

Cytomorphological Study of Lymph Node in Tertiary Care Hospital

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Abstract:

Introduction: Lymphadenopathy, marked by enlarged lymph nodes, poses diagnostic challenges. Fine Needle Aspiration Cytology (FNAC) emerges as a valuable tool, offering minimal invasiveness and cost-effectiveness. While FNAC is less ideal for lymphomas, it aids in distinguishing cervical organ issues. Globally, lymphadenopathy's causes vary, with tuberculosis prevalent in developing nations like India.

Aims and Objectives: The study focused on identifying common cytological patterns in lymph node lesions and correlating factors associated with these lesions.

Materials and Methods: A prospective study was undertaken at Belagavi Institute of Medical Sciences focused on FNAC for clinically suspected lymph node lesions over a period of 12 months (July 2022-June 2023). Inclusive of all ages and genders, the study performed up to four FNAC attempts, with PAP and Giemsa staining for immediate evaluation. Granulomatous cases underwent Ziehl-Nielsen staining.

Results: The study encompassed 252 cases with lymph node presentations, spanning ages 9 months to 85 years. The majority were males (152) compared to females (100). Cervical lymph nodes dominated presentations (208 cases), with 49 cases in the 10-20 age group. Malignant cases exhibited a male preponderance (51 cases) compared to females (21). Malignancies correlated significantly with age above 40 ($p < 0.00001$). Metastatic squamous cell carcinoma prevailed (54 cases), notably in cervical lymph nodes. Tubercular lymphadenitis, predominantly in females, accounted for 27 cases. Despite left-sided prevalence, females showed slightly more right-sided cases. Overall, the study delineated age, gender, and pathology patterns in lymph node presentations.

Conclusion: Fine Needle Aspiration Cytology (FNAC) serves as an excellent first line investigation for assessing the nature of lesions in lymph nodes, offers a reliable and readily acceptable diagnostic tool in the diagnosis of tuberculosis, primary and metastatic malignancies, reactive lymphadenitis and suppurative lesions as it is quick and minimally invasive procedure.

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Introduction

Lymph nodes play a crucial role in the human immune system and lymphadenopathy occurs when a lymph node is unusually large in size and number or displays atypical consistency [1], [2]. The causes of lymphadenopathy produce a large spectrum of disorders ranging from suppuration to lymphadenopathy [3] and it is difficult to ascertain the cause based only on history and clinical examination [2].

Many a times in cases of cervical lymphadenopathies other neck organs with salivary glands particularly are often confused for cervical lymph nodes, Fine Needle Aspiration Cytology (FNAC) are often helpful in distinguishing those cases [2]. Compared to a tissue biopsy a FNAC has several advantages primarily due to its minimal

invasiveness, speed and cost effectiveness [4], [5], [6]. While FNAC is generally regarded as providing lower-quality diagnostic material compared to trucut/core needle biopsy, particularly for diagnosing lymphomas, it offers several advantages. Firstly, it is a convenient office procedure without the necessity for a prior hematological workup and secondly, the adequacy of material can be promptly assessed, and repeat FNAC can be conducted simultaneously. Additionally, FNAC boasts an exceptionally low complication rate [7].

Lymphadenopathy is a common presenting sign in the clinical setup particularly in developing nations such as India due to the increased prevalence of tuberculosis in the population [8]. In addition to the above FNAC can also provide insights into whether

the etiology of lymphadenopathy is systemic or localized [9]. In view of these factors it can be well established that the disease pattern is varied in countries due to various geographical and socio-economic reasons [10], [11], [12]. The common cytomorphological patterns presented are divided into reactive, suppurative, granulomatous and malignant, with the malignant ones divided into metastatic deposits or lymphomas [13].

The current study was aimed towards finding out the most frequent cytological patterns of lymph node lesions and correlating the various factors associated with the lesions of the lymph nodes attending the cytology department of our tertiary care hospital.

Materials and Methods

In the Department of Cytopathology, a prospective observational study was undertaken at Belagavi Institute of Medical Sciences, Belagavi over a period of 12 months between July 2022 and June 2023.

Selection of Study Sample

This is a hospital based descriptive study. The source of data for the intended study is collected from subjects referred to the Department of Pathology at Belagavi Institute of Medical Sciences, Belagavi, with clinically suspected lymph node lesions (visible/palpable) during July 2022 and June 2023. The obtained material is spread across three slides: two air-dried and one fixed with alcohol. The

alcohol-fixed slide undergoes Papanicolaou (PAP) staining, while one air-dried smear is stained with Giemsa, and a third slide is reserved for Ziehl-Nielsen staining. The slides are screened under a bright field microscope and classified as Reactive, Suppurative, Granulomatous, and Malignant. Ziehl-Nielsen stain is performed on patients diagnosed and categorized as Granulomatous lymphadenitis.

The study included all the patients, irrespective of age and gender who presented to the cytology section with a referral for lymph node fine needle aspiration cytology and we excluded inadequate samples.

Data analysis is done using SPSS (Statistical Package for Social Sciences).

Descriptive statistics like frequencies and percentages for categorical variables and mean and standard deviation is calculated for continuous variables.

Chi-square test and Fisher test (if appropriate) is used to find the association between clinical presentation, diagnosis and other parameters in the study. p value < 0.05 is considered significant.

Results

In the present study the least age of presentation was 9 months or 0.75 years and the maximum age of presentation was 85 years with a mean age of 35.72 years, median age of 35 years and mode age of 40 years.

Table 1: Age wise distribution of patients

Age range (in years)	No of cases
0-10	26
10-20	49
20-30	28
30-40	34
40-50	43
50-60	30
60-70	27
70-80	14
80-90	1
Total	252

Maximum cases were in the 10-20 age group accounting for 49 cases followed by ages 40-50 years which accounted for 43 cases. The least number of cases were observed in the 80-90 age group which accounted for 1 case which was of a 85 year old female diagnosed as necrotizing granulomatous lymphadenitis. Females accounted for 100 cases whereas males accounted for 152 cases. Cervical lymph node FNACs accounted for a lion's share of the total number of cases (208 out of the total 252 cases), inguinal and axillary lymph nodes followed with 22 cases each. While maximum

number of cases had one lymph node levels involved, in two cases 2 different levels of lymph nodes were involved both being cervical and axillary. One of those was of a 70 year female who was diagnosed as breast carcinoma and had both axillary and cervical (supraclavicular) groups of lymph nodes involved and the other was of a 29 year old male who had both cervical and axillary lymph nodes enlarged and was diagnosed as Necrotizing Granulomatous lymphadenitis with Ziehl-Nielsen stain for acid fast bacilli being positive for tubercular bacilli.

Table 2: Side distribution of cases

Side	No of cases
Left	117
Right	111
Bilateral	18
Midline	6

Table 3: Side distribution according to sex

Side	Male	Female
Left	72	45
Right	65	46
Bilateral	12	6
Midline	3	3

18 of the cases had palpable lymph nodes on the bilateral aspects but being on the same level as their right and left counterparts. Overall the lesions which were diagnosed were characterized as Reactive, Suppurative, Granulomatous and Malignant.

Majority were characterized as reactive followed by malignancies which accounted for 72 cases. Malignant cases showed a male preponderance with 51 cases diagnosed as Malignant compared to females which showed only 21 cases as Malignant.

Table 4: Categorization of cases according to sex

Category	Female	Male	Grand total
Reactive	41	57	98
Suppurative	3	7	10
Granulomatous	33	35	68
Malignant	21	51	72
None	2	2	4
Grand total	100	152	252

When compared to the non-malignant and malignant lesions in males it was observed that there was a significant correlation between males having more incidence of malignancy than females, with a p value of 0.0447(by Fisher's exact test).

Table 5: Categorization of cases according to side of lymph nodes

Side	Reactive	Suppurative	Granulomatous	Malignant	None	Grand Total
Bilateral	8	0	1	9	0	18
Left	38	3	32	43	1	117
Midline	4	0	2	0	0	6
Right	48	7	33	20	3	111
Grand Total	98	10	68	72	4	252

50% of all the cases which showed bilateral presentation were diagnosed as Malignant compared to left which had 36.7% cases and right side accounted for 19.8% cases but when compared for statistical correlation it was found out that there was no statistically significant correlation as the p value on fisher's exact test was found to be >0.05 at 0.0549.

Table 6: Categorization of cases according to age range

Age range (in years)	Category					
	Reactive	Suppurative	Granulomatous	Malignant	None	Grand total
0-10	16	1	8	1	0	26
10-20	32	3	10	3	1	49
20-30	10	2	15	1	0	28
30-40	14	1	11	6	2	34
40-50	12	1	14	15	1	43
50-60	7	1	5	17	0	30
60-70	5	1	2	19	0	27
70-80	2	0	2	10	0	14
80-90	0	0	1	0	0	1
Grand total	98	10	68	72	4	252

When categorized the lesions in comparison to their age it was observed that in cases of reactive lesions of lymph nodes majority of the cases (72 out of 98 cases) were observed in ages below 40 and in cases of malignant lesions (61 out of 72 cases) were observed in the ages above 40 indicating that in ages above 40 incidences of malignancies are higher. P

value both by Chi square and Fisher's exact test showed a significant correlation between age and incidence of malignancy in lymph nodes in ages above 40 with a p value of <0.00001. The average age for malignant lesions was 52.139 years, whereas the average for non malignant lesions was 29.237 years.

Table7: Distribution of lesions above and below age of 40 with Malignancy correlation

	Non malignant	Malignant	P value
<40 years	126	11	Chi square: <0.00001
>=40years	61	54	Fisher's test: <0.00001

A majority of the malignant cases were observed in the cervical lymph nodes (60 out of total 72 cases) however a statistical correlation could not be established between Malignancies and location of the lymph nodes.

Table 8: Level of lymph involved by malignant and non malignant lesions.

Level of lymph nodes	Non malignant	Malignant	P value
Cervical	142	60	Chi square: >0.05
Axillary	15	7	Fisher's exact test: >0.05
Inguinal	18	4	
Cervical and axillary	1	1	

Table 9: Age and sex distribution of Tubercular lymphadenitis

Age Group	Male	Female	Grand total
0-10	1	2	3
10-20	2	1	3
20-30	1	5	6
30-40	4	2	6
40-50	3	5	8
50-60	0	0	0
60-70	0	0	0
70-80	0	1	1
80-90	0	0	0
Grand total	11	16	27

Table 10: Side and location wise distribution of tubercular lymphadenitis

Side	Cervical	Axillary	Cervical and axillary	Grand total
Left	12	1	1	14
Right	11	2	0	13
Grand Total	23	3	1	27

Granulomatous lymphadenitis was seen in a total 68 cases in which 27 were categorized as Tubercular lymphadenitis as they showed presence of acid fast bacilli, except for a single case in a 9 month old child with left axillary lymph node swelling which was diagnosed as BCG lymphadenitis and categorized as Granulomatous lymphadenitis, the Ziehl-Nielsen stain for acid fast bacilli showed presence of acid fast bacilli. In cases of tubercular lymphadenitis it was observed to have a female preponderance as they composed 59.3% (16/27) cases. The side and location showed preponderance to cervical lesions with a slight deviation towards left side's lesions. Malignant lesions accounted for 72 cases ranging

from ages of 5 years to 77 years. In ages below the ages of 20 the observed lesions were exclusively lymphoproliferative lesions, in spite of metastatic squamous cell carcinoma being the commonest encountered malignant entity at 54 cases out of a total 72 cases. The youngest patient to have a diagnosis of metastatic squamous cell carcinoma was in a 30 year old patient in the cervical lymph nodes. One case of metastatic adenocarcinoma was noted in the left supraclavicular lymph node (Virchow's node). A case of Anaplastic Large Cell Lymphoma in a male child aged 12 with left cervical lymphadenopathy.

Table 11: distribution of malignant lesions.

Malignant lesions	Total
Lymphoproliferative lesion	2
Lymphoproliferative lesion (Hodgkin's Lymphoma)	2
Lymphoproliferative lesion Non Hodgkin's Lymphoma	5
Metastatic adenocarcinoma	1
Metastatic breast carcinoma	7
Metastatic Deposits	1
Metastatic Squamous cell carcinoma	54
Grand Total	72

Discussion

The current study was conducted for a period of 12 months between July 2022 to June 2023.

Lymphadenopathy, presenting clinically as a manifestation of regional or systemic diseases, provides valuable insights into the underlying condition. Its occurrence can be attributed to either benign or malignant lesions, influenced by geographical and socioeconomic factors [14]. The cytology of lymph nodes has emerged as a diagnostic window for various diseases, owing to its prompt results, simplicity, and minimal trauma with fewer complications. FNAC is endorsed as a practical alternative, particularly in resource-constrained developing countries, offering cost-effective diagnostics compared to surgical excision biopsies. The combination of optimal material and expertise elevates cytological diagnosis to a level of significance comparable to histopathology. In clinical scenarios, distinguishing between reactive and neoplastic lymphadenopathy poses challenges and it requires considerable expertise, practice and training for an accurate diagnosis. In such instances, understanding the patterns of lymphadenopathy becomes a valuable asset for clinicians grappling with diagnostic dilemmas [15].

The current study showed a material adequacy rate of 98.41% which correlated with the studies done by Sharma RI et al (100%), Hemalatha et al (98%), Gupta et al (85.2%) and Badge SA et al (98.4%) [16], [17], [18], [19]. The number of males outnumbered the number of females by a ratio of 1.52:1 which contrasted with the study done by Malhotra AS et al which showed a female preponderance of 1.12 female patients per 1 male patient, but was concurred with the study done by Pathy C et al which showed a male to female ratio of 1.46:1 [20], [21].

In our study it was observed that the primary cause of lymphadenopathy was reactive lymphadenopathy constituting 98/252 (38.9%) cases which contrasted with study done by Hashmi AA et al, Malhotra AS, Badge SA et al, Sharma RI et al which showed tuberculosis to be a primary cause of lymphadenopathy at 40%. But this was in concordance with the study done by Pathy PC *et al*

as they too had reactive lymphadenitis as the most common cause of lymphadenopathy [7], [20], [21], [16], [19]].

Granulomatous lymphadenitis constituted 26.98% of cases and was the third most prevalent lesion in the study however it was observed that only 27 of those cases were positive for Ziehl-Nielsen stain and could be definitively classified as tubercular lymphadenitis. Of the cases it was observed that females comprised of a higher number of cases compared to male in this category (16 cases were female whereas 11 cases were males). It was also observed that cervical lymphadenopathy showed a higher chance of tuberculous granulomatous lymphadenitis. This was partly correlatable with studies done by Badge SA et al, and Sharma RI et al [19], [16]. This could be attributable to the prevalence of tuberculosis in India with the lack of awareness about tuberculosis treatment particularly in female population.

Malignant cases comprised 26.9% of the study, which was a significantly higher proportion when compared to studies done by Badge SA et al (4.83%) and Shamsad SS et al (13.6%) [19], [22]. But a lower proportion compared to study done by Pathy PC et al which showed malignancy in 48.27% cases. The maximum numbers of benign cases were observed in the 2nd decade (45 out of 49) and 3rd decade (27 out of 28 cases) of life. Whereas malignant cases were typically seen in the ages above 40, with 70% of the cases encountered in the 60-70 and 70-80 age group. This was partly concordant with the studies done by Pathy C et al which showed more chances of encountering a malignant cause of lymphadenopathy after the age of 40 but in that study the maximum number of malignant cases were observed in the 5th decade of life whereas in our study they were observed in the 7th decade of life [21].

Cervical lymph nodes bagged a lion's share in the patients undergoing FNAC for lymph node lesions as they comprised of 80.15% cases followed by axillary with 8.73 % cases which correlated by similar options by Sharma I et al, Badge SA et al and Khajuria et al a [16], [19], [23]. Of the malignant lesions it was observed that metastasis from squamous cell carcinoma was the most common,

followed by adenocarcinoma which correlated with studies done by Sharma RI et al [16], these lesions were primarily metastasis from lesions in the buccal cavity and the larynx and can be attributed to the heavy prevalence of Gutkha and tobacco chewing in the geographical location. Diagnosis of Hodgkin's and Non-Hodgkin's lymphoma is difficult on basis of FNAC however in our study we encountered 2 cases and 4 cases of Hodgkin's and Non-Hodgkin's Lymphoma respectively, along with 2 cases of Lymphoproliferative lesion which could not be placed on either attributable to the limitations of FNAC. This incidence of lymphoproliferative lesion with a possibility of malignancy concurred with studies done by Sharma RI et al (2.3%), Vimal S et al (2.67%), Arul P et al (3.0%) and Bhavani et al(1.2%) [16], [23], [24], [25]. But with a slightly higher percentage of (3.57%).

Conclusion

Fine Needle Aspiration Cytology (FNAC) serves as an excellent, quick, and minimally invasive first-line investigation for assessing the nature of lesions in lymph nodes, offering a reliable and readily accepted diagnostic tool. Utilizing ZN stain in cases with granulomas, necrosis, or suppuration proves highly valuable for diagnosing tuberculosis economically and conveniently, making it an alternative to open lymph node biopsy. The study revealed diverse cytomorphological patterns of lymphadenopathy and a substantial burden of tuberculous lymphadenitis. FNAC demonstrates high accuracy, sensitivity, and specificity, serving as a specific tool for early detection of primary malignancies and metastatic lesions, particularly beneficial in resource-limited settings.

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