



DIFFERENTIAL DIAGNOSIS AND EVALUATION OF LYMPHADENOPATHY AT A TERTIARY CARE CENTRE

Dr. K. Mercy Saranya	3 rd Year Post Graduate,
Dr P. Uma Rani*	Associate Professor, *Corresponding Author
Dr G.Vahini	Professor,
Dr Vijay	Prof ,SPM,
Dr Rajendra Prasad	Professor And HOD, Pathology,

KEYWORDS :

INTRODUCTION

Lymph nodes enlargement is a very common presentation of many benign and malignant diseases. Peripheral lymphadenopathy has a wide differential diagnosis, including infection, autoimmune disorders, and a number of reactive conditions(1). The most common benign condition encountered is infective, while the most common malignant disorder found is lymphoma(2). Etiological profile of lymphadenopathy varies from region to region. In developing countries like India, tuberculosis is the main cause while in developed countries secondary carcinoma is the most frequent cause for lymphadenopathy(3). Lymphomas are a heterogeneous group of cancers that have a variety of clinical presentations ranging from an indolent course to aggressive disease. The diagnosis of lymphoma often presents as a diagnostic challenge(4). Lymph nodes are the most common site of metastatic malignancy and sometime constitute the first clinical manifestation of a disease(5).

Most cases of lymphadenopathy are primarily assessed by FNAC procedure and also it is a simple, quick, inexpensive and equally reliable procedure which can be used as a routine OPD procedure but the frequency of indeterminate or incorrect diagnosis is higher in comparison to excisional biopsy. Aspiration cytology of lymphoma is difficult to interpret and distinguish reliably between Hodgkin lymphoma (HL), non-Hodgkin lymphoma (NHL) as well as subtype of either. So excisional biopsy is the procedure of choice in suspected lymphoma.

Histologic diagnosis depends on changes in the overall architectural pattern of the lymph node as well as identification of individual cell. Excisional biopsy yields more tissue for diagnostic studies facilitating preparation of multiple histological sections for routine and special stains as well as providing adequate material for culture. Although the advent of new immuno-histochemical analytic technique has improved the diagnostic accuracy, however histological examination of lymphoid tissue remains the gold standard for diagnosis(6).

AIMS and OBJECTIVES :

To evaluate and frame the differential diagnosis of the cases presenting with lymphadenopathy at a tertiary care centre.

MATERIALS AND METHODS :

This is a Retrospective study conducted in department of pathology in ASRAM medical college from February 2017 to September 2021, for a period of 3year 9months.

METHOD OF DATA COLLECTION:

In all patients, biopsy was performed as an out-patient procedure with minimal morbidity and no mortality. The

clinical details were provided by the respective clinical departments. Sections were prepared from formalin fixed, paraffin embedded blocks and stained with Hemotoxylin and Eosin in all cases. Special stains including Ziehl Neelsen, periodic acid Schiff and Gomori's methenamine silver were used wherever needed. Selected cases were additionally stained with Immunohistochemistry (IHC) using a panel of antibodies or markers through avidin-biotin peroxidase method. The lymphadenopathy cases detected as lymphoma, were classified according to WHO classification of hematolymphoid malignancies (2016).

INCLUSION CRITERIA:

A total of 75 cases of lymphadenopathy which are histopathologically confirmed were included in this study.

EXCLUSION CRITERIA:

Cases where Histopathological studies were inconclusive due to lack of adequate material and cases with En bloc lymphnode dissection with known cases of primary or associated with evidence of primaries elsewhere in the body were excluded from the study.

STATISTICAL ANALYSIS:

Data were entered into the computer and analysed using software SPSS trial version 26.0. The mean[standard deviation(SD)] was computed for all the quantitative variables, the frequency and percentage were computed for all the qualitative variables.

RESULTS :

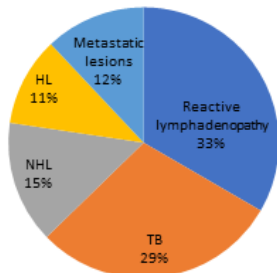
Out of the total of 75 lymph node biopsies, 53.3% (40 cases) were males and 46.6% (35 cases) were females giving a male to female ratio of 1.1:1. The age range was 3-75 years in case of male and 13-75 years in case of female(Tab/Fig3,4).The most common lymph node involved is cervical region showing 40 cases (53.3%)(Tab/Fig 1). Out of 75 lymph node biopsies analyzed, the non-neoplastic lesions were more common comprising 47 cases(62.6%), which included 22 cases (29.3%) of non-specific reactive lymphoid hyperplasia, 3 cases (4%) of specific lymphoid hyperplasia, 22 cases (29.3%) of tuberculous lymphadenitis. The neoplastic lesions were 28 cases (37.3%), which included 11cases (14.6%) of non-Hodgkin lymphoma (NHL), 8 cases (10.6%) of Hodgkin lymphoma (HL) and 9 cases (12%) of metastatic lesions(Tab/Fig2,4).

Tuberculous lymphadenitis comprising 22 cases (29.3%) of nonneoplastic lesions and the second most common histologic pattern encountered occurred predominantly in young adult female and 19 cases (86.3%) occurred before the age of 40 years with a peak between 21 and 30 years with slight female preponderance (M:F-0.83:1).

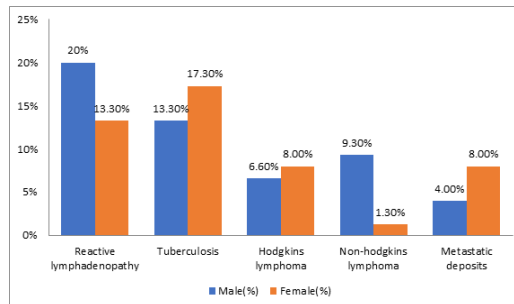
Table/Fig1. Distribution of lymphadenopathy cases.

Lymphadenopathy	Cervical	Axillary	Inguinal	Submandibular	Supraclavicular	Parotid	Tonsillar	Mesentric	Others
1.Reactive	11	1	4	1	1	2	-	5	-
2. Tuberculosis	18	-	-	1	1	-	-	-	2
3.HL	4	2	1	-	-	-	-	-	1
4.NHL	3	-	4	1	-	-	2	-	1
5.Metastatic	4	1	3	-	-	-	-	-	1

Table /Fig2: Distribution of different types of lesions on lymphnode biopsy.



Table/Fig3: Gender wise distribution of lymphadenopathy



Table/Fig4. Age and gender distribution of patients

Lymphadenopathy	Sex	<10yrs	11-20 yrs	21-30 yrs	31-40 yrs	41-50 yrs	51-60 yrs	61-70 yrs	> 70 yrs	Total	%
1.Reactive lymphadenopathy	M	1	3	1	2	2	2	1	3	15	20%
	F	-	2	2	2	1	1	1	1	10	
2. TUBERCULOSIS	M	1	2	2	2	1	1	1	-	10	13.3%
	F	-	5	7	-	-	-	-	-	12	
3. HODGKIN'S lymphoma	M	2	2	-	1	1	-	-	1	7	6.6%
	F	-	-	-	-	-	-	1	-	1	
4. NHL	M	-	-	-	2	-	1	2	-	5	9.3%
	F	-	-	2	-	1	3	-	-	6	
5. Metastatic deposit	M	-	-	-	-	1	2	-	3	3	4.0%
	F	-	-	1	1	2	1	1	6	6	

Among the non-neoplastic lesions, reactive lesions were by far most common accounting for 25 cases (33.3%). There was male preponderance showing M:F ratio of 1.5:1. Common age group affected was 11-20 years. Among the non-specific reactive lymphoid hyperplasia, 16cases(21.3%) showed follicular hyperplasia, 6 cases(8%) showed sinus histiocytosis. The rest 3cases (4%) had other specific patterns of lymphoid hyperplasia comprising of 2 cases(2.6%) of kimura disease and 1 case(1.3%) of castleman’s disease.

There were 8 cases(10.6%) of HL which constituted 42.1% of all lymphomas. The most common age group was between 11yrs to 20 yrs of age with male preponderance (M:F - 7:1). Nodular sclerosis (NS) was the most common subtype of HL(Figure5).

Table/fig5. Distribution of cases according to subtype of Hodgkins lymphoma

Subtype	No of cases(%)
1. Nodular sclerosis	4(5.3%)
2. Mixed cellularity	3(4.0%)
3. Lymphocyte predominant	1(1.3%)

There were 11 cases(14.6%) of NHL which constituted 57.8% of all lymphomas. The most common age group affected was 51 and 60 years with a female preponderance (M:F = 0.5:1). A single case(1.3%) of T-cell lymphoma and 10 cases (13.3%) of B-cell lymphoma which includes 4 cases (5.3%) of diffuse large B-cell lymphoma (DLBCL) being the most common subtype. Other subtypes are 2cases(2.6%) of follicular lymphoma(FL), 1case (1.3%) of burkitt lymphoma, 3 cases(4%) of chronic lymphocytic lymphoma/small lymphocytic lymphoma (CLL/SLL). A single(1.3%) of T-cell variant of NHLs which is angioimmunoblastic T-cell lymphoma (AITL) type(Figure6)

Table/fig 6.Distribution of cases according to subtype of Non-Hodgkins lymphoma

Subtype	No of cases(%)
1. Diffuse large B cell lymphoma(DLBCL)	4(5.3%)
2. Small cell lymphoma(SLL)	3(4.0%)
3. Follicular lymphoma	2(2.6%)
4. Burkitt's lymphoma	1(1.3%)
5. Angioimmunoblastic T cell lymphoma	1(1.3%)

Metastases constituted the remaining malignancies representing 12% of total lymph node biopsies. The majority of cases were found within the age group 50-70 years. The M:F ratio was 0.6:1. Out of 9 cases of metastatic lymphadenopathies, 5 cases (6.6%) adenocarcinoma and a single case(1.3%) each of squamous cell carcinoma, papillary carcinoma of thyroid, sebaceous carcinoma and poorly differentiated carcinoma respectively(Figure7).

Table/fig7. Metastatic deposits with their unknown primary site

Deposits with Unknown primary site	No of cases
1. Squamous cell carcinoma	1(1.3%)
2. Adenocarcinoma	5(6.6%)
3. papillary carcinoma thyroid	1(1.3%)
4. Sebaceous carcinoma	1(1.3%)
5. Poorly differentiated carcinoma	1(1.3%)

DISCUSSION

Palpable lymph nodes offer an important diagnostic clue to the etiology of the underlying condition. 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. Our study shows that males were more commonly affected. Patients with benign etiology were younger, whereas those with malignant

etiology were older which was similar to the findings of the study conducted by Arun roy et al(7).

The most common lymph node involved is cervical region showing 40 cases (53.3%) which was similar Sarsu SB et al(8) study, where the most commonly involved lymphnode was cervical followed by inguinal and mesenteric.

In our study unilateral lymphadenopathy was 98% and bilateral was 2% which was similar to the study conducted by Nasheen bagali et al(9).

The present study showed, Reactive lymphnodal hyperplasia similar to the study conducted by Zahir et al and Thomas et al. In Zahir et al reactive lymphnodal hyperplasia was followed by malignancy and infectious disease(10). In Thomas et al study reactive lymphnodal hyperplasia followed by granulomatous pathology and malignancy(11).

Tuberculous lymphadenitis is the second most common cause of lymphadenopathy in our present study involving cervical lymphnodes of female of younger age(21-30) which was similar to the study conducted by Albasri AM et al(12).

In our study lymphoma was the most common malignant pathology. Non-Hodgkins lymphoma was more common than hodgkins lymphoma which was similar to the study conducted by Groves FD et al(13) . Most of the lymphomas shows size >1cm with hard consistency and fixed texture. The features are similar to the study conducted by Bosch et al(14).

Hodgkins lymphoma was the most common in younger age (45years), while the distribution of NHL was equal among both <45 and >45 years group. This finding was in consistent with the study conducted by Reddy DL et al(15).

Among B-cell lymphomas, DLBCL is accounting for 36.3% similar to Naresh et al(16) study. DLBCL is considered as single largest subset of NHLs in India.

Among HL, nodular sclerosis is the most common subtype comprising 5.3% of cases. In USA and Europe it comprises 70% of classical HL; however, rate varies greatly among other geographical regions and the risk is the highest among those with high socio-economic status.

In Metastatic lymphadenopathy the deposit of adenocarcinoma is most common(6.6%) which is similar to Henry P et al study (17).

CONCLUSION :

- Reactive lymphadenopathy is the most common type of lymphnodal enlargement.
- Cervical lymphnodes are the common site of lymphadenopathy.
- There by we conclude that lymphadenopathy, though worrisome, biopsy is the diagnostic methodology to categorise the etiology.

REFERENCES

1. Nixon S, Bezverbnaya K, Maganti M, Gullane P, Reedijk M, Kuruvilla J, Prica A, Kridel R, Kukreti V, Bennett S, Rogalla P. Evaluation of lymphadenopathy and suspected lymphoma in a lymphoma rapid diagnosis clinic. *JCO oncology practice*. 2020 Jan;16(1):29-36.
2. Hussain MI, Bukhari MH, Aftab MZ. Lymph node biopsies: Evaluation of disease pattern and role of surgery—Our experience from South Punjab, Pakistan. *Acta Medica International*. 2019 Jan 1;6(1):7.
3. Nasheen bagali, maheboob bagali, Praveen kumar,. "cervical lymphadenopathy- a clinicopathological review". *International journal of current research*.2020 ;12(01):9652-9655.
4. KühnlA, CunninghamD, HutkaM, etal: Rapid access clinic forum explained lymphadenopathy and suspected malignancy: Prospective analysis of 1000 patients. *BMC Hematol*.2018:18-19.
5. Goyal S, Kaur Brar R, Sehgal S. Histopathological and cytological spectrum of lymphadenopathy: a window to preliminary diagnosis. *Int J Med Res Rev*. 2017 Oct.;5(10):900-7
6. Patel, Komal; Patel, Mubin I.; JHA, Bharti M.. Histopathological analysis of lymph nodes in patient with clinical lymphadenopathy - 266 cases. *International Journal of Research in Medical Sciences*, 2016 Dec: 1655-1660.

7. Roy A, Kar R, Basu D, Badhe BA. Spectrum of histopathologic diagnosis of lymph node biopsies: a descriptive study from a tertiary care center in South India over 5½ years. *Indian Journal of Pathology and Microbiology*. 2013 Apr; 56(2):103-7
8. Sarsu SB, Sahin K. A retrospective evaluation of lymphadenopathy in children in a single center's experience. *J Pak Med Assoc* 2016;66:654-7.
9. Nasheen bagali, maheboob bagali, Praveen kumar, s.p2020. "cervical lymphadenopathy- a clinicopathological review". *International journal of current research*.12(01):9652-9655.
10. Zahir S, Azimi A. Histopathologic findings of lymph node biopsy cases in comparison with clinical features. *Pak J Med Sci* 2009;25:728-33.
11. Thomas JO, Ladipo JK, Yaw T. Histopathology of lymphadenopathy in a tropical country. *East Afr Med J* 1995;72:703-5.
12. Albasri AM, El-Siddig AA, Hussainy AS, Alhujaily AS. Pattern of lymph node pathology in Western Saudi Arabia. *Asian Pac J Cancer Prev* 2014;15:4677-81.
13. Groves FD, Linet MS, Travis LB, Devesa SS. Cancer surveillance series: Non-Hodgkin's lymphoma incidence by histologic subtype in the United States from 1978 through 1995. *J Natl Cancer Inst* 2000;92:1240-51.
14. Bosch X, Coloma E, Donate C, et al: Evaluation of unexplained peripheral lymphadenopathy and suspected malignancy using a distinct quick diagnostic delivery model: Prospective study of 372 patients. *Medicine (Baltimore)*.2014. 93:95.
15. Reddy DL, Venter WD, Pather S. Patterns of lymph node pathology; fine needle aspiration biopsy as an evaluation tool for lymphadenopathy: A retrospective descriptive study conducted at the largest hospital in Africa. *PLoS One* 2015;10.
16. Naresh KN, Srinivas V, Soman CS. Distribution of various subtypes of non-Hodgkin's lymphoma in India: A study of 2773 lymphomas using R.E.A.L. and WHO classifications. *Ann Oncol* 2000;11(1):63-7.
17. Henry P, Longo D. Enlargement of lymph nodes and spleen. In: Braunwald E, Hayser SL, Fauci AS, Longo DL, Kasper DL, Jameson JL, editors. *Harrison's Principles of Internal Medicine*. 16th ed. New York: McGraw-Hill; 2005:343-8