Original Article

Frequency and Clinico Pathological Features of Diffuse Large B Cell Lymphoma - A Tertiary Care Center Experience

Ambareen Hamid[1], Sobia Ashraf[1], Muhammad Azhar Farooq[2] and Adil Iqbal[3]

ABSTRACT

Objective: To determine the frequency and study the clinicopaological features of DLBCL.
Study Design: Descriptive study
Place and Duration of Study: This study was conducted at the Department of Pathology, King Edward Medical University , Lahore from 2013 to 2017.
Materials and Methods: One hundred and seventy two consecutive cases of Non Hodgkins lymphoma referred for bone marrow biopsy were enrolled in the study. All the cases were diagnosed on histological biopsies. The patients receiving chemotherapy or radiotherapy were excluded from the study.
Results: Out of 172 patients 05 (2.9%) had T cell NHL and 167 (97.1%) had B cell lymphoma. Out of these B cell NHL 46 (26.7%) cases were of diffuse large B cell lymphoma. Cytopenias were observed in 32.6 % of patients. In 13 % patients bone marrow was infiltrated. The pattern of infiltration was diffuse.
Conclusion: DLBCL is a frequently presenting aggressive NHL having hcetrogenous clinical behavior.

Key Words: Clinico Pathological Features, Diffuse Large B Cell, Lymphoma

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INTRODUCTION

Lymphomas are group of malignancies arising from the lymphoid system. The term lymphoma is used when the primary site of origin is out of bone marrow. Lymphomas are broadly classified into Hodgkin Lymphoma (HL) and Non Hodgkin Lymphoma (NHL). Collectively, lymphoid neoplasms are the fourth most common cancer and the sixth leading cause of cancer death in the United States. The lymphoma comprise 3.37% of all malignant neoplasms and the incidence of malignant lymphoma around the world has been increasing at a rate of 3-4% over the last 4 decades.[1,2]

Diffuse large B cell lymphoma (DLBCL) is the most common histologic subtype of nonHodgkin lymphoma (NHL) accounting for approximately 25 percent of NHL cases.[2]. The diagnostic category of "DLBCL" is quite heterogeneous in terms of morphology, genetics, and biologic behavior and a number of subcategories are included in the revised 2017 World Health Organization (WHO) classification.[3]

DLBCL is a malignancy of large B lymphocytes. Common cell of origin is germinal centre centroblast in 80% of cases, immunoblast in 10% of cases. Other morphologic variants include the T-Cell–Rich/ Histiocyte-Rich variant which has a prominent background of reactive T cells and histiocytes, anaplastic type, where the cells are morphologically similar to those of T/null ALCL while Plasmablastic DLBCL, a very uncommon subtype, often occurs in HIV-positive patients.

A variety of chromosomal alterations have been detected in DLBCL. The most common abnormality involves alterations of the BCL-6 gene at the 3q27 locus, which is critical for germinal center formation. A substantial number of cases of DLBCL have complex karyotypes.[4]

In the majority of cases, patients present with either a nodal or extranodal mass lesion. At diagnosis, DLBCL involves the bone marrow in approximately 15-25% of cases. However, the bone marrow may reveal discordant morphology from the lymph node, usually in indolent lymphoma[5]. DLBCL is an aggressive tumor, the second most common lymphoma to secondarily involve the marrow, comprising 16% of bone marrow biopsies infiltrated by NHL at one institution[6].

MATERIALS AND METHODS

This descriptive study was conducted in Department of Pathology, King Edward Medical University, Lahore from 2013 to 2017. One hundred and seventy two consecutive cases of Non Hodgkins lymphoma referred for bone marrow biopsy were enrolled in the study. All the cases were diagnosed on histological biopsies. The patients receiving chemotherapy or radiotherapy were excluded from the study.

1. Department of Pathology / Paediatric Medicine[2] / Medicine[3], King Edward Medical University, Lahore.

Correspondence: Dr. Ambareen Hamid, Associate Professor of Pathology, King Edward Medical University, Lahore.
Contact No: 0306-4466699
Email: dr_ambareen@hotmail.com

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Data Collection and Analysis: After informed consent the socio demographic information was entered on the specially designed proforma. The clinical data regarding site of involvement, organomegaly was noted. Bone marrow aspiration and trephine biopsy was performed according to standard protocol. Bone marrow aspirate smears were stained by Giemsa Wright stain. Trephine was decalcified and the paraffin embedded sections were prepared. Histological sections were stained with haematoxylin and eosin. Bone marrow aspirate and trephine biopsy were examine for infiltration of marrow, its pattern and any other significant finding. The data was analysed and expressed as frequency and perectages using IBM SPSS version 20.

RESULTS

A total of consecutive one hundred and seventy two biopsy proven non hodgkins lymphoma (NHL) patients referred for bone marrow biopsy were included in the study. Out of these 172 patients 05 (2.9%) had T cell NHL and 167(97.1%) had B cell lymphoma. Out of these B cell NHL 46 (26.7%) cases were of diffuse large B cell lymphoma. In these 46 patients of DLBCL 34 were male and 12 were female (male to female ratio 2.8 1. (figure 1).

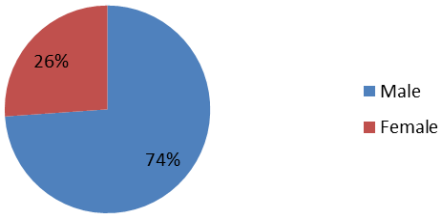

Figure No.1: Gender distribution

Figure 1: Gender distribution in patients of DLBCL Age ranged from 18-80 years and peak age group was seventh decade followed by 6th decade..(figure 2)

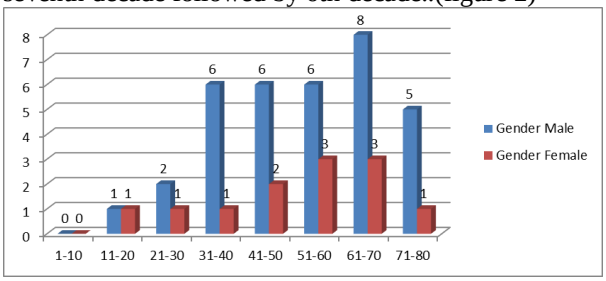

Figure No.2 : Age and gender distribution in patients of DLBCL

The primary site of involvement was nodal in 41 patients (89%) and extra nodal in 05 (11%) patients. Cervical, axillary, 4attern4i4lar and supraclavicular were enlarged in majority of patients (35 patients – 76%), inguinal lymph nodes in 02 patients (04 %) and para aortic in 04 patients (08 %).

We also examined the patients for organomegaly. Spleen was enlarged in 04 patients. No other organ involvement was found in rest of patients. Cytopenias were observed in 15 (32.6 %) patients, 14 had anemia only while 1 patient had both anemia and thrombo-cytopenia. Bone marrow was performed to see infiltration of marrow. (Table 1)

Table No.1: Morphological findings of Bone marrow in DLBCL

Bone marrow infiltration						Total
Present (n= 06)				Absent n= (40)		
Pattern of infiltration				Reactive lymph follicles		
Diffuse	Focal	Interstitial	Paratra-becular	Present	Absent	
06 (13%)	0	0	0	03 (6.5%)	37 (80.5%)	46

DISCUSSION

NHL is a heterogeneous neoplasm considering clinical presentation, its response to therapy and outcome of disease. The DLBCL, a morphological subtype of non 5attern's lymphoma exhibits significant heterogeneity pertaining to the underlying genetics, morphological pattern, immunophenotypes and clinical expression. Therefore, there is variation in both response to treatment as well as the prognosis of disease.[7] It is an aggressive tumour. The 5 year survival with current standard chemotherapy is estimated to be 60 – 70 %.[8]

This study was conducted to determine the frequency of DLBCL and study its clinio pathological features. A total of 172 patients of biopsy proven non hodkins lymphoma were enrolled in the study. Majority of our patients presented in 7th decade. Nagi et al in a study on non hodgkins lymphoma found that most of the patients presented in 5th – 7th decades with the mean age being 43.2 years.[9] Uzma et al found that the mean age of presentation of patients of NHL was 46.7 years[10]. In a study conducted by Sultan et al it was seen that the mean age was 48.5 ± 16.0 years with the median age of 50 years.[11] Bajwa et al found Mean age at presentation was 54.66 ±16.73 years in cases of lymphoma.[12] In our study the age of patients of DLBCL, a subset of NHL ranged from 14 to 80 years with a mean age of 53.6 years. The wide range of age at first presentation is attributed to the diverse genetics and morphological subtypes[7,8].

The male to female ratio was 2 8:1. In a study conducted by Bajwa et al found a male to female ratio of 5:1[12]. Naz E et al found a male to female ratio of 2.6:1 in sixty two patients of non hodgkins lymphoma[13]

In the modern era of medicine, underdeveloped countries like Pakistan still face economic constraints. The less presentation of females can partly be explained by less health care facilities available to females.

Sultan et al conducted a study on 184 patients of non hodgkins lymphoma and found out that B cell

lymphoms were more common than T cell lymphoma.[11] The study conducted by Naz E e tal revealed that B cell NHL were 85.5 % as compared to 14.5 % of T cell lymphoma[13]. The findings of our study are in concordance with theses local studies, showing a percentage of 97 of B cell NHL .

We found in that 26.7 % of patients. had DLBCL 28 patients of NHL were broadly classified as B cell NHL. Further catagarization was not done due to financial constraints. The exact percentage of DLBCL may be higher. The studies conducted in this region mostly report a higher frequency of DLBCL. In a study by Nawaz et al, the reported percentage is 55 %.[14] Whang C et al. found that the most common subtype of NHL was diffuse large B-cell lymphoma (55.0%)[15] In a study Sultan et al found that Diffuse large B-cell lymphoma constituted major subtype, in 67.9% of cases.[16] Aggressive behavior of this neoplasm compels the patient to seek medical attention leading to its frequent presentation.

In our study anaemia was most frequent haemtological manifestation, presenting in 14 patients while anaemia and thrombocytopenia was present in only one patient. Cytokine release, anorexia leading to malnourishment and marrow infiltration and failure are all contributory factors towards development of cytopenias.

Majority of patients had nodal involvement at presentation. In our study most common site of involvement was lymph nodes above the diaphragm. In extra nodal site gastrointestinal tract was most commonly involved site. International studies show that gastrointestinal tract is the most common primary site of extranodal diffuse large B-cell lymphoma , and approximately one-third of extranodal DLBCL occurs in the GI tract.[17] The findings are consistent with recent studies conducted internationally in which they found out that most common extra nodal involvement is gastro intestinal tract in 32% and 34% patients respectively.[17,18,19]

Bone marrow infiltration reflects advance stage of disease. It is associated with poor prognosis in newly diagnosed cases of lymphoma. Bone marrow biopsy was done to stage the disease. In our study 06 (13%) patients had bone marrow infiltration at presentation. The pattern of infiltration was diffuse in all cases. These findings are similar to the results reported in international studies by Hantaweepant C, et al, and Vishnu P, et al, who found 12.2%, 13% of bone marrows involved by DLBCL at presentation respectively.[20,21]

CONCLUSION

Diffuse large B cell lymphoma is a frequently presenting non hodgkins lymphoma. Being an aggressive, tumor compels the patient to seek medical help at an earlier stage. .

Author's Contribution:

Concept & Design of Study:	Ambareen Hamid
Drafting:	Sobia Ashraf
Data Analysis:	Muhammad Azhar Farooq, Adil Iqbal
Revisiting Critically:	Ambareen Hamid, Sobia Ashraf
Final Approval of version:	Ambareen Hamid

Conflict of Interest: The study has no conflict of interest to declare by any author.

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