



SPECTRUM OF HISTOPATHOLOGIC PATTERNS OF LYMPH NODE BIOPSIES: A DESCRIPTIVE STUDY FROM A TERTIARY CARE CENTER OVER 2 YEARS

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ABSTRACT

Background: Lymph node plays an important role in retaining and reacting to foreign antigens. Lymph nodes are affected by many types of lesions, both non-neoplastic and neoplastic. Clinical diagnosis is usually delayed due to nonspecific symptoms, so a lymph node biopsy is necessary to arrive at a proper diagnosis. **Aims:** Present study aims at studying the spectrum of lesions in lymph node biopsies and evaluating the neoplastic and non-neoplastic disorders with respect to the site, age and sex. **Materials and Methods:** This was a prospective study of 200 cases of lymph node biopsies carried out in the histopathology section of a tertiary care hospital. **Observation and Results:** Non-neoplastic lesions were more common comprising 90.5% (181 cases) which included 96 cases (48%) of tuberculous lymphadenitis, 71 cases (35.5%) of reactive hyperplasia of lymph node, 6 cases (3%) of granulomatous lymphadenitis, 3 cases (1.5%) of the vascular transformation of the lymph node and 1 case (0.5%) each of Kikuchi lymphadenitis, Castleman's disease, Infectious mononucleosis, Dermatopathic lymphadenopathy and Kimura disease were encountered. 9.5% (19 cases) were neoplastic lesions which included 9 cases (4.5%) of primary lymphoma and 10 cases (5%) of metastatic lesions. Primary lymphomas included 2 cases (1%) of Non-Hodgkins lymphoma and 7 cases (3.5%) of Hodgkins lymphoma. **Conclusions:** Lymph node excision biopsy remains the "gold standard" for diagnosis of lesions. In the present study, tuberculous lymphadenitis was the predominant lesion, (95 cases, 48%) followed by reactive hyperplasia of lymph node (71 cases, 35.5%) and metastatic lesions (10 cases, 5%).

KEYWORDS : Lymphadenopathy, lymphadenitis, lymphoma.

INTRODUCTION

Lymphadenopathy refers to lymph nodes that are abnormal either in their size, number, or consistency. In general, lymph nodes greater than 1 cm (cervical and axillary) and greater than 1.5cm (inguinal) in diameter are considered to be abnormal [1]. Lymphadenopathy can be neoplastic or non-neoplastic. The former includes mainly hematolymphoid malignancies and metastases while the causes of non-neoplastic lymphadenopathy are varied such as infections (bacterial, viral, fungal), drug reactions (including certain vaccines), lipid storage disorders, and a wide variety of miscellaneous non-neoplastic lymphoproliferative disorders such as Castleman disease, Rosai Dorfman disease, Kimura disease, Kikuchi Fujimoto disease, and systemic lupus erythematosus [2]. Imaging studies such as ultrasonography, computed tomography, or magnetic resonance imaging are helpful in the diagnosis. Though fine needle aspiration cytology is commonly used to establish the etiological diagnosis, excision biopsy of the lymph node remains the "gold standard" for diagnosis [3].

MATERIALS AND METHODS

The prospective study of 200 cases of lymph node biopsies was carried out in the histopathology section of the Department of Pathology for a duration of 2 years from June 2018 to June 2020 after obtaining necessary ethical approval from the Institutional Ethics Committee (Reference no.-IEC/PG/363/Oct/2018, Date-19/10/2018).

Inclusion Criteria:

- All types of lymph node biopsy specimens from patients of all ages above one year.

Exclusion Criteria:

- Inadequate samples
- Poorly preserved tissue

- Specimens of lymph node dissection.

The detailed clinical history like age, sex, site, presenting complaints, and clinical diagnosis along with relevant investigations were noted from histopathology requisition forms and medical records. All the specimens of lymph node biopsies were received in 10% formalin.

On examination of the specimens, gross morphological features like size, shape, colour, consistency, and presence of necrosis were noted. Sections were taken which were processed in an automated tissue processor. 4-5micron thick sections were taken from formalin fixed, paraffin embedded blocks. The sections were stained with Hematoxylin and Eosin (H&E).

Special stains including Ziehl Neelsen (ZN), periodic acid Schiff (PAS), and Gomori's methenamine silver (GMS) stains were used as indicated.

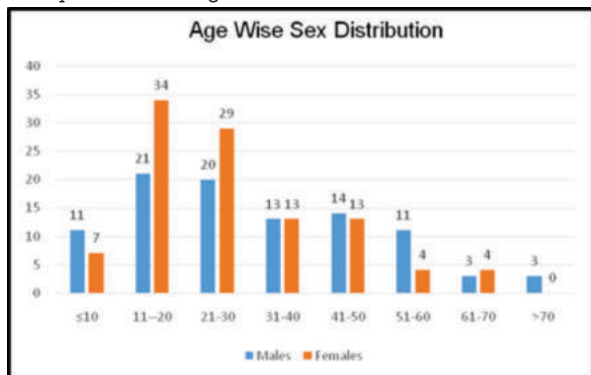
Immunohistochemistry was also performed using relevant antibodies according to the histomorphological features. After digitalization of the data, appropriate statistical analysis was done.

OBSERVATION AND RESULTS

The overall age range noted in this study was 1.5 to 80 years. The age range among males was 1.5-80 years while it was 4-69 years among females.

In both males and females, the maximum number of cases were in the age group 11-20 years. The least number of cases among males were noted in the age groups 61-70 and above 70 years. Among females age group above 70 years showed the least number of cases. The present study included 57 cases (28.5%) of lymphadenopathy in the pediatric age group

(1-18 years) [Table/Fig.1].



[Table/Fig 1]: Age-wise Sex Distribution (n=200)

Considering the gender-wise distribution, out of the 200 cases, 106 cases (53%) were females and 94 cases (47%) were males with a male to female ratio of 1:1.1, showing a slight female preponderance.

The most commonly affected group of lymph nodes were the cervical nodes (58%) followed by mesenteric (22%), axillary and inguinal (8% each). Rest 4% included mediastinal, intraparotid, postauricular, periportal, perigastric and gastroduodenal lymph nodes [Table 2].

[Table 2]: Sites of lymphadenopathy (n=200)

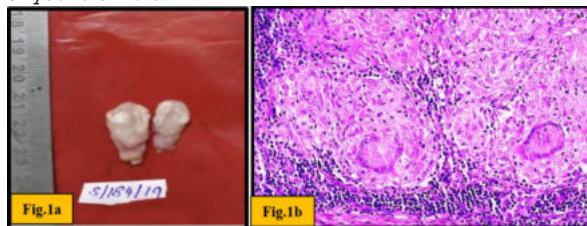
Site of lymphadenopathy	No of cases (n=200)	Percentage (%)
Cervical	117	58
Mesenteric	45	22
Inguinal	16	8
Axillary	15	8
Others	7	4
Total	200	100

Maximum number of patients (139) came with the complaint of lymph node swelling whereas remaining 61 patients, lymphadenopathy was found incidentally during a clinical examination or surgical procedures. The constitutional symptoms such as fever, loss of weight, loss of appetite, local pain, and cough were also seen. The lymph node lesions were categorized into neoplastic and non-neoplastic. Out of 200 lymph node biopsies analyzed, 181 cases (90.5%) of non-neoplastic lesions and 19 cases (9.5%) of neoplastic lesions were observed [Table 3].

[Table 3]: Distribution of Various Histopathological Lesions (n=200)

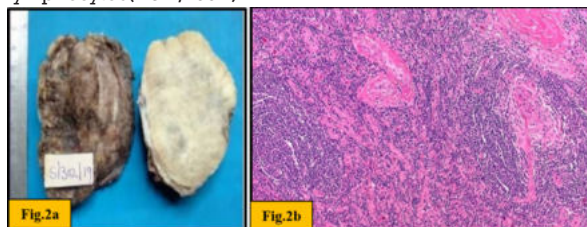
Lesion	Number of cases	Percentage (%)	
Tuberculous lymphadenitis	96	48	
Reactive hyperplasia of lymph node	71	35.5	
Granulomatous Lymphadenitis including Toxoplasma lymphadenitis and sarcoidosis	6	3	
Vascular Transformation of Node	3	1.5	
Infectious Mononucleosis	1	0.5	
Castleman disease	1	0.5	
Dermatopathic lymphadenopathy	1	0.5	
Kikuchi Lymphadenitis	1	0.5	
Kimura Disease	1	0.5	
Primary Lymphomas	Hodgkin's Lymphoma	7	3.5
	Non- Hodgkin's Lymphoma	2	1
Metastatic lesions	10	5	
Total	200	100	

The non-neoplastic lesions included 48% tuberculous lymphadenitis [Fig.1a,1b], 35.5% reactive hyperplasia of lymph node, 3% granulomatous lymphadenitis, 1.5% vascular transformation of lymph node and 0.5% each of infectious mononucleosis, Castleman disease [Fig.2a,2b], Kikuchi lymphadenitis, Dermatopathic lymphadenopathy and Kimura disease [Fig.3]. Out of the 3% of granulomatous lymphadenitis, one was diagnosed as sarcoidosis. The patient had high serum ACE (Angiotensin converting enzyme) levels and bilateral hilar lymphadenopathy on chest X-Ray and CT thorax. The second case was toxoplasma lymphadenitis in a 34 year old male.



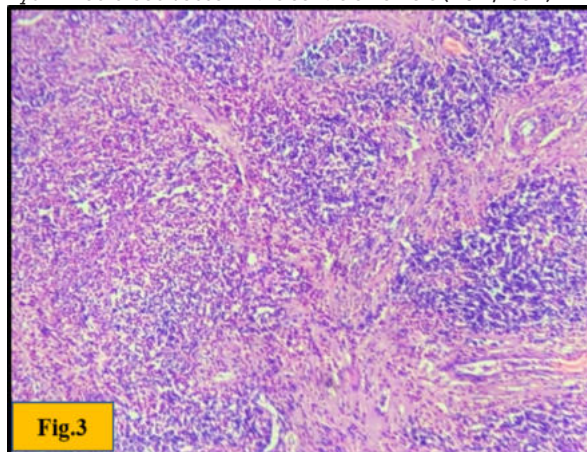
[Fig. 1a]- Gross image- Greyish white, soft cut surface of tuberculous lymph node showing cheesy white necrosis

[Fig. 1b]- Histopathology of Tuberculous Lymphadenitis showing well-formed epithelioid cell granuloma comprised of Langhan's giant cell, epithelioid cells and peripheral cuff of lymphocytes(H&E,200X)



[Fig. 2a]- Gross image- Greyish white, firm cut surface of lymph node mass in Castleman Disease

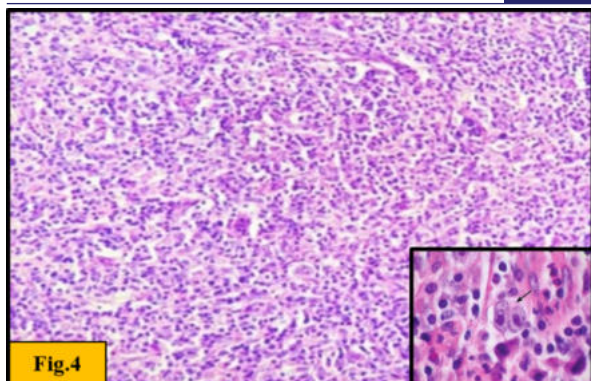
[Fig. 2b]- Histopathology of Castleman's disease showing hyalinized blood vessel in the centre of follicle (H&E,400X)



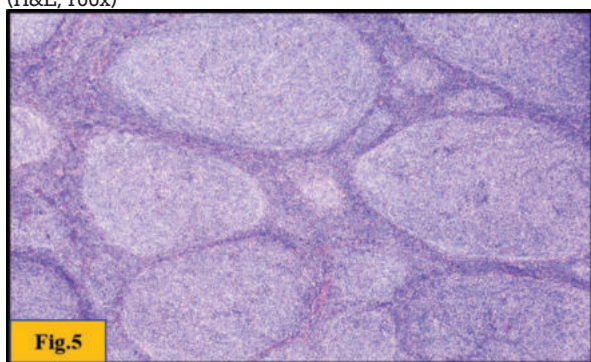
[Fig.3]- Histopathology of Kimura disease showing hyperplastic follicles along with prominent vasculature and eosinophilic infiltrate in the interfollicular area (H&E,100X)

The neoplastic lesions comprised of 9.5% cases. 4.5% of the cases were primary lymphoma and 5% were metastatic lesions [Table 3].

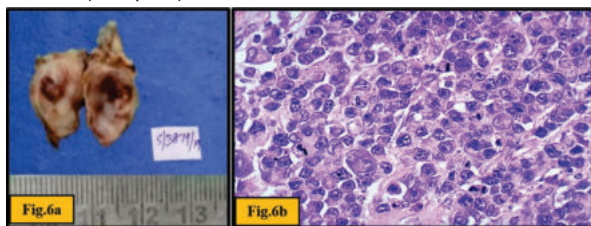
Out of the primary lymphomas, 3.5% of Hodgkin's lymphoma [Fig.4] and 1% of non-Hodgkin's lymphoma [Fig.5] was noted. 7 cases of Hodgkin's lymphoma were encountered of which 6 were of mixed cellularity type and 1 was of lymphocyte depleted type. Among the Non-Hodgkin's lymphoma, 1 case was of Diffuse Large B cell lymphoma [Fig.6a,6b] and the other was Burkitt lymphoma.



[Fig. 4]- Histopathology of Hodgkin's Lymphoma showing mononucleate and (Inset) binucleate Reed Sternberg cells along with polymorphous cell population (H&E, 100x)

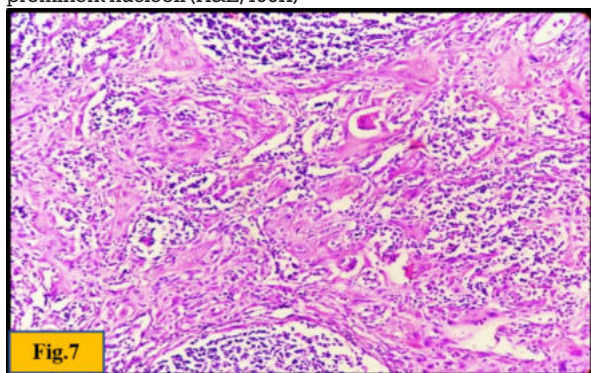


[Fig.5]-Non-Hodgkin's Lymphoma, Follicular variant showing increased monotonous appearing follicles, with ill-defined borders (H&E, 40x).



[Fig.6a]- Gross image -Soft, fleshy, greyish white cut surface of right cervical lymph nodes showing areas of haemorrhage in Diffuse Large B Cell Lymphoma

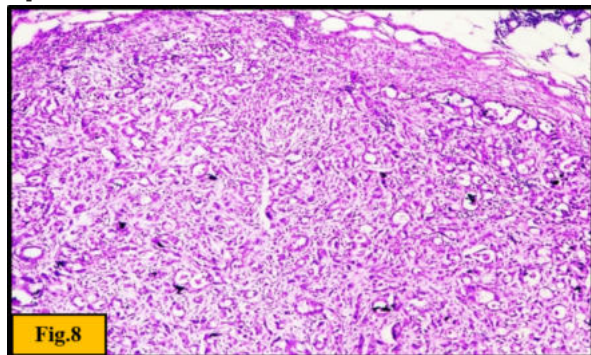
[Fig.6b)- Histopathology of Diffuse large B-cell lymphoma showing large lymphoid cells with vesicular nuclei and prominent nucleoli (H&E, 400X)



[Fig.7]- Histopathology of lymph node metastases of squamous cell carcinoma showing tumour arranged in sheet (H&E, 400X)

Metastatic malignancies accounted for 5% cases. Maximum (5) cases included metastases from squamous cell

carcinomas [Fig.7] followed by 3 metastases from invasive ductal carcinoma of breast and 1 case each of metastases from adenocarcinoma [Fig.8], and papillary carcinoma of the thyroid.



[Fig. 8]- Histopathology of lymph node with metastatic adenocarcinoma showing tumour arranged in back to back glandular pattern (H&E, 200X)

In the present study, 171 cases clinically diagnosed as benign, 164 were histopathologically diagnosed as benign and 7 came malignant. In contrary, out of 29 clinically diagnosed malignant cases, 19 came out to be truly malignant and 10 came benign on Histopathological examination.

With respect to the determination of benign and malignant lesions, the sensitivity was 63.2%, whereas specificity was 90.6%. The positive predictive value was modest at 41.3%. The negative predictive value was 95.9%. Thus, the accuracy of Histopathological examination is 85.5%, when compared to clinical diagnosis. [Table 4]

[Table4]: Association Between The Clinical Diagnoses And Histopathological Diagnoses.

Clinical Diagnosis	Total	Histopathological Diagnosis	
		Benign	Malignant
Benign	171	164	7
Malignant	29	10	19
Total	200	174	26

DISCUSSION

The lymph node is an important component of the immune system. Thus, proliferation and expansion of one or more of its cellular components occur following an immune response leading to significant lymph node enlargement. As lymphadenopathy is a very common clinical presentation, lymph node biopsy and histopathological examination are important to determine the non-neoplastic and neoplastic causes of nodal enlargement.

The present study was carried out over 2 years from June 2018 to June 2020 to evaluate the different histopathological patterns of lymph node biopsies. Slight female preponderance was noted with 53% females and 47% males with a male: female ratio of 1:1.1. This finding is in concordance with studies done by Pagaro PM et al[4] (51%), Kamat GC[5] (52.45%), Tiwari M et al[6] (56%). On the contrary, studies carried out by Agale et al [1] (42.35% females, 57.65% males), Arun Roy et al [7] (36.8% females, 63.2% males) and Sujata R[8] (40.9% females, 59.1% males) showed a male preponderance.

The predominant age group observed was 11- 20 years. Studies conducted by Amrita et al[3], Kamat GC[5] and Damle et al[9] also showed the maximum number of cases in the age group of 11-20 years.

Least number of cases (3 cases, 1.5%) were seen above 70 years of age, which was in agreement with the studies carried out by Pagaro PM et al[4] and Kamat GC[5].

The cervical lymph nodes were predominantly involved in the study which included 117 out of the 200 cases accounting for 58%. This finding is in agreement with studies by **Pagaro PM et al[4]**, **Tiwari M et al[6]**, **Vidyadhar R et al[10]**, **Damle et al[9]** and **Potti et al[11]** which showed maximum cases of cervical lymphadenopathy accounting to 39%, 49%, 39%, 65.86%, and 60% respectively. The cervical nodes are one of the major group of lymph nodes draining the head and neck area which is a common primary site of various infections and malignancies thus, explaining the preponderance of cervical lymphadenopathy.

Non-neoplastic lesions (90.5%) were much more common than neoplastic lesions (9.5%) and these results were consistent with the studies done by **Kamat GC[5]** and **Vidyadhar R et al[10]** having 82.92% and 75.6% non-neoplastic lesions respectively. On contrary, studies like **Arun Roy et al[7]** and **Pagaro PM et al[4]** both showed 53% of predominantly neoplastic lesions.

Out of non-neoplastic lesions, tuberculous lymphadenitis was the predominant lesion (48%) followed by reactive hyperplasia of lymph node (35.5%). Similar findings were noted in the study done by **Tiwari M et al[6]** and **Amrita et al[3]** where tuberculosis was the most common lesion with 47.2% and 40.4% respectively followed by reactive hyperplasia. Unlike the above mentioned studies, the study done by **Damle et al[9]** reported reactive hyperplasia (52.87%) as the predominant lesion in non-neoplastic lesions. Several authors have reported that tuberculosis is one of the most common causes of lymphadenopathy in developing countries such as India. Social determinants like poverty, malnutrition, and overcrowding have been proved to have a significant role in the propagation of tuberculosis in developing countries.

Out of the 96 cases of tuberculous lymphadenitis found in the present study, only 13 (15.4%) were positive for Acid Fast Bacilli (AFB) on Ziehl Neelsen (ZN) stain. Similarly, in the study carried out by **Sujata R[8]**, out of 23 cases of tuberculous lymphadenitis, 5 (21.7%) showed positivity for AFB. **Ahmed H et al[12]** reported AFB positivity in only 3 cases (3%) out of the 100 tuberculous lymph nodes studied.

Though detection of AFB is confirmatory for tuberculous lymphadenitis, it has several limitations and lacks sensitivity. AFB positivity depends on the bacillary load of the specimen. It was reported that the absence of AFB in samples showing an otherwise characteristic histopathological picture should not weigh against the diagnosis of tuberculosis [12]. Although in high tuberculosis prevalent areas like India, histopathology is the gold standard for diagnosis of tuberculous lymphadenitis where features such as Epithelioid cell granulomas, Langhans giant cells and caseous necrosis strongly suggest tuberculosis.

Out of total (9.5%) neoplastic lesions, maximum (5%) were metastatic disease followed by Hodgkin's lymphoma (3.5%) and Non-Hodgkin's lymphoma (1%). This was in agreement with the results obtained by **Sujata R[8]** showing 14.75% cases of metastases, 9.83% cases of Hodgkin's lymphoma and 6.55% cases of Non-Hodgkin's lymphoma. Similarly, **Dasari P et al[13]** reported 12.33% of metastatic lesions, 7.5% of Hodgkin's lymphomas and 4.1% of Non-Hodgkin's lymphoma.

Our study showed more cases (3.5%) of Hodgkin's lymphoma than Non-Hodgkin's lymphoma (6.5%) which included 6 cases of mixed cellularity type and 1 case of lymphocyte depleted type. Similar findings were seen in study done by **Sujata R[8]** showing predominantly Hodgkin's lymphoma accounting for 6 (9.83%) cases which included 4 cases of mixed cellularity and 2 cases of Lymphocyte rich type. Also, in the study by **Potti**

et al[11], Hodgkin's lymphomas included 15 cases of mixed cellularity, 2 cases of nodular sclerosis, 1 case of lymphocyte depleted and 1 case of nodular lymphocyte predominant type. In the study done by **Pagaro PM et al[4]**, predominantly cases were of Non-Hodgkin's lymphomas (8%) followed by Hodgkin's lymphomas (3%). Similar trend was shown by **Kamat GC[5]**, reporting 3.27% of Non-Hodgkin's lymphoma, and 0.4% Hodgkin's lymphoma. Geographic variations, the number of patients included in the study and their immunological status would have been responsible for the difference in the above findings.

Maximum cases (26%, n=10) of metastases were from squamous cell carcinomas. This finding was concordant with the studies like **Pagaro PM et al[4]** and **Kamat GC[5]**, which were showing 58.6% and 66.6% cases of metastases from squamous cell carcinoma. It was discordant with the findings of **Amrita et al[3]** and **Vidyadhar et al[10]** where metastases from adenocarcinoma was the most common finding showing 38.6% and 77.5% respectively. The higher number of squamous cell carcinoma metastasis in our study could be due to the high consumption of various types of tobacco in our area leading to malignancies.

CONCLUSION

Lymphadenopathy is one of the most frequently encountered clinical presentation among patients of all age groups and both sexes attending both outpatient and inpatient departments. Non-neoplastic conditions are much more common than neoplastic ones.

While investigating the cause of enlarged lymph nodes, a histopathological examination helps in establishing early and definitive diagnosis. It is not only a less expensive and faster method of diagnosis but remains the gold standard in early diagnosis thus, reducing morbidity and improving patient's prognosis.

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