with epithelioid cell granulomas with necrosis (72.22%) followed by necrosis without granulomas (23.63%) (Table 4).

Non Hodgkin's lymphoma showed predominantly monomorphic population of lymphoid cells.(Figure 3a & 3b). Hodgkin's lymphoma showed a mixed cell population with characteristic Reed-sternberg giant cells (Figure 4a & 4b).

Metastatic squamous cell carcinoma showed tumor cells showing squamoid nature and atypia (Figure 5).

A cytohistopathological correlation was done in 54 cases. Out of 54 cases, 12 were of reactive hyperplasia, 11 of which were true positive and 01 were false positive which turned out to be tuberculous lymphadenopathy on histological examination .

In 178 cases of tuberculous lymphadenitis, histological correlation was seen in 08 cases that were exactly correlated. A total 54 malignant lymphadenopathy cases were correlated in which 11 were lymphomas and 23 were of metastatic carcinoma. Out of 11cases, 03 were of Hodgkins lymphoma and 08 were of nonHodgkins lymphoma (Table 5).

Table 6: Comparison of AFB positivity on ZN staining

Study	AFB positivity on Z-N Staining (%)
S shamshad et al	46.4%
Adhikari et al	41.6%
Hirachand S et al	50%
Hemlatha et al	52%
Patel MM et al	31%
Present study	39.9%

Table 7: Statistical analysis of lymphnode lesions

Cytological diagnosis	No of cases	Reactive	Histopathological diagnosis			Sensitivity (%)	Specificity (%)	Diagnostic accuracy (%)
			Tuberculosis	Lymphoma	Metastasis			
Reactive	12	11	01			91.6%	99%	97.3%
Tuberculosis	08		08			100%	100%	100%
Lymphoma	11			11		100%	100%	100%
Metastatic tumor	23				23	100%	100%	100%
Total	54	11	09	11	23			
Overall						97.9%	99.75%	99.32%

Table 8: Comparison of statistical analysis

Studies	Sensitivity	Specificity	Diagnostic accuracy
Vijaya bharathi et al	97.18%	98.74%	98.26%
Shamshad s et al	94.6%	98.50%	97.6%
Present study	97.9%	99.75%	99.32%

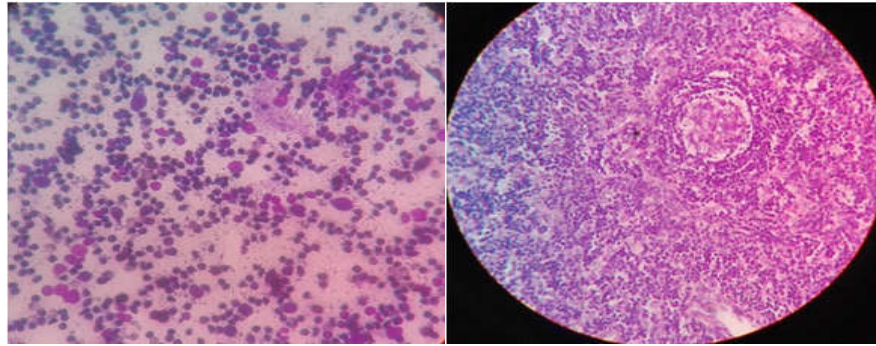


Fig. 1a: Reactive Hyperplasia:FNAC smear showing polymorphous population of lymphoid cells.MGG 40X. **Fig. 1b:** Reactive Hyperplasia:Section shows lymphoid follicle with germinal centre. H&E 40X

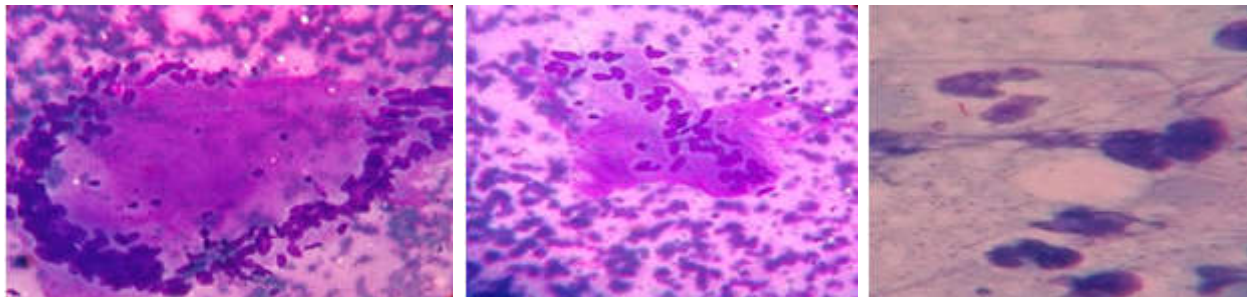


Fig. 2a: Tuberculous Lymphadenitis.:FNAC smear showing granuloma(MGG). **Fig. 2b:** Langhans giant cell(MGG) and Fig 2c: AFB positivity. ZN 40X

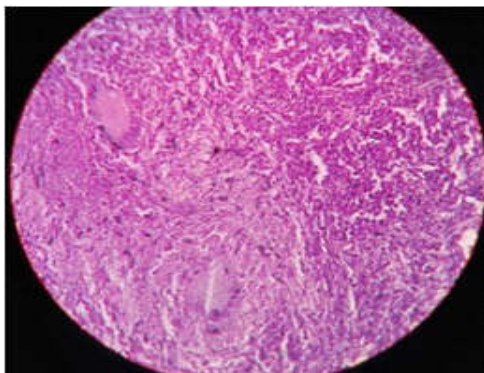


Fig. 2d: Tuberculous Lymphadenitis.Biopsy section showing granuloma,Langhans giant cell .H&E 40X

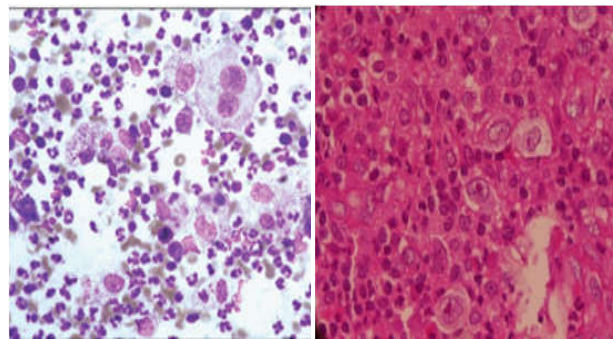


Fig. 4a: Hodgkins lymphoma..FNAC smear showing Reedsternberg cells and reactive cells. MGG 40X . **Fig. 4b:** Hodgkins lymphoma.Biopsy sections showing Reed Sternberg cells H&E 40X

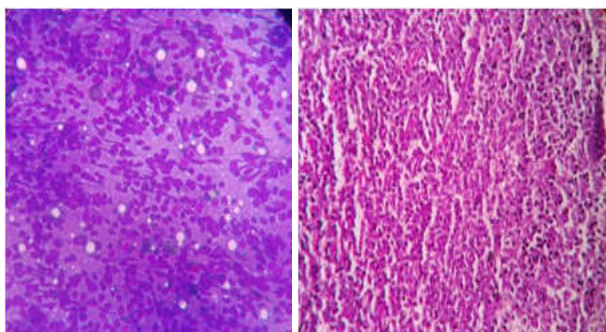


Fig. 3a: Non Hodgkins Lymphoma: FNAC smear showed predominantly monomorphic population of small lymphoid cells. MGG40X. **Fig. 3b:** Non Hodgkins lymphoma:Section shows effacement of lymphnode architecture by small lymphoid cells.H&E 40X

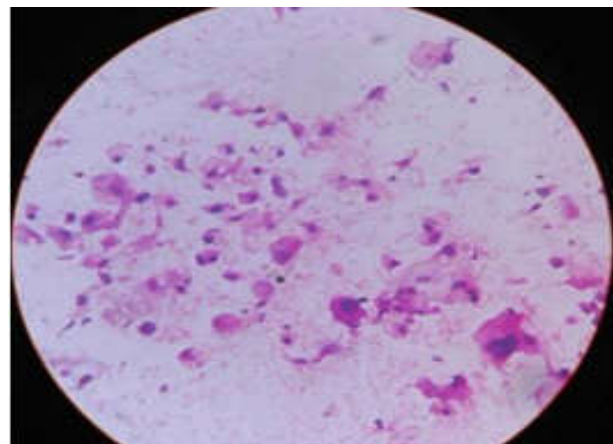


Fig. 5: Metastatic Squamous Cell Carcinoma.FNAC smear showing malignant squamous cells. H&E 40X.

Discussion

Fine needle aspiration cytology is a simple, safe, inexpensive and reliable investigative procedure. With the recent advances in ultrasound and CT scan technologies, deep lesions can be aspirated using these procedures and helps in preventing surgical intervention [12].

The lesions arising in the lymph node can be found in patients ranging from early to advanced age. In our study youngest patient was less than 1 year old and oldest was 80 years of age. These figures come in close comparison to S.S. Ahmad et al study of 1000 patients where the youngest patient was 2 years old and oldest was 95 years old.

In our study, a male preponderance was noted with a male to female ratio of 1.4:1 which correlated with Sumyra K.Q et al study which showed a M:F ratio 1.5:1

Cervical region was the most frequent site of lymphadenopathy in our study (84%). Many other studies also found [(Mandakini M.P et al (83.9%), Sumyra K. Q et al (76%), S.S. Ahmed et al (73.5%)] cervical region to be the most common site of involvement.

In our study most of the cases were benign (82.62%) and 17.37% were malignant. Our findings were similar to findings of Arjun Singh et al study (85.4% and 14.6%).

Out of benign lesions, reactive lymphadenopathy was most common (59.32%) and 18.85% were tubercular which correlates closely with findings of Sumyra K.Q et al (36.9% and 9.1% respectively).

We reported 15 cases (1.58%) of lymphomas and 149 cases (15.78%) of metastasis to lymph nodes which correlate with findings of S.S. Ahmed et al (16.6%). Majority of the metastatic nodes sampled were squamous cell carcinoma (65%).

In the present study, the second most common cytological diagnosis was tuberculous lymphadenitis (178 cases). Predominant cytomorphological pattern was epithelioid cell granuloma with caseous necrosis (40.44%) which is comparable to findings of Mandakini M.P et al (64.85%).

AFB positivity was seen in 71 cases (39.8%) and was maximum with epithelioid cell granulomas with necrosis (72.22%) followed by necrosis without granuloma pattern (23.63%) which is comparable with the findings of Patel MM et al (31%), Adhikari et al (41.6%), S shamshad et al (46.4%), Hirachand S et al [13] (50%), Hemalatha et al study (52%) (Table 6).

A cytohistopathological correlation was possible in 54 cases. Out of 54 cases, 12 were of reactive hyperplasia, 11 of which were true positive and 01 was false positive which turned out to be tuberculous lymphadenopathy on histological examination.

In 178 cases of tuberculous lymphadenitis, histological correlation was possible in 08 cases that were exactly correlated. A total 34 malignant cases were correlated in which 11 were lymphomas and 23 were of metastatic carcinoma. Out of 11 cases, 03 were of Hodgkins lymphoma and 08 were of non Hodgkins lymphoma and were correlated with histopathology.

In the present study overall sensitivity, specificity and diagnostic accuracy of FNAC 97.9%, 99.7% and 99.3% respectively (Table 7).

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