

Distribution of lymphoid neoplasm in eastern India: An experience from a tertiary care cancer research institute

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Abstract

Introduction: The classification of lymphoid neoplasm has witnessed significant revisions over the years with the recent one simplifying the diagnosis and management of lesions at the very initial stages of lymphomagenesis. Different subtypes of lymphoid neoplasm vary in the different geographical locations. The present study aimed to probe the distribution of lymphoid neoplasm in Eastern India.

Materials and Methods: A total of 79 cases of lymphadenopathy were included over a period of two years and were subjected to categorization according to WHO classification, using light microscopy and immunohistochemistry studies.

Results: Of the 79 cases of lymphadenopathy studied, 35 cases were NHL, 21 cases were HL and rest other types. The ratio of NHL to HL as per our study was 1.66:1. Among NHL cases B-cell lymphomas were the predominant type accounting for 77.78% of all NHL cases, while T-cell lymphomas constitute 17.78% cases. Among HL, mixed cellularity variant was the commonest type (52.38%), followed by nodular sclerosis (33.33%) and lymphocyte predominance (9.52%).

Conclusion: While DLBCL was the most common prevalent B cell NHL subtype followed by follicular lymphoma, Burkitt's lymphoma and High Grade B Cell lymphoma, ALCL was the most common T-cell lymphoma subtype followed by peripheral T cell lymphoma and Mycosis fungoides. Mixed cellularity was found the most common subtype of HL followed by the nodular sclerosis.

Keywords: Hodgkin's lymphoma, Lymphoid neoplasm, Non-Hodgkin's lymphoma.

Introduction

The lymphomas are a heterogeneous group of disorders and accounts for up to 3% of all malignancies. The classification of lymphomas has undergone many changes over the last two decades.¹ In 2001, the World Health Organization (WHO) produced a consensus classification encompassing immunophenotype, genetic abnormalities and clinical features.² The 2008 WHO classification of hematopoietic and lymphoid tumors and the associated monograph represented the established guidelines for the diagnosis of malignant lymphomas; however, subsequently there were major advances with significant clinical and biologic implications, which led to a major revision in the nearly 8-year-old classification of the lymphoid neoplasms.³ The 2016 WHO classification of mature lymphoid, histiocytic, and dendritic neoplasms thus clarified the diagnosis and management of lesions at the very early stages of lymphomagenesis, refined the diagnostic criteria for some entities, detailed the expanding genetic/molecular landscape of numerous lymphoid neoplasms and their clinical correlates, and referred to investigations leading to more targeted therapeutic strategies.³

Non-Hodgkin lymphoma is the eighth leading cause of cancer death in the United States. Non-Hodgkin lymphoma is more common in men than women, and among individuals of Caucasian descent. According to SEER statistics of NHL, the number of new cases was 19.5 per 100,000 men and women per

year, while the number of deaths was 5.9 per 100,000 men and women per year. These rates were however age-adjusted and based on 2010-2014 cases and deaths.⁴ As per 2012-2014 data, it is posed that approximately 2.1 percent of men and women will be diagnosed with non-Hodgkin lymphoma at some point during their lifetime. In 2014, there were an estimated 661,996 people living with non-Hodgkin lymphoma in the United States. The prognosis and treatment of NHL depend on the subtype, stage and associated comorbid conditions. While adequate information is available on the epidemiological profile of NHL from developed nations, such data is sparse from low middle income countries (LMICs) like India. The present study thus attempted to probe the distribution of various lymphoid neoplasms in a tertiary care Cancer institute in Eastern India.

Materials and Methods

The present study was a hospital based prospective research conducted in a dedicated tertiary care Cancer institute in Eastern India for a period of two years. Cases of enlarged lymphnodes were enrolled in the study. Those with metastatic and tubercular lymphadenopathy were excluded.

All patients with enlarged lymphnodes were subjected to fine needle aspiration cytology. Each patient with non-specific/inconclusive FNAC reports was subjected to lymph node excision biopsy. The cytology slides were prepared after aspiration and fixed.

After fixation, the slides were stained with hematoxylin and eosin. The surgically biopsied lymph was fixed in 10% buffered formalin. After gross examination, entire or representative sections were taken followed by paraffin embedding, cutting and slide preparation and finally stained with hematoxylin and eosin. Both histopathology and FNAC slides were examined under light microscope.

Immunohistochemistry was performed according to avidin-biotin peroxidase complex method, after

pretreatment of antigen retrieval, by heating in microwave oven in 0.01M citrate buffer (p H-6.0). The panel of immunohistochemistry (IHC) markers included CD45 (LCA), CD45RO, CD79, CD20, CD23, CD10, CD5, CD3, CD56, CD4, CD8, CD15, CD30, CD34, EMA, MUM1, BCL6, TdT, BCL2, MIB1/KI67, ALK1, Kappa and lambda light chains. The results were tabulated and recorded individually. (Fig. 1)

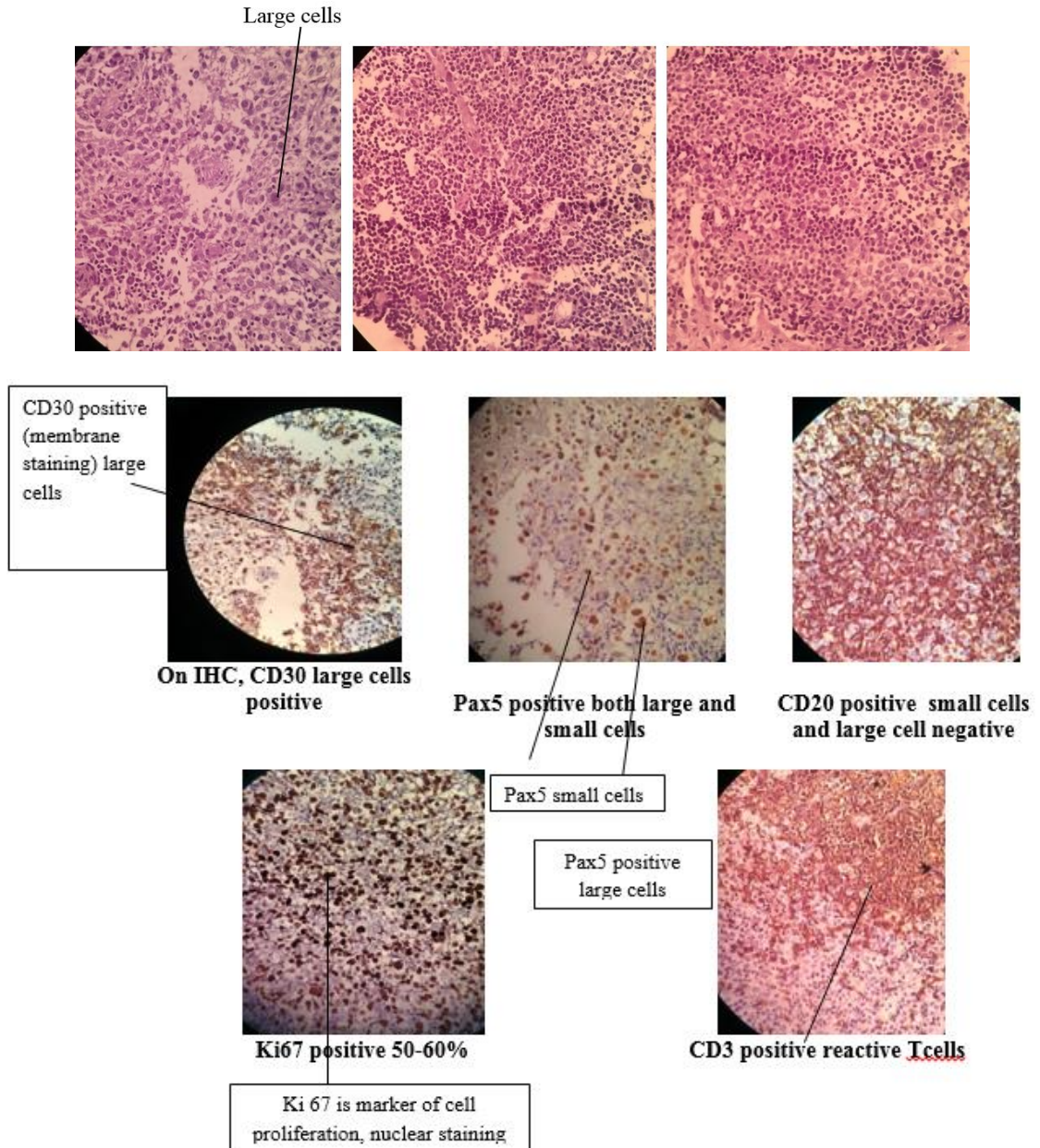


Fig. 1: Histopathological and immunohistochemistry presentations (Final diagnosis was confirmed by IHC as CD30 positive diffuse large B cell lymphoma)

There was 100% concordance between the light microscopy and IHC studies.

All patients were subjected to routine hematological (estimation of hemoglobin, total, and different leucocyte count, platelet count, peripheral

smear for abnormal/ blast cells etc.) and biochemical (liver function tests, urea, creatinine, uric acid) investigations. The radiological examination included chest radiograph, computed tomography, and ultrasonography of abdomen.

Results

Of the 79 cases of lymphadenopathy studied, 35 cases were NHL, 21 cases were HL and rest other types. (Table 1)

Table 1: Distribution of various causes of lymphadenopathy (N=79)

Causes of Lymphadenopathy	Frequency (%)	Mean Age (Range)	Gender (M/F)
NHL	45 (56.96)	49.42 (4-67)	26/19
HL	21 (26.58)	43.5 (5-61)	15/6
Atypical Lymphoid Hyperplasia	06 (7.59)	40.66 (32-51)	4/2
Reactive Lymphoid Hyperplasia	05 (6.33)	54.33 (45-63)	4/1
Meningoma	01 (1.26)	53	1/0
Adnexal Tumor	01(1.26)	38	0/1

NHL: Among 45 cases of NHL, 26 patients were males (57.78%) and 19 were females (42.23%). Male to female ratio was 1.36:1

The age range was 5-68 years with a mean age of 42.86 years. Among NHL cases B-cell lymphomas were the predominant type (35 cases) accounting for 77.78% of all NHL cases. T-cell lymphomas constitute 8 cases (17.78%).

Of the B-cell neoplasms, diffuse large B-cell lymphoma (DLBCL) was the most common subtype (18 cases, 40%), followed by follicular lymphoma (10 cases, 22.22%). Among the follicular lymphomas, Grade 3 was most common type (6 cases), followed by

Grade 2 (3 cases) and Grade 1 (1 cases). Third common B-cell NHL was Burkitt's lymphoma (04 cases, 8.8%) followed by High Grade B Cell lymphoma (02 cases, 4.44%) and Plasmablastic lymphoma (01 case, 2.22%). (Table 2)

T-cell lymphoma comprised of 8 cases (17.78%) and anaplastic large cell lymphoma (ALCL) was the most common subtype (05 cases, 11.11%), followed by peripheral T cell lymphoma (02 cases, 4.44%), and Mycosis fungoides (01 cases, 2.22%).

There were two cases of aggressive NK cell leukemia subtype. (4.44%).

Table 2: Distribution of NHL (N=45)

Subtypes of NHL	Frequency (%)	Mean Age (Range)	Gender (M/F)
B Cell Lymphoma			
Diffuse Large Cell B Cell	18 (40)	47.81 (30-59)	10/08
Follicular Lymphoma	10 (22.22)	44.37 (41-63)	06/04
Burkitt's Lymphoma	04 (8.88)	9.25 (5-13)	02/02
Plasmablastic Lymphoma	01 (2.22)	44	00/01
High Grade B Cell Lymphoma	02 (4.44)	58.5 (55-62)	01/01
T Cell Lymphoma			
Anaplastic Large Cell Lymphoma	05 (11.11)	23.36 (12-26)	03/02
Peripheral T Cell Lymphoma	02 (4.44)	64 (60-68)	02/00
Mycosis fungoides	01 (2.22)	53	00/01
NK Cell Lymphoma			
Aggressive NK cell leukemia	02 (4.44)	41.5 (36-47)	02/00

HL: Out of 21 cases of HL, 15 patients were males and 6 patients were females with a male-female ratio of 2.5:1. The age range for HL was 27-63 years with a mean age range of 31.3 years. All cases of HL were of nodal origin and no extra nodal case was detected in the study. The most frequent site was cervical group of lymph nodes (12 cases, 57.14%) followed by axillary nodes (6 cases, 28.57%), mediastinal nodes (2 cases, 9.52%) and others. (Table 3)

Mixed cellularity variant was the commonest type (11 cases, 52.38%). followed by nodular sclerosis (7 cases, 33.33%) and lymphocyte predominance (2 cases, 9.52%).

Among the 7 cases of nodular sclerosis, five cases were Grade 1 and two cases were Grade 2.

Table 3: Distribution of HL (N=21)

Subtypes of HL	Frequency (%)	Mean Age (Range)	Gender (M/F)
Classical Hodgkin's lymphoma			
Classical mixed cellularity	11 (52.38)	39.56 (28-63)	8/3
Classical nodular sclerosis	7 (33.33)	41.42 (27-56)	5/2
Lymphocyte predominance	2 (9.52)	38.5 (36-41)	1/1
Nodular lymphocyte predominant	1 (4.76)	55	1/0

Discussion

The classification of malignant lymphomas has witnessed significant revisions over the years with the recent one simplifying the diagnosis and management of lesions at the very initial stages of lymphomagenesis. However limited availability of the panel of IHC markers has posed a challenge to the investigations in resource constraint settings. Moreover geographical variations in lymphoid malignancies are also well known. In India, the first population based cancer registry was established in Mumbai by the Indian Cancer Society in 1964.⁵ Under the network of National Cancer Registry Program (NCRP) of Indian Council of Medical Research, other urban registries have been available in Delhi, Chennai, Bhopal and Bangalore. However, such registry data from Eastern India has been scarce. The present study tried to probe the distribution of malignant lymphomas in a dedicated cancer research centre in Eastern India.

Our study investigated a total of 79 cases of lymphadenopathy of which 35 cases were NHL, 21 cases were HL and rest were cases of atypical lymphoid hyperplasia, reactive lymphoid hyperplasia, meningoma and adnexal tumor. The ratio of NHL to HL as per our study was 1.66:1 which is similar to another Indian study reporting 1.58:1 ratio.⁶ Our study showed 26.58% ML cases to be HL, and appears to be in concurrence with studies from surrounding Eastern Mediterranean countries as well as other studies from India.⁷⁻¹⁴ A retrospective study involving 347 cases in Jordan revealed much higher percentage.¹⁵ On the contrary, much lower frequency of HL was seen in Asian countries like Japan (7%),¹⁶ Thailand (8.5%),¹⁷ and China (6.6%).¹⁸

On studying the HL subtypes, mixed cellularity was found the most common subtype (52.38%) followed by the nodular sclerosis subtype (33.33%). Similar trend was found in Pakistan¹⁹ and also in one Indian study.⁶ However, in Jordan, Europe, USA and other western world, nodular sclerosis is the most common subtype.¹⁵ Increased incidence of mixed cellularity subtype in and around Indian subcontinent may be due higher risk of childhood exposure to Epstein Barr virus that is more likely to be associated with a mixed cellularity than nodular sclerosis.²⁰ Mixed cellularity as well as nodular sclerosis was more prevalent in males than females. Studies in Western Ethiopia of Africa reported lymphocyte predominant subtype as the common type of HL.²¹

Our study showed 56.96% of the cases as NHL. Of NHL subtypes, our study revealed DLBCL as the most common prevalent subtype (40%). DLBCL has also been reported to be the most common NHL in most studies worldwide, but it varies considerably from region to region.²² The percentage of DLBCL noted in the current study is much in concurrence with other Indian studies reporting the figures to be 33–37%.^{7,23,24} However the figures are quite higher as in Pakistan 66.1%.¹⁹ UAE at 59%,¹⁰ Northern Iraq 52.2%,¹⁴ Kuwait 47.6%,²⁵ Egypt 49%,²⁴ Jordan 43.8%–53%,^{15,26} and Turkey at 41%.²⁷

Follicular lymphomas were the second most common subtype of NHL (22.22%) in our study, which is comparable in other Indian study.²³ A higher proportion is noted in Western studies (28–32%). Lower incidence of follicular lymphoma (4–8%) was reported from Saudi Arabia, Egypt, UAE, North Jordan and Pakistan.^{10,14,19,24,26} Among the follicular lymphomas, Grade 3 was most common type, followed by Grade 2 and Grade 1 respectively. Low rates of follicular lymphoma in developing countries might be due to the fact that many DLBCL progresses from previously undiagnosed follicular lymphoma and those unique environmental or genetic factors may contribute to such progression.²³ Third common B-cell NHL was Burkitt's lymphoma (8.8%) followed by High Grade B Cell Lymphoma (4.44%) and Plasmablastic lymphoma (2.22%). T-cell lymphoma comprising of 17.78% of NHL cases revealed ALCL as the most common subtype (11.11%), followed by peripheral T cell lymphoma (4.44%), and Mycosis fungoides (2.22%). Our study noted two cases of aggressive NK cell leukemia subtype. However, the small study sample size posed to be the main limitation for the study.

Conclusion

The present study revealed the ratio of NHL to HL being 1.66:1. Of the HL subtypes, mixed cellularity was found the most common subtype followed by the nodular sclerosis. DLBCL was the most common prevalent B cell NHL subtype followed by follicular lymphoma, Burkitt's lymphoma and High Grade B Cell lymphoma. ALCL as the most common T-cell lymphoma subtype followed by peripheral T cell lymphoma and Mycosis fungoides.

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