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Original Research Paper

Pathology

INCIDENCE OF NON-HODGKIN'S LYMPHOMA ALONG WITH ITS CYTOHISTOPATHOLOGICAL PICTURE: A REPORT FROM SRI KRISHNA MEDICAL COLLEGE & HOSPITAL, MUZAFFARPUR, BIHAR

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ABSTRACT The malignant lymphomas constitute a group of neoplasms, of varying degrees of malignancy, derived from the basic cells of lymphoid tissue, the lymphocyte, and histiocytes in any of their developmental stages. Methodology: A secondary data analysis was done by the Department of Pathology, Sri Krishna Medical College & Hospital, Muzaffarpur, Bihar. A total of 42 patients of NHL were diagnosed in the Department of Pathology over a period of one and half years that is from July 2019 to January 2021. Clinical information regarding age, sex, and site of the biopsy was noted and hematoxylin and eosin-stained sections were examined. Results: A total of 52 cases of NHL were diagnosed confirmatively over the given duration of study. Majority of the patients (38.5%) belonged to the age range of 40-60 years. Male female ratio was calculated to be 2.47:1. Conclusion: Most common lymphoma is DLBCL. Incidence of FL is much less common compared with the west. T cell NHL is more common than the West, but is less prevalent than some Asian countries.

KEYWORDS : Non-Hodgkin's Lymphoma, Cytohistopathological Picture

Introduction

The malignant lymphomas constitute a group of neoplasms, of varying degrees of malignancy, derived from the basic cells of lymphoid tissue, the lymphocyte, and histiocytes in any of their developmental stages. Lukes defined malignant lymphoma as "a neoplastic proliferative process of the lymphopoietic portion of the reticuloendothelial system, that involves cells of either the lymphocytic or histiocytic series in varying degrees of differentiation, that occurs in an essentially homogeneous population of a single cell type." The character of histologic involvement is either diffuse (uniform) or nodular and the distribution of involvement may be regional or systemic (generalized); however, the process is basically multicentric in character.[1]

NHL (Non-Hodgkin Lymphomas) are a heterogenous group of lymphoproliferative malignancies that are much less predictable than Hodgkin's lymphomas and have a far greater predilection to disseminate to extranodal locations. Nearly 25% of NHL cases arise in extranodal locations and most of them are seen involving both nodal and extranodal sites.[2]

The most common NHL subtypes by far in developed countries are diffuse large B-cell lymphoma (about 30%) and follicular lymphoma (about 20%). All other NHL subtypes have a frequency of less than 10%.[3] NHL is the sixth most common cause of cancer-related death in the USA after prostate, breast, lung, colorectal, and bladder cancer. Oropharyngeal lymphomas are the second most common malignant disease in the oral region after squamous cell carcinoma.[4]

According to Globocan (2012), the estimated incidence of non-Hodgkin's lymphoma (NHL) is 5/100,000 (385,741 new cases), with a mortality rate of 2.5/100,000 (199,630 deaths) worldwide.[5] The burden of NHL in 2012 for India was estimated to have an incidence rate of 2.2/100,000 (23,801 new cases) and a mortality rate of 1.5/100,000 (16,597 deaths). Within the country, the incidence of NHL is higher in urban areas compared to rural registries.

Immunohistochemistry (IHC) has set the way for possible understanding of the pathogenesis of NHL as well as aiding in identifying the immunophenotype of most NHL cases. [6] Recently, IHC has become an important step in the investigation of diagnostic pathologic studies of NHL. It is used for classifying lymphatic neoplasms into B cell and T-cell phenotypes as well as for differential diagnosis with other malignant proliferations. CD20 is a cell surface marker expressed precisely on a majority of human B-cells. [7] Moreover, it has also been reported to be expressed on more than 90% of B-cell lymphomas; thus, it has become a good molecular goal for monoclonal antibody therapy [8, 9].

Due to the limited data of the histopathological presentation of NHL in in this part of the country, a thorough insight into this aspect of NHL is essential for proper diagnosis and optimum treatment.

METHODOLOGY

A secondary data analysis was done by the Department of Pathology, Sri Krishna Medical College & Hospital, Muzaffarpur, Bihar. A total of 42 patients of NHL were diagnosed in the Department of Pathology over a period of one and half years that is from July 2019 to January 2021. Clinical information regarding age, sex, and site of the biopsy was noted and hematoxylin and eosin-stained sections were examined. Cases diagnosed provisionally as NHL on light microscopy were taken up for immunohistochemistry (IHC).

Some cases, which were reported as lymphoma on light microscopy but turned out reactive after examining the excision biopsy specimen or application of IHC (like Kikuchi disease, Castleman disease, Rosai-Dorfman disease, and reactive lymphadenopathy), were excluded from this study. Cases who were difficult to diagnose with the available set of IHC markers were referred to higher centers and hence excluded from the study. Plasmacytoma and multiple myeloma cases were also not included in this study.

The panel of antibodies used for IHC included CD2, CD3, CD5, CD7, tdt, CD10, CD15, CD19, CD20, CD23, CD30, CD45, CD56, CD117, CD1A, BCL2, BCL6, cyclin D1, K i -67, and ALK-1. Panel of antibodies used in a given case was dependent on the morphological evaluation and varied from 5 to 11.

IHC was performed based on horseradish peroxidase polymer chain two step indirect technique. Antigen retrieval was done using pressure cooker with Tris- EDTA buffer (pH-9.0).

Results

A total of 52 cases of NHL were diagnosed confirmatively over the given duration of study. Majority of the patients (38.5%) belonged to the age range of 40-60 years. Male female ratio was calculated to be 2.47:1.

Table 1 shows Age and sex distribution

Age group (In years)	B cell lymphoma		T cell lymphoma	
	Male	Female	Male	Female
0-20	5	1	2	1
21-40	6	2	3	1
41-60	8	4	6	2
Above 60	5	2	2	2

Nearly one-fourth (27.2%) of NHL were extranodal with the most common site being the gastrointestinal tract. Oropharynx and oral cavity were the next most common sites followed by nasal and nasopharyngeal.

The ratio of incidence of B-cell NHL to T-cell NHL was found in this study to be 1.74 that implies 63.5% of the samples were diagnosed to have B-cell NHL. Diffuse large B cell lymphoma (DLBCL) was the most common lymphoma diagnosed. These lymphomas presented with a high proliferation index (ki67 more than 50%). CD30 was applied whenever the morphology was anaplastic and three cases were CD30 expressing DLBCL. There were four cases of T cell rich large B cell lymphoma (TCRLBCL) type of DLBCL. These cases showed diffuse effacement of architecture of the lymph node with a predominant CD3 positive T cell population and singly scattered large B cells expressing CD20, Pax5, and negative for CD30. Whenever these large B cells had a tendency to form sheets, these cases were excluded from TCRLBCL group and kept in DLBCL.

Table 2 shows distribution of samples according to the variety of lymphoma

Type of lymphoma	Number (%)
B-cell NHL	
Diffuse Large B-cell Lymphoma	24 (44.2%)
Small lymphocytic lymphoma	4 (7.7%)
Mantle cell lymphoma	3 (5.8%)
Follicular lymphoma	1 (1.9%)
Marginal zone B cell lymphoma of MALT type	1 (1.9%)
Precursor B cell lymphoblastic lymphoma	1 (1.9%)
T-cell NHL	
Anaplastic large cell lymphoma	13 (25.0%)
Precursor T cell lymphoblastic lymphoma	3 (5.8%)
Peripheral T cell lymphoma NOS	3 (5.8%)

Four cases (7.7%) presented with small lymphocytic lymphoma (SLL). All the cases were above 50 years of age. The neoplastic B cells expressed CD5 and CD23 and were negative for CD10 and cyclin D1. Two cases with diagnostic difficulty showing weak to absent CD5 expression were sent to the higher center for diagnosis. These cases were LEF1 positive. Mantle cell lymphoma was reported in 5.8% of all NHL cases. They were composed of small uniform cells with cleaved or angulated nuclei without nucleoli. These cases had a low proliferation index and were expressing cyclin D1. SOX11 was used in cyclin D1 negative cases. One case of follicular lymphoma (FL) was reported. It expressed CD10 and BCL2 and had a low proliferation index. Grading of the tumor based on the number of centroblasts was done. Marginal zone B cell lymphoma of mucosa-associated lymphoid tissue (MALT) type was also seen in 1 case, that was found in the stomach. It was low-grade B cell lymphomas with lack of CD5 and CD10 expression and strong immunoglobulin M (IgM) expression.

Among the T cell NHL, the most common group comprising 25.0% cases was anaplastic large-cell lymphoma (ALCL). The presenting age group ranged from 20 years to 60 years. All the cases expressed CD30 and two thirds expressed Alk-1. The second group of NHL was peripheral T cell lymphoma not otherwise specified (PTCL NOS) accounting for 5.8% cases. This was a heterogenous group of T cell lymphoma expressing the T antigens CD3, CD5, CD7, CD2 in variable proportions and always negative for follicular helper T cell markers, CD4, CD10, Bcl6, and PD1. There was one case expressing CD3, CD5, CD4, and negative for CD7, CD10, CD2 with aberrant expression of CD20 but the tumor cells were Pax5 negative. Maximum cases belonged to 50 to 70 years of age group.Of the 3 cases of T cell lymphoblastic lymphoma, two involved the mediastinum and one was in the bone. All the cases were seen in patients less than 30 years of age. The tumor cells had a high proliferation index (> 70%) and expressed nuclear antigen tdt along with T specific antigens.

DISCUSSION

The classification of lymphoma is evolving over the years with the expansion of our knowledge and the development of better techniques for its detection and characterization. The World Health Organization (WHO) classification of tumors has now become a household name among pathologists, continuously updating us about the newer entities. In the present study, we have classified lymphoma based on the recent 2017 edition of WHO. [10] The incidence of lymphoma is higher in the developed nations. In India also, lymphoma is more common in the urban areas as compared the rural. [11, 12] Urban population has a higher socioeconomic status and their lifestyles also lean toward the west whereas the rural population has a more traditional lifestyle. This variation in socioeconomic and environmental factors in the rural and urban areas may be responsible for the difference in the occurrence of lymphoma. [13] The global burden of lymphoma is increasing and the disease is more common in males. Male to female ratio of incidence of HL and NHL, worldwide, is 1.6:1 and 1.3:1, respectively. [14] Two studies from south India have reported a slightly higher incidence in males compared with the global data. According to these studies, male:female ratio in HL is 2.5:1, while that in NHL is 2.2 to 2.8:1. [15, 16] In our study, both HL and NHL are thrice as common in males as in females. One study from eastern India reports results similar to our results. [17] Maximum cases of HL in our study were less than 25 years of age (64.7%) and those of NHL belonged to the age group of 41 to 60 years. This is in concordance with the other Indian studies. [15, 16, 17]Extranodal presentation is common in some lymphomas like DLBCL, Burkitt lymphoma, MALT lymphoma, and PTCL. Studies from Western countries have shown that extranodal NHL are seen in 24 to 48% of all NHL. [18] Our neighboring countries like China and Japan have even higher incidence of extranodal lymphoma ranging from 44 to 60% as per literature. [19, 20] This may be because of the higher prevalence of extranodal NK/T cell lymphoma in these countries compared with India. Two studies from south India, Padhi et al and Mishra et al have reported the incidence of extranodal lymphoma to be 22 and 22.6% of all NHL, respectively. [21, 22]Padhi et al reported the central nervous system as the most common site, followed by the gastrointestinal tract, whereas Mishra et al reported head and neck and gastrointestinal tract as the most common site. In our study, 27.2% patients presented with extranodal disease and the most common sites were the gastrointestinal tract and head and neck. The results of the study from eastern India by Mondal et al are similar to our study with 27.7% extranodal presentation. [17]

DLBCL is the most common lymphoma in India as well as other countries with 40 to 50% of cases. We reported 44.2% DLBCL in our study. One of the largest studies from India by Arora et al reported FL as the second largest group among the

NHL with 10.9% cases, followed by SLL at 4.1%. Our study differs slightly, with the second most common NHL being SLL (7.7%), followed by mantle cell lymphoma (5.8%). FL forms only 1.9% of all NHL in our study. This maybe because the two studies from India are done in south India that is socioeconomically more developed compared with Bihar. FL is known to be more common in countries with higher socioeconomic status. In the West, SLL is the second most common lymphoma (21.9%) after DLBCL, whereas in China only 4.6% cases are SLL. Another 1.9% cases were lymphoblastic lymphoma in the present study. [15, 18, 19, 23]

The incidence of T cell NHL appears to increase worldwide as we move from West to East. About 26.1% T cell NHL was reported in China, while in the USA it was found in only 7% cases. The frequency of T cell NHL reported in India is ~20%. [15, 23] In the present study, also 25.0% NHL were of T cell type. Naresh et al have reported T lymphoblastic lymphoma as the commonest T cell NHL. They might have included the cases presenting with leukemia, without lymphadenopathy in their study giving a higher incidence. In our study, we have only included the cases with lymphoma, similar to Arora et al. But we got higher incidence of TLBL (5.8%) compared with them (2.2%). Among another T cell NHL, PTCL NOS and ALCL were the most common in India. [15, 23] A similar trend was seen in our study as well. AITL is the next common T cell NHL in India with the reported incidence of 1 to 2%. In the present study, we couldn't report ant case of AITL. While ENKTCL is rare in the west, it is very common in the eastern part of the world. [19, 24] In China, it is the commonest T cell NHL. In India, the incidence of ENKTCL has been reported to be 0.7 to 0.9%. However, in our study there was no case. We also reported one rare case of FTCL. FTCL was kept in the PTCL NOS group in WHO 2008, 18 but is a separate entity in the recent 2017 edition 4 along with other tumors arising from follicular helper T cells.

CONCLUSION

This study documents the frequency of different types of lymphoma in a tertiary care center in Bihar. Most common lymphoma is DLBCL. Incidence of FL is much less common compared with the west. T cell NHL is more common than the West, but is less prevalent than some Asian countries.

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