

## Patterns of Lymph Node Lesions on Fine Needle Aspiration Cytology in a Territory Hospital in Nepal

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**Introduction:** Lymphadenopathy is the clinical manifestation of wide spectrum of diseases ranging from non-neoplastic to neoplastic etiology. FNAC plays a vital role in solving such issues which is a simple, safe, reliable, cost effective tool to render a diagnosis after which proper and timely management can be done.

**Objectives:** The study was undertaken to establish various cytomorphological patterns of lymphadenopathies with special reference to tuberculosis.

**Materials and methods:** This retrospective study was conducted on 144 patients with lymphadenopathy at Department of Pathology in our tertiary care center who had undergone FNAC. The cytomorphological patterns were analyzed.

**Results:** The most frequent cause of lymphadenopathy was tuberculosis followed by reactive, metastatic carcinomas and lymphomas.

**Conclusion:** Our study demonstrated the role of FNAC to elicit various cytomorphological patterns of lymph node enlargement and revealed a high burden of tuberculosis.

**Keywords:** AFB, FNAC, Lymph nodes, Lymphadenitis, Tuberculosis, ZN Stain.

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**L**ymph nodes are bean shaped, encapsulated structure widely distributed in our body and are an integral part of our immune system.<sup>1</sup> There are about 450 lymph nodes in our body mainly located in neck, axilla, groins, mediastinum, mesentery of bowel and para-aortic areas.<sup>2</sup> Lymph nodes can be enlarged in a wide spectrum of conditions ranging from infectious to neoplastic etiology and are commonly seen in clinical practice.<sup>3, 4, 5</sup>

Fine needle aspiration cytology (FNAC) is the study of cellular material which is obtained by applying fine needle under negative pressure. The history of FNAC dates back to 1904 first performed by Greig and Gray for the diagnosis of Sleeping Sickness.<sup>6</sup> Thereafter, Guthrie in 1921 systemically performed FNAC on lymph nodes for diagnostic purpose.<sup>7</sup> FNAC is a safe, simple, rapid, reliable, cost effective and minimally invasive procedure which has a diagnostic role in evaluation of lymphadenopathies.<sup>8, 9, 10, 11</sup> It can be done on an outpatient basis or conveniently on bedside patients. This study highlights the cytomorphological spectrum of various lymph node lesions with special emphasis on cytological pattern in diagnosis of tuberculosis.

**Material and Methods**

This is a retrospective study done at the Department of Pathology, B & B Hospital which is a tertiary care center to evaluate

the different cytological features in non-neoplastic and neoplastic lymph node lesions. This study duration was of three years from January 2018 to December 2020. The detailed clinical history, relevant laboratory parameters and radiological findings were noted. After taking the written consent, FNAC was performed with 20-22 gauge needle attached to 10 ml syringe. The aspirate was smeared and fixed. May Grunwald Giemsa stain was done in air dried smears and Papanicolaou stain in alcohol fixed smears. Zeihl Nelsen (ZN) Stain was done whenever cheesy material was aspirated and all cytological cases of granulomatous lymphadenitis.

**Results**

A total of 144 FNACs were done from the lymph node lesions out of which 109 were

Cytological diagnosis	Number of cases
Tuberculosis	56 (39%)
Reactive	45(31%)
Metastasis	29(20.5%)
Lymphoma	6(4%)
Granulomatous lymphadenitis	5(3.5%)
Suppurative lymphadenitis	3(2%)
<b>Total</b>	<b>144 (100%)</b>

*Table 1: Distribution of FNAC diagnosis of 144 patients*

non neoplastic and 35 were neoplastic. Among the non-neoplastic cases, 56 (39%) were tubercular and 45 (31%) showed reactive features. There were 5(3.5%) cases of granulomatous lymphadenitis and

3(2%) cases of suppurative lymphadenitis. Thirty-five cases were malignant lymphadenopathy: 6(4%) were lymphoma and 29(20.5%) were metastasis to lymph nodes (**Table 1**).

Age	Tuberculosis	Reactive	Tumor	Granulomatous lymphadenitis	Suppurative lymphadenitis	Total
0-10	0	9	0	0	0	9(6%)
11-20	15	8	0	0	0	23(16%)
21-30	20	8	0	4	1	33(23%)
31-40	13	8	4	1	0	26(18%)
41-50	5	1	2	0	2	10(7%)
51-60	3	2	9	0	0	14(10%)
61-70	0	1	12	0	0	13(9%)
71-80	0	5	4	0	0	9(6%)
Above 80	0	3	4	0	0	7(5%)
<b>Total</b>	<b>56</b>	<b>45</b>	<b>35</b>	<b>5</b>	<b>3</b>	<b>144(100%)</b>

*Table 2: Age distribution of patients of lymphadenopathy*

Out of 144 cases, 70(48%) were male and 75 (52%) were females. **Table 2** Shows age distribution of patients with lymphadenopathy. The maximum incidence of lymphadenopathy was seen in the age group 21-30 years. The youngest age of presentation was 2 years and oldest was 98 years in this study. The most common group of lymph nodes aspirated were cervical (69.4%) followed by supraclavicular (10%), axillary (6%), inguinal (5%), submandibular (3.5%), preauricular (3.5%), submental (2%) and

sub occipital lymph nodes (0.6%) as shown in **Table 3**.

The majority of cases recorded were those of tubercular lymphadenitis out of which 43(77%) were from cervical group of nodes. The incidence of tubercular lymphadenitis was more in females than males with ratio of 2:1. The most common age group was 21-30 years (36%). According to the cytomorphological features, we classified the smears into three categories: well-formed epithelioid granulomas without necrosis (**Figure. 2a**)

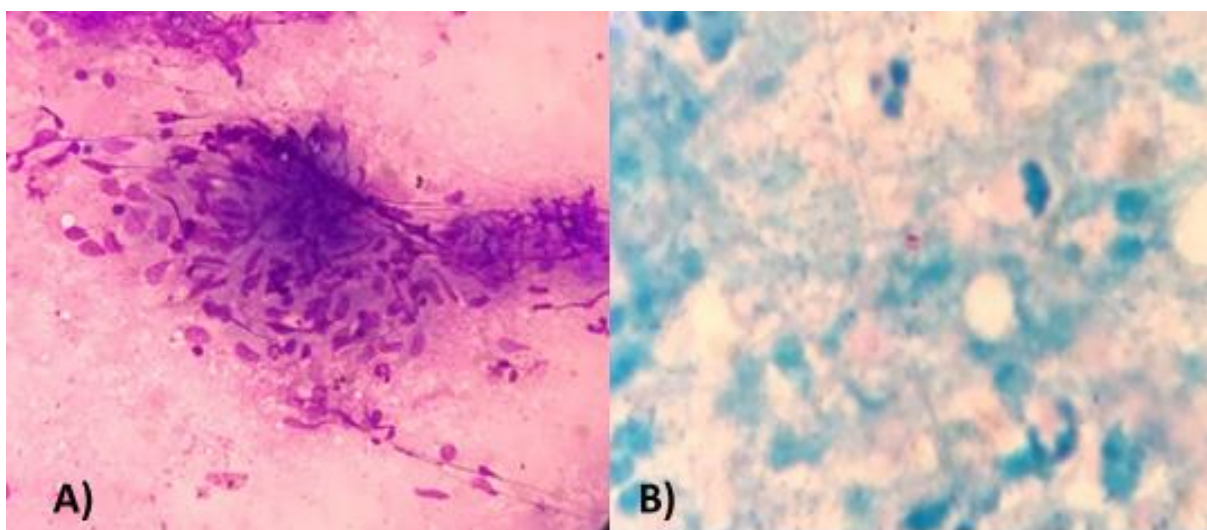
## Fine Needle Aspiration Cytology

Site	Tuberculosis	Reactive	Tumor	Granulomatous lymphadenitis	Suppurative lymphadenitis	Total
Cervical	43	32	20	5	0	100(69.4%)
Supraclavicular	3	4	6	0	1	14(10%)
Axillary	3	3	3	0	0	9(6%)
Inguinal	2	0	5	0	0	7(5%)
Preauricular	1	2	1	0	1	5(3.5%)
Submandibular	4	1	0	0	0	5(3.5%)
Submental	0	2	0	0	1	3(2%)
Sub occipital	0	1	0	0	0	1(0.6%)
<b>Total</b>	<b>56</b>	<b>45</b>	<b>35</b>	<b>5</b>	<b>3</b>	<b>144(100%)</b>

*Table 3: Lymph node group involved in various types of lymphadenopathy*

Cytological findings	Number of cases	Percentage	ZN positive
Granuloma alone	11	19.7%	2 (18%)
Granulomas and necrosis	37	66%	20 (54%)
Necrosis alone	8	14.3%	8 (100%)
<b>Total</b>	<b>56 (100%)</b>	<b>100%</b>	<b>30</b>

*Table 4: Cytological findings of 56 cases of tubercular lymphadenitis*



*Figure 1: Granulomas and necrosis. (a) Pap stain; (b) MGG stain*

FNAC diagnosis	Number of cases
Squamous cell carcinoma	14
Adenocarcinoma	9
Small cell carcinoma	4
Papillary thyroid carcinoma(PTC)	1
Mucoepidermoid carcinoma(MEC)	1
Total	29

Table 5: Distribution of Different types of metastatic tumor

epithelioid granulomas with necrosis (**Figure 1**) and caseation or only necrotic material without epithelioid granulomas. ZN stain (**Figure. 2b**) was done in all 56 cases out of which Acid Fast Bacilli (AFB) was seen in 30(53.5%) cases. Out of eleven cases of granuloma without necrosis, two (18%) showed AFB

positivity and out of 37 cases with both granulomas and necrosis, AFB was demonstrated in 20(54%) cases. All eight cases (100%) with presence of necrosis alone showed tubercle bacilli. The cytological picture of 56 cases of tubercular lymphadenitis with AFB results are shown in Table 4. Aspirates were not subjected to culture and ancillary test in this study.

Reactive lymphadenitis was the second most common pattern seen in this study with 45(31%) cases. Majority of the cases presented with cervical lymphadenopathy. Clinical history in many patients revealed an infective etiology mostly in upper respiratory tract.

A total of 35 cases were diagnosed as neoplastic cause in our study. A male preponderance was noted with 61-70 being the most common age group followed by 51-60 years. The maximum number of

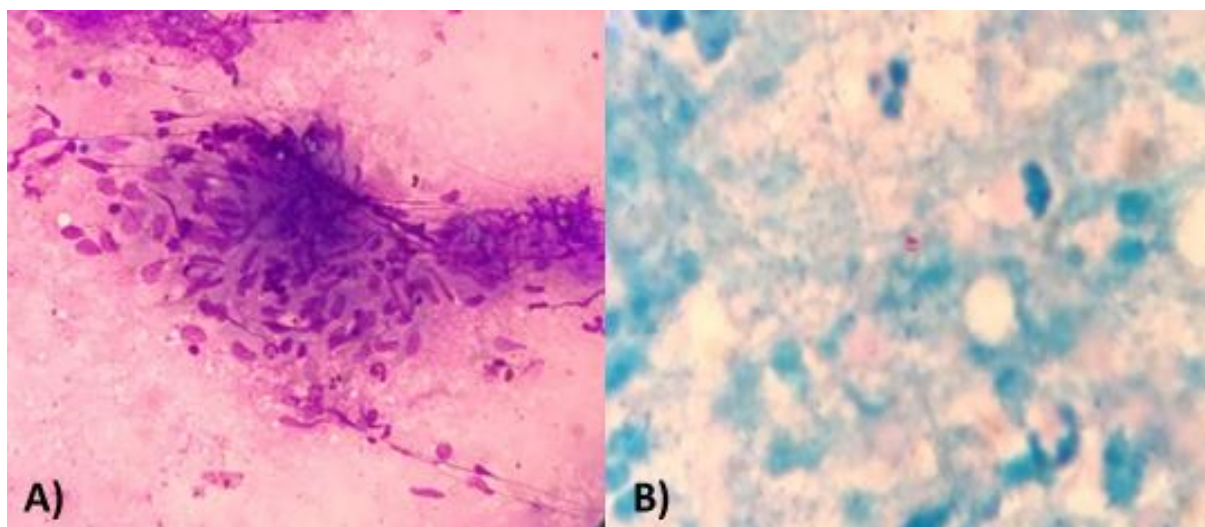


Figure: 2 (a) Epithelioid granuloma (MGG stain); (b) AFB (ZN stain)

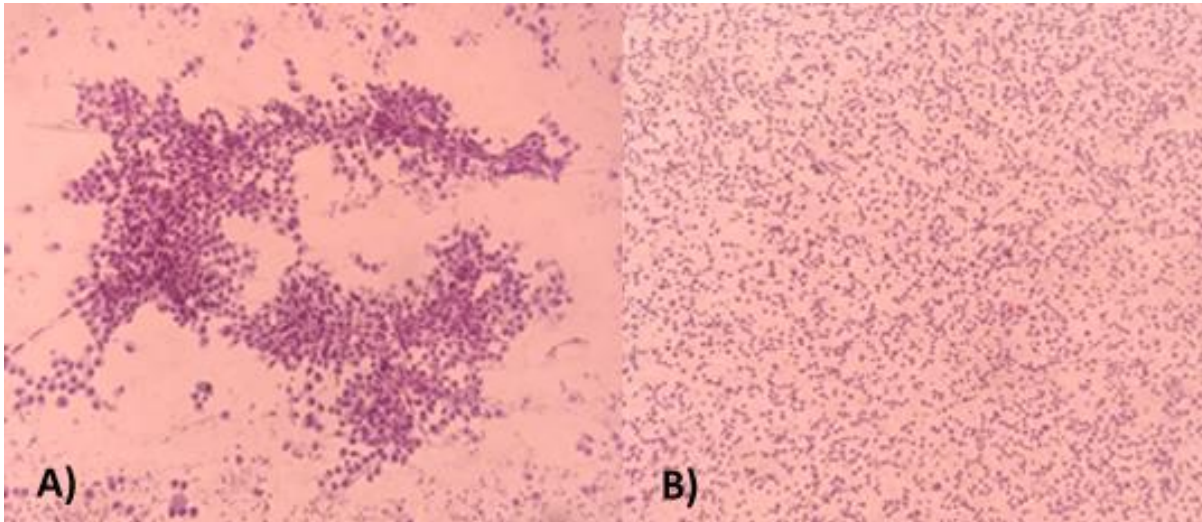


Figure: 3 (a) Metastatic deposit of SCC; (b) NHL

cases was recorded in the cervical group of lymph nodes (48%) followed by supraclavicular (20%). The most common metastatic deposits were from SCC (42%) (Figure. 3a) followed by adenocarcinomas (34%). On further workup, six cases of SCC had primary lesion in lung. Two cases of cutaneous SCC and one cervical SCC presented with metastatic deposits in inguinal lymph nodes. Four cases of adenocarcinoma of lung and single case of breast carcinoma showed secondaries in cervical and axillary lymph nodes respectively. There were four cases of small cell carcinomas (16%) of lung, one mucoepidermoid carcinoma (4%) and one papillary thyroid carcinoma (4%). Out of all cases of lymphomas diagnosed cytologically as Non Hodgkin Lymphoma (NHL) (**Figure: 3b**), biopsy was done in 4 and showed same results. Follow up was lost in 2 patients.

The presence of poorly developed vague

granuloma and occasional histiocytes were categorized as granulomatous lymphadenitis which comprised of 5 (3.5%) cases. ZN stain was done in all and was negative. Out of five cases, biopsy evaluation was done in 2 cases and one showed epithelioid histiocytes with well-formed granulomas and foci of caseous necrosis. The other one showed non caseating granulomas at periphery of hyperplastic follicles consistent with features of toxoplasmosis. Follow up was lost in rest three patients.

### Discussion

Peripheral lymphadenopathy is the clinical manifestation of regional or systemic disease and is always accessible for FNACs which provides great aid in the diagnosis of disease especially in developing countries like Nepal. FNAC provides quick and reliable diagnosis in many cases reducing the need for surgical

biopsy even though it is considered gold standard.<sup>1, 11,12,13,14</sup>

In the present study, maximum number of patients were of second decade with slight female preponderance which correlated with other studies.<sup>1, 2, 3</sup> The most common lymph node involved was cervical lymph node followed by supraclavicular, axillary, inguinal node and others similar to studies conducted by Biradar et al and Sharma et al.<sup>4, 7, 12</sup> This could be attributed to rich supply of lymphatics in the neck region.<sup>1, 2</sup>

In the present study tubercular lymphadenitis was the most common cause of peripheral lymphadenopathy followed by reactive cause which is similar to many other studies.<sup>3, 5, 12, 15</sup> It is the most common cause of extra pulmonary manifestation. The high incidence of tuberculosis in our part of world could be due to ignorance, low socioeconomic status, incomplete treatment or resistance to therapy.<sup>1,8</sup> This is in sharp contrast to very low incidence of only 1.6% in western world.<sup>16</sup> The most common age group of tubercular etiology belonged to 21-30 years and in decreasing trend after that age group in this study which is similar to study done by Shilpa et al and Kochchar et al.<sup>11,16,17</sup> However, others have observed that no age group is exempted from the disease.<sup>1,6</sup> The cervical lymph node was the most common site involved with female preponderance

which is in accordance with other studies.<sup>6,8,11,15</sup> The frequent involvement of cervical lymph nodes could be due to easy entry of organism via tonsillar lymphoid tissue.<sup>13</sup>

The cytomorphological patterns for diagnosis of tuberculosis are epithelioid histiocytes forming granulomas, multinucleated langhans giant cells and caseous necrosis but all these features may not be seen. The presence of granulomas is highly suggestive of Tuberculosis as it is the most common cause of granulomatous disease in Nepal where there is high burden of TB. The most common pattern in our study was presence of necrosis and granulomas both which was seen in more than half cases of tubercular lymphadenitis, followed by epithelioid granulomas only in 11 cases and necrosis only in 8 cases. ZN staining was done in all and showed the detection of AFB varies with the cytomorphological features and was lowest in those with epithelioid granulomas with absence of necrosis and highest with presence of necrosis only. The other possibilities that can be considered in AFB negative cases are sarcoidosis, cat scratch disease, collagen vascular disease, leprosy, toxoplasmosis and fungal infection.<sup>1</sup> Nevertheless, many authors have reported that in areas with high burden of tuberculosis, the presence of epithelioid granulomas without necrosis

in conjunction with clinical features, should be considered as tuberculosis unless proven otherwise.<sup>2,3,5,7</sup>

The presence of necrotic material only is highly suggestive of TB as AFB was detected in all our cases.<sup>2, 13, 14, 15</sup> According to some studies, necrosis is associated with high multiplication of tubercle bacilli whereas the presence of epithelioid granulomas and multinucleated giant cells have some role in suppressing the growth of AFB.<sup>3,4,7</sup> Therefore, the cytological pattern and bacterial load can be correlated with the immune condition of the patient to some extent. However, we must be aware that metastatic SCC may also yield cheesy material on aspiration which looks cytologically similar to caseous necrosis.<sup>10, 11, 15</sup> Therefore, a careful search for tumor cells coupled with ZN stain is required to arrive at a correct diagnosis especially in elderly population. Reactive lymphadenitis was the second common pattern identified in our study and was seen mostly in first decade which is similar to various studies.<sup>1,7,9</sup> Smears showed polymorphous population of lymphoid cells comprising of centrocytes, centroblasts, dendritic reticulum cells, tingible body macrophages derived from germinal centre and plasma cells, immunoblasts, endothelial cells derived mainly from interfollicular region. Reactive lymphadenitis occurs as an

immune response against variety of antigens like bacterial, viral, fungal or nonspecific etiologies. However, it was the most common case of lymphadenopathy in study reported by Lakhey et al, Biradar, Mainali et al, Gayatri et al and Vimal et al.<sup>4, 8,9, 2</sup>

Metastatic deposits in lymph nodes were seen in 29 cases which was predominantly in elderly male population in agreement with other studies.<sup>17</sup> The most common cause of metastatic deposit was Squamous cell carcinoma followed by adenocarcinoma and small cell carcinoma. Many other studies observed SCC as the predominant metastatic deposit and this could be attributed to high incidence of smoking and tobacco consumption in their region.<sup>1,3,11,13</sup> Metastatic deposit from small cell carcinoma of lung showed cells with scant cytoplasm, inconspicuous nucleoli, nuclear molding, numerous apoptotic bodies and smearing artifact. Secondary deposit in cervical lymph node from PTC showed sheets and papillae of cells with oval clear nuclei with intranuclear inclusions. These cytomorphological features helped us in providing some clue towards the primary origin of the tumor. Lymphomas comprised of 4% cases similar to other authors and all were NHL.<sup>3, 15, 5</sup> Out of these, excisional biopsy was done in four cases and correlated with FNAC findings.



However, the role of FNAC in diagnosing lymphomas is controversial especially in low grade ones.<sup>2</sup>

There were 3 cases of suppurative lymphadenitis and 5 cases of granulomatous lymphadenitis which is similar to observation by other authors.<sup>1</sup> Out of 5 cases of granulomatous lymphadenitis, excisional biopsy was done in two cases and one showed abundant caseous necrosis and epithelioid granulomas consistent with tubercular lymphadenitis. FNAC covers only a portion of lymph node and sometimes the pathology may involve only a focal area which may not be reached during aspiration as FNAC is a blind procedure. Therefore, the aspirate may not be representative of the entire lesion and may pose diagnostic challenge. It has been observed that in early phase of the disease, the aspirate may simulate reactive lymphadenitis and follow-up re-aspiration after one to two weeks may be performed if the clinical suspicion is high.<sup>6</sup> The other one showed small noncaseating granulomas at periphery of hyperplastic follicles consistent with toxoplasmosis which was later on confirmed by serology.

### **Conclusion**

FNAC has a valuable role in diagnosis of non-neoplastic as well as neoplastic lesions of lymph node where it also

provides clue regarding the origin of primary tumor. The most common cause of lymphadenitis was tuberculosis in our study. Even though detection of AFB is required for confirmed diagnosis of tuberculosis, the presence of epithelioid granulomas in conjunction with clinical features is considered as tuberculosis in our part of world.

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