

Clinical and Pathological Characteristics of Nodal Lymphomas- A Tertiary Care Centre Study in North INDIA

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ABSTRACT

Aim: Neoplasms originating in lymphoid tissue comprise a diverse but closely related group of neoplasms with varied clinical presentations, histomorphology, immunophenotype and genetics. . We aimed to study the clinicopathological patterns of nodal lymphomas in a tertiary care centre of J&K.

Materials and Methods: This was a two year retrospective, single centre observational study conducted at the Department of Pathology, Sher-e-Kashmir Institute of Medical Sciences. All patients with lymphomas in their lymph node biopsies were included.

Results: A total of 137 patients were enrolled in the study with male predominance. 97 were Non-Hodgkins Lymphoma and 40 Hodgkins Lymphoma. The mean age of patients was 43.5 yrs±18.9 yrs. In NHL category 5 cases (5.1%) belonged to the pediatric age group while 92(94.8%) were adults. In Hodgkins lymphoma there were 9 (22.5%) pediatric cases and 31 adults (77.5%). The most common presenting complaint of these patients was swelling in the cervical, axillary or inguinal region. The most common subtype of Non-Hodgkins Lymphoma was Diffuse Large B Cell Lymphoma (DLBCL) and the most common subtype of Hodgkins Lymphoma was Mixed Cellularity (MC).

Conclusion: We conclude that most of the nodal lymphomas in our region are Non-Hodgkins lymphoma with a male predominance. Cervical lymph nodes are more commonly affected and the most common subtype is DLBCL. Peripheral T-Cell Lymphoma NOS is the most common nodal T cell lymphoma. HL is the predominant nodal lymphoma in children and mixed cellularity is the commonest subtype. A unimodal age peak is found in HL in our population as against the bimodal peak in Western countries.

Significance: The epidemiological differences in our population can provide an insight into the biology of nodal lymphomas and pave the way for future research. There should be awareness in our population regarding screening for palpable nodal swellings and early reporting if present.

Keywords: lymphomas, Lymph nodes, DLBCL

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INTRODUCTION

Neoplasms originating in lymphoid tissue comprise a diverse but closely related group of neoplasms with varied clinical presentations, histomorphology, immunophenotype and genetics². However, they can broadly be divided into Hodgkin Lymphoma (HL) and Non-Hodgkin Lymphoma (NHL)³. Most (85-90%) of NHLs are of B-cell origin, with most of the remaining cases being T-cell neoplasms and only rarely are tumours of NK cell origin encountered. Non-Hodgkins lymphomas arise in lymph nodes and other lymphoid tissues and are known as nodal lymphomas. Those originating in lymphatic cells of other organs are known as extranodal lymphomas⁴. Both nodal and extranodal lymphomas have different etiologies,

presentation, behaviour and survival and should therefore be considered distinct entities⁴. Also, nodal lymphomas are not a single disease but a diverse group of neoplasms, each with a different geographical distribution, developmental path, age profile and prognosis. We aimed to study the clinicopathological patterns of nodal lymphomas in a tertiary care centre catering to people from all regions of Kashmir.

MATERIALS AND METHODS

This was a two-year retrospective, single-centre observational study conducted at the Department of

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Patient Selection and biopsy processing

The database of the department was searched to identify all patients with lymphomas in their lymph node biopsies. The common patterns of lymphomas were included in the analysis. Repeat biopsies, biopsies with inadequate clinical details and extranodal lymphomas were excluded from the study.

Paraffin-embedded blocks were used to obtain the tissue sections. Standard processing techniques were followed for all the biopsies. All tissues were stained with hematoxylin and eosin, cytochemical and relevant immunohistochemical stains.

Classification

All lymphomas were classified either as Hodgkins Lymphoma or Non-Hodgkins Lymphoma. Each broad category was further classified according to the WHO classification of lymphoid neoplasms⁵.

Data Source And Variables

Clinical data, demographic details, histological details as well as treatment received by these patients were obtained from the medical record files.

Statistical Analysis

The statistical analysis used SPSS Version 23.0 (IBM Corp., Armonk, NY, USA). Categorical variables expressed as numbers or percentages were compared using Chi-Square and Fisher's exact test (as applicable). Continuous variables reported as mean or median (depending on the normality of data) were compared using Wilcoxon rank-sum methods.

RESULTS

A total of 137 patients were enrolled in the study. The mean age of patients was 43.5 yrs $\pm$ 18.9 yrs. The mean age of Non-Hodgkins Lymphoma (NHL) patients was 48 $\pm$ 17.6 years, while the mean age of Hodgkin's lymphoma (HL) patients was 30 $\pm$ 15.5 years. In the NHL category, 5 cases (5.1%) belonged to the pediatric age group, while 92(94.8%) were adults. Hodgkin's lymphoma had 9 (22.5%) pediatric cases and 31 adults (77.5%). Out of the 137 patients, there were 89(64.9%) males and 48(35.03%) females. There were 63 males (64.9%) and 34 females (35.05%) in NHL. There were 26 males (65%) in HL and 14 females (35%).

These patients' most common presenting complaint was swelling in the cervical, axillary or inguinal region. One hundred and three patients (75.1%) had regional and 34 (24.8%) had generalized lymphadenopathy at presentation. Patients with regional lymphadenopathy showed involvement in either one region or two regions. In 75 (54.7%), there was single regional involvement, and two areas were involved in 28 (20.4%) patients. In patients with single regional lymphadenopathy most common site was cervical lymphadenopathy accounting for 48 cases, followed by axillary (8 cases), mediastinal (6 cases), abdominal (8 cases), inguinal (3 cases) and retroperitoneal (2 cases). B-Symptoms were present in a total of 58 patients (42.3%). Breathlessness was present in patients with mediastinal lymphadenopathy (10 points, 7.2%). Cough was present in 7 patients (5.1%). Pleural Effusion was present in 9 (6.5%) patients. One patient (0.7%) presented with SVC Obstruction syndrome. Splenomegaly was present in 5 patients (3.6%), and Hepatosplenomegaly was present in 6 (4.3%) patients. Ascitis was present in 4 (2.9%) patients.

Non-Hodgkins Lymphoma constituted 97(70.8%) cases, while Hodgkins Lymphoma accounted for 40 (29.2%) cases. The subclassification of NHL and HL in our study is shown in table 1 and table 2, respectively. The demographic and clinical profile of NHL patients is shown in Table 3. Finally, the IHC profile of the most common NHL patients is shown in Table 4.

DISCUSSION

Geographic and ethnic differences have been noted in the incidence and pattern of lymphomas. In this study, we aimed to study the distribution of lymphomas involving lymph nodes in a primary tertiary care centre of J&K.

Lymphomas constituted 3.1 % of the total malignancies in our patients. The worldwide incidence of malignant lymphomas is around 3.37%, with Non-Hodgkins lymphoma consistently higher than Hodgkins Lymphoma². Non-Hodgkins lymphoma cases comprised more than twice that of Hodgkin's lymphoma cases in our study. The average age of presentation of our patients with NHL was in the fifth decade, with a mean age of 48.86 $\pm$ 18.9 yrs. This is somewhat between the average age group noted in other parts of India and Western countries where the mean age of presentation was in the fourth decade⁶ and sixth decade,

Table 1: Table Showing Pattern of Non Hodgkins Lymphoma in Our Patients (n=97)

Type of Lymphoma	Frequency	Percent
DLBCL ¹	51	52.57
Follicular Lymphoma	12	12.37
CLL/SLL ²	8	8.24
Peripheral T Cell Lymphoma	8	8.24
Mantle Cell Lymphoma	6	6.18
Anaplastic Large Cell Lymphoma Alk 1 ³	3	3.02
T Cell Lymphoblastic Lymphoma	3	3.09
Burkitt Lymphoma	2	2.06
B Cell Lymphoblastic Lymphoma	2	2.06
Alk + Large B cell Lymphoma	1	1.03
Anaplastic Large Cell Lymphoma Alk 1-	1	1.03
Total	97	100.0

1. DLBCL: Diffuse Large B Cell Lymphoma;
2. CLL/SLL: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma;
3. ALK: Anplastic Lymphoma Kinase.

Table 2: Showing Pattern Of Hodgkins Lymphoma In Our Patients(n=40)

Type of Hodgkins Lymphoma	Frequency	Percentage
HODGKINS LYMPHOMA -MC	21	52.5%
HODGKINS LYMPHOMA- NS	13	32.5%
HODGKINS LYMPHOMA - LR	3	7.5%
NODULAR LP HODGKINS LYMPHOMA	3	7.5%

MC: Mixed Cellularity; NS: Nodular Sclerosis; LR: Lymphocyte Rich; LP: Lymphocyte Predominant

Table 3: Characteristics Of Non-Hodgkins Lymphoma Patients In Our Study(N=97)

	Percentage	AGE (mean)	M:F	B-Symptoms	BM Involvement (number)	HSM ⁹	SM ¹⁰
DLBCL ¹	52.5	50	2:1	39.2	5/52	NIL	NIL
Alk+ B Cell ²	1.03	60	1 F	1	NIL	NIL	NIL
FL ³	12.3	41	1.4:1	41.6	4/12	NIL	1
CLL ⁴	8.2	52.2	3:1	31.5	1/8	NIL	NIL
PTC-NOS ⁵	8.2	46	1.6:1	37.5	1/8	1	2
MCL ⁶	6.1	60.6	2:1	50	2/6	2	1
Alk+ T cell	3.09	43	1.5:1	1	NIL	NIL	NIL
BL ⁷	2	38.5	1:1	1	NIL	NIL	NIL
TALL ⁸	3	13	2:1	1	NIL	NIL	NIL
B-ALL	2	17.5	1:1	1	NIL	1	NIL
Alk-T Cell	1.03	48	1 M	1	1	NIL	NIL

1.DLBCL: Diffuse Large B Cell Lymphoma; 2. Alk: Anplastic Lymphoma Kinase 3.Follicular Lymphoma 4. CLL/SLL: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma; 5. PTC-NOS: Peripheral T Cell Lymphoma – Not Otherwise Specified. 6 MCL: Mantle Cell Lymphoma 7 BL: Burkitt Lymphoma 8. ALL: Acute Lymphoblastic Lymphoma 9. HSM: Hepatosplenomegaly 10.SM: Splenomegaly.

Table 4 : showing the IHC profile of most common NHL patients.

NHL TYNHLPE	CD20	CD5	CD23	CD10	Bcl2	Bcl6	CyclinD1	CD3	CD 4
DLBCL	+	-	-	+(45%)	-	+(45%)	+	-	-
FL	+	-	-	+	+(95%)	+(5%)	-	-	-
SLL	+	+	+	-	-	-	-	-	-
MCL	+	+(66%)	-	-	-	-	+	-	-
PTCL	-	-	-	-	-	-	-	+	+

DLBCL: Diffuse Large B cell lymphoma ; FL: Follicular Lymphoma ; SLL: Small cell lymphoma ; MCL: Mantle Cell Lymphoma ; PTCL: Peripheral T Cell Lymphoma.

respectively^{7,8}. There was also a difference in the age of presentation for Hodgkin's lymphoma cases between our studies and those from the West. In our study, the mean age of presentation was 30 years, with a unimodal peak of presentation. We did not find bimodal peaks in our research.

The most common lymphoma in children was Hodgkins Lymphoma in our study, accounting for 6.5% of the total lymphomas. Hodgkins Lymphoma was also the most typical nodal lymphoma in children in other studies⁹.

The male-female ratio in our study was 1.8:1. A male predominance was seen in lymphomas in other studies as well^{10,11}. This male predominance was consistently seen in all lymphomas, including follicular lymphoma. This male predominance of follicular lymphomas is also seen in other studies from India¹² but contrasts with the studies from West¹³, where follicular lymphomas have a female preponderance. The cervical region was the most commonly involved site. One of the reasons for cervical presentation may be that it is the most accessible site for palpation and is noticed quickly by the patient compared to other sites.

The most common type of lymphoma in our population was DLBCL occurring in almost half of the NHL patients. In DLBCL centroblasts subtype was the most common subtype. Other studies from India and Asian countries have also shown a considerable percentage of people having DLBCL ranging from 40.3%¹¹ to 59%. In USA and Europe, it constituted 25-30% of the NHL patients⁵. Therefore, a higher percentage in our population than in the West may be due to the genetic predisposition of our population to this type of lymphoma. Also, many of these patients seek medical attention late in developing countries, and these patients may have DLBCL from the transformation of initial low-grade Lymphomas. A similar trend was seen in follicular lymphomas, where the most common type was grade 2 in our study as opposed to other studies where grade 1 was the most common¹⁴.

The most common T cell lymphoma involving lymph nodes was peripheral T cell lymphoma-NOS. The most common type of Hogkins lymphoma in our patients was mixed cellularity. Although studies from India and other Asian countries show mixed cellularity to be the commonest subtype, Western countries have a predominance of nodular sclerosis subtype. Increased incidence of mixed cellularity

subtype in India and other Asian countries may be due to a higher risk of childhood exposure to Epstein Barr virus, which is more likely to be associated with mixed cellularity than nodular sclerosis¹⁵.

The epidemiology of lymphomas is complicated, the reasons being manifold: many subtypes, each having unique biology, complex association with infectious causes, genetic predisposition, etc². Our knowledge of nodal lymphomas is rapidly changing as more and more data becomes available on genetic alterations and their prognostic and treatment implications. More extensive studies are required to understand and predict these cases thoroughly.

CONCLUSION

We conclude that most of the nodal lymphomas in our region are Non-Hodgkins lymphoma with a male predominance. Cervical lymph nodes are more commonly affected, and the most common subtype is DLBCL. Peripheral T-Cell Lymphoma NOS is the most common nodal T-cell lymphoma. Hodgkin's lymphoma is the predominant nodal lymphoma in children, and mixed cellularity is the commonest subtype. There should be awareness in our population regarding screening for palpable nodal swellings and early reporting if present. A unimodal age peak is found in Hodgkins Lymphoma in our people as against the bimodal peak in Western countries. These epidemiological differences can provide insight into the biology of these cases and pave the way for future research.

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