Pattern of histopathological diagnosis of lymph node biopsies at a tertiary care hospital in Northeast India

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Abstract
Biopsy and histopathology plays an important role in establishing the cause of lymphadenopathy. Knowledge of the characteristic histopathological findings and causes of lymphadenopathy may spare patients from unnecessary and management. To study the most frequent cause of enlarged lymph nodes in our set up. To assess the spectrum of lymphadenopathy in various age groups. The study was a hospital based cross-sectional study. Total 75 numbers of patients from July 2015 till June 2016 were recruited. All specimens of lymph node biopsies damaged specimens, known cases were excluded. The diagnosis of was made on the basis of gross morphology and light microscopic features. Ziehl Neelson staining, immunohistochemistry were done whenever required. There were more male cases. Most frequently affected age group was between 40-49 years. The cervical region was most commonly affected. Benign cases were more common. Out of 44 benign cases, 55 % were reactive hyperplasia, 43% were granulomatous lesions and Castleman's disease in 1 case. Tubercular lymphadenitis was the most frequent entity among granulomatous lesions. Of 31 malignant lesions, 55% were non-hodgkin's lymphoma 26% were hodgkin's lymphoma and 19% were metastatic. Lymph node biopsy remains a valuable diagnostic tool as it allows for the architecture of the gland to be viewed thereby given an accurate and concise diagnosis with minimal risk to the patient.

Keywords: Histopathology, Immunohistochemistry, Lymphadenopathy.

Introduction
Lymph nodes are discrete, ovoid lymphoid structures that are widely distributed throughout the body. Lymphadenopathy refers to nodes that are abnormal in size, consistency or number, caused by the invasion or propagation of either inflammatory cells or neoplastic cells into the nodes. Clinically, lymphadenopathy may be peripheral or visceral. Peripheral lymphadenopathies are easily detected by routine physical examination and are often biopsied as they are easily accessible for lymphadenectomy, which is a minor surgical procedure. Visceral lymphadenopathy on the other hand, requires laparotomy or sophisticated imaging techniques for detection.

Among the peripheral nodes, those in the upper part of the body (cervical, supraclavicular, axillary) are preferentially biopsied than lower limb nodes (popliteal, inguinal or femoral) as the former are more likely to yield definitive diagnosis whereas the latter are often characterized by non-specific reactive or chronic inflammatory and fibrotic changes.[1,2]

Lymphadenopathy is a common clinical problem and biopsies are usually undertaken to determine the cause of nodal enlargement. Various reports document tuberculosis and infectious etiology as major causes of lymph node enlargement[3,4] whereas malignancies as a predominant cause in the developed countries.[5,6] Increase in incidence of tuberculosis attributed to the advent and preponderance of HIV infection has been documented worldwide.[7-9]

Considering the plethora of diseases that may cause lymphadenopathy, it is essential to define the pattern of disorders presenting primarily as lymph node enlargement in a particular environment.[10] Pattern of lymph node enlargement is different in different age group. Metastatic deposit is common in adults whereas it is rare in children.[11,12] Reactive hyperplasia to minor stimuli has been reported as a significant cause of lymphadenopathy in children.

Materials and Methods
The hospital-based descriptive study was conducted in the Department of Pathology, Assam Medical College and Hospital, Dibrugarh, Assam to study the commonest cause of enlarged lymph nodes in our set up, to assess the spectrum of lymphadenopathy in various age groups. The study was a hospital based cross-sectional (non-interventional) type of study. Total 75 patients from July 2015 till June 2016 were recruited. All excised lymph node specimens received in the Department constituted the study material. The specimens were processed for histopathological examination. All the lymph node studies were grouped into one of the following broad categories: Reactive hyperplasia, Granulomatous lymphadenitis, Metastatic lymph node, Lymphoma.

History was noted from the case records, which included the age, presenting symptoms and clinical diagnosis whenever available. The diagnosis of lymph node lesions was made on the basis of clinical features, morphology and light microscopic features. All the specimens of lymph nodes received at the Pathology Department of Assam Medical College & Hospital

satisfying the inclusion and exclusion criteria were taken up for the study.

Inclusion Criteria: All surgically resected and biopsied specimens of lymph node tissue from all age groups received at the Department of Pathology, Assam Medical College & Hospital, Dibrugarh, for histopathological examination.

Exclusion Criteria: Specimens of known cases of primary malignancy were excluded, which were 8 in number. Badly handled and poorly preserved lymph node specimens were excluded which were 4 in number. Data was collected using predesigned proforma.

Results

The present study was conducted in the Department of Pathology, Assam Medical College and Hospital, Dibrugarh, Assam to study the commonest cause of enlarged lymph nodes in our set up, to assess the spectrum of lymphadenopathy in various age groups. We found that out of 75 cases, 7% were below 10 years of age, 9% in the 10-19 years age group, 19% in the 20-29 years age group, 11% in the 30-39 years age group, 27% in the 40-49 years age group, 15% in the 50-59 years age group and 13% were above 60 years of age. (Table 1)

Table 1: Age wise distribution of lymphadenopathy

Age group (in years)	Number (n)	Percentage (%)
<10	5	6.67
10–19	7	9.33
20–29	14	18.67
30–39	8	10.67
40–49	20	26.67
50–59	11	14.67
>/=60	10	13.33
Total	75	100.00

Table 2: Sex Distribution

Sex	Number (n)	Percentage (%)	Ratio (Male: Female)
Male	61	81.33	4.35 : 1
Female	14	18.67	
Total	75	100.00	

We observed that out of 75 cases, 81% were males and 19% were females. Male to Female ratio was approximately 4:1. (Table 2)

Table 3: Age wise distribution of lymph node biopsy

Age group (in years)	Reactive	Tubercular Granuloma	Granulomatous	Metastatic	Non-Hodgkin's Lymphoma	Hodgkins Lymphoma	Castleman's Disease	Total	
								n	%
<10	2	0	0	0	1	1	0	4	5.33
10–19	1	3	2	0	1	0	0	7	9.33
20–29	4	6	1	0	1	1	0	13	17.33
30–39	3	1	1	0	2	2	1	10	13.33
40–49	6	0	3	3	4	0	0	16	21.33
50–59	4	2	0	1	4	0	0	11	14.67
≥60	4	0	0	2	4	4	0	14	18.67
Total	24	12	7	6	17	8	1	75	100.0

The present study includes patients of all age groups. The peak incidence of age group suffering from the disease was 40-49 years (21.33%) followed by cases which are above 60 years of age (18.67%).

Majority of the benign lesions were in the age group of 20-29 years of age followed by 40-49 years of age group, being 25% and 20.45% respectively. (Table 3)

Table 4: Final diagnosis of lymphoma cases

Final Diagnosis	Number (n)	Percentage (%)
Classical Hodgkin's Lymphoma	5	20.00
Follicular Lymphoma	4	16.00
Anaplastic Large Cell Lymphoma (anaplastic lymphoma kinase negative)	2	8.00
Anaplastic Large Cell Lymphoma (anaplastic lymphoma kinase positive)	2	8.00
B Cell Lymphoblastic Lymphoma	2	8.00
Mantle Cell Lymphoma	2	8.00
Nodular Lymphocyte Predominant Hodgkin's Lymphoma	2	8.00
Diffuse Large B Cell Lymphoma	2	8.00
B Cell Non-hodgkin's Lymphoma	1	4.00
Mixed Phenotypic Acute Leukemia	1	4.00

Marginal Zone Lymphoma	1	4.00
Peripheral T Cell Lymphoma	1	4.00
Total	25	100.00

Out of all the lymphoma cases, 5 cases (20%) were diagnosed as classical Hodgkin's lymphoma, 4 cases (16%) as follicular lymphoma, anaplastic large cell lymphoma (alk negative) in 2 cases (8%), anaplastic large cell lymphoma (alk positive) in 2 cases (8%), B cell lymphoblastic lymphoma in 2 cases (8%), mantle cell lymphoma in 2 cases (8%), diffuse large B cell lymphoma in 2 cases (8%), marginal zone lymphoma in 1 case (4%), peripheral T cell lymphoma in 1 case (4%) and unclassifiable in 1 case (4%). (Table 4 and Fig. 1-4)

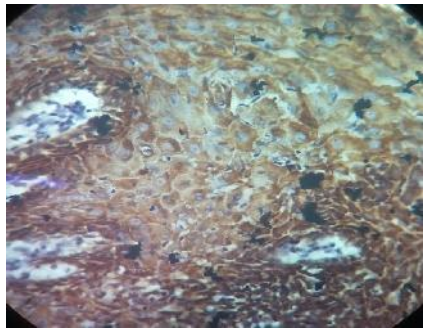

Fig. 1: Cytokeratin positive in metastatic lymph node

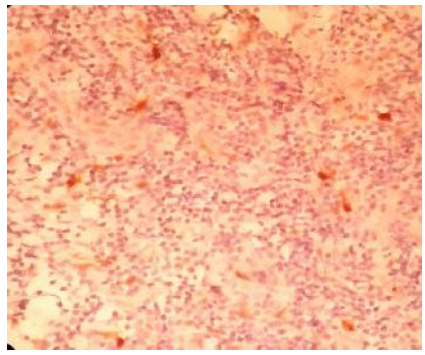

Fig. 2: Cyclin D1 positive in Mantlecell lymphoma

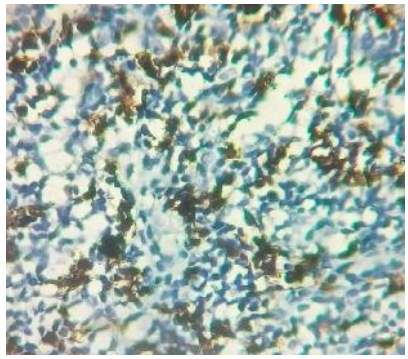

Fig. 3: CD 20 positivity in tumour cells of Nodular lymphocyte predominant Hodgkin's lymphoma

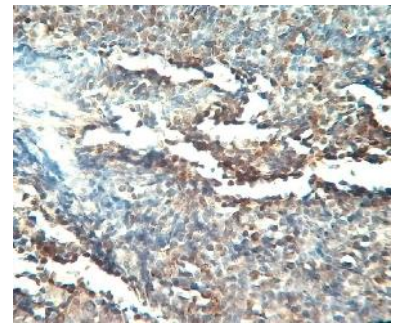

Fig. 4: Ki 67 positivity in more than 30% cells in a case of high grade lymphoma

Discussion

In studies conducted by Henry et al,[13] YeuTsu N et al[14] and in India by Kamat et al,[15] it has been found that benign lesions are much more common than malignant lesions.

Rao M N et al[16] reported that, lymphadenopathy due to malignancy were 22 (44%), non-malignant causes were 28 (56%).In the present study, lymphadenopathy due to benign (non-malignant cases were 44 (59%) and due to malignant involvement in 31 cases (41%).

In present study, 32% cases were reactive hyperplasia and 26% cases were granulomatous. Vacchani et al,[17] reactive hyperplasia was 51% and granulomatous lymphadenitis was 24%. Tiwari et al[18] reported reactive hyperplasia to be 36% and granulomatous lymphadenitis to be 49 %.

Kamat et al[15] reported reactive hyperplasia to be 30.73 % and granulomatous lymphadenitis to be 58.19%.

Tuberculosis has also been reported by several authors as the predominant lesion in adults in the tropics. Rahman et al[19] in his study found that tuberculosis was the commonest cause of lymphadenopathy accounting for 33.5% of cases.

In the present study lymphoid malignancies accounted for 33% of cases and metastatic lymph node accounted for 8% of cases. In the present study, lymphoma accounted for 33% of cases out of which non-hodgkin's lymphoma constituted 68% of total lymphoma cases and Hodgkin's lymphoma constituted 32% of total lymphoma cases. In study conducted in Nigeria by Akinde et al,[20] lymphoma cases constituted 16.85 % of cases. In study conducted in India (Karnataka) by Kamat et al[15] and in Nepal by Tiwari et al[18] and in Gujarat by Vachhani et al,[17] frequency of lymphoma cases are 3.7%, 2% and 2% respectively. In the Western world non-hodgkin's lymphoma is reported to be 3 to 4 times more common than Hodgkin's lymphoma. In our study we found 6 cases (8%) of metastatic lymph node satisfying the inclusion and

exclusion criteria. Three of them were metastatic squamous cell carcinoma and three were metastatic adenocarcinoma.

Kamat et al,[15] Tiwari et al,[18] Akinde et al,[20] Sibanda et al,[21] Anunobi et al,[22] the percentage of cases with metastatic deposits found in the lymph node were 7.37%, 11%, 12.4%, 14.9%, 2.62%, 33.60%, 36.50% respectively.

Table 5: Distribution of lymphoma and metastatic lesions

Authors	Number of Cases	Place	Non Neoplastic Lesions (%)			Neoplastic Lesions (%)	
			Reactive	Granulomatous	Other	Metastatic	Lymphoma
Sibanda et al[21]	2194	Zimbabwe	33	27		33	7
Thomas JO et al[23]	427	Nigeria	37	28		36	
Rao MN et al[16]	50	India	65			44	
Moore et al[24]	1877	USA	47.8	36		2.6	8.5
Henry et al[13]	220	USA	63	21		16	
Ochicha et al[25]		Nigeria	27	30		19	24
Tiwari et al[18]	55	Nepal	36	47	4	11	2
Anunobi et al[22]	720	Nigeria	34	17.4		33.6	14.2
Kamat et al[15]	244	India (Karnataka)	30.7	58.2		7.37	3.67
Akinde et al[20]	733	Nigeria	31	24		37	17
Rahman et al[19]	191	Bangladesh	30.9	34.6	4.7	12.6	17.3
Vachhani et al[17]	100	India (Gujarat)	51	24		23	2
Present Study	75	India (Assam)	32	26	1	8	33

Conclusion

Lymphadenopathy is an important finding in the diagnosis of many diseases. The histopathological examination helps us in assessing the architecture of the tissue. Combined with immunohistochemistry, it can be a useful tool in clinching a diagnosis. The history, blood examination and cytological correlation are required. The major limitation of our study was the small number of cases owing to the short duration of the study. Many cases were lost to follow up, some of the cases expired owing to malignant disease. Another limitation was that some of the specimens were badly preserved due to poor fixation by formalin.

We are planning to increase the number of cases in the years to come and maintain proper records of the patients so that they are not lost to follow up.

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