Pattern of Diffuse Large B cell Lymphoma (DLBCL) in Aden, Yemen

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Abstract

Background:

DLBCL is part of aggressive lymphomas with limited survival in the absence of effective treatment.

Aim:

The aim of this study was to determine the frequency and the pattern of presentation of DLBCL in patients diagnosed in Aden.

Methods and Material:

It was conducted prospectively in Aden, at Al-Amal Oncology Unit of Al-Gamhouria Modern General Hospital. All patients confirmed to have NHL by histopathology were selected from Jan. 1st to Dec. 31st, 2009. They were clinically examined and investigated for clinical staging and classification.

Data analysis:

Data analysis was conducted by the SPSS 18 program, using the Chi square, Fisher Exact, hypothesis test (Z-test) and student t-tests.

Results:

The frequency of DLBCL was 35%. In DLBCL, the median age was 51.5 years, with male to female ratio of 3.67:1. Clinically, most patients were nodal and B symptoms were present in 64.3% of them; weight loss and sweating were reported more than in the other subtypes of NHL. Investigations showed that 64.3% were anemic, 35.7% with high ESR and high β2 microglobulin, 21.4% with low albumin and high uric acid. Half of them presented in stage III and IV disease and according to the IPI scoring, 64.3% presented with intermediate to high risk disease. Comparison with other NHL subtypes was performed and showed that DLBCL is associated with aggressive pattern of presentation.

Conclusion:

This study concluded that DLBCL is an aggressive NHL at presentation and needs immediate diagnosis and intervention to improve the outcome.

Keywords:

DLBCL, NHL, Lymphoma, Pattern, Aden, Aggressive

Introduction

Diffuse large B-cell lymphoma (DLBCL) is the frequent non-Hodgkin's lymphoma (NHL) subtype, accounting for up to 25 - 40% of newly diagnosed cases.[1,2] It is a fast-growing lymphoma, that can arise in lymph nodes or outside of the lymphatic system, in the gastrointestinal tract (GIT), testes, thyroid, skin, breast, bone or brain.[3,4]

DLBCL is a part of aggressive lymphomas, survival of which is limited in the absence of effective treatment. Currently, it may be cured in a significant percentage of patients depending on the initial characteristics of the disease. The treatment of DLBCL patients has been revolutionized in recent years, with the addition of rituximab to combination chemotherapy,

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resulting in an increased proportion of cured patients.[5,6]

In Aden, lymphomas are among the most common cancers encountered in the oncology unit. The Cancer Registry of Aden in 1998,[7] reported lymphomas as the third most common cancer (12.1%) after gastrointestinal (14.3%) and breast cancers (12.4%), and the last report in 2006 by Basaleem et al,[8] for the period 2002-2006, showed that NHL alone (7.8%) was the third common cancer after breast cancer (16.6%) and leukemia (12.6%).

This study was conducted in Aden to determine the frequency and the characteristics of patients with DLBCL among other subtypes of NHL in Aden.

Patients and Methods

This is a prospective study conducted in Al-Amal Oncology Unit during the period Jan. 1st - Dec. 31st, 2009, where 40 patients were proven by histopathology to have NHL and among which 14 patients were found to be DLBCL by immuno-histochemistry.

After detailed history taking, all patients were examined clinically and investigated thoroughly and staged according to the Cancer Staging Manual (Ann Arbor staging of NHL).[9]

All patient data were processed by the SPSS 18 program and classified into two groups: the first group as DLBCL and the second group included all the other subtypes of NHL. The data of patients with DLBCL were compared to that of other subtypes of NHL using the Chi square, Fisher exact and hypothesis tests.

For ethical consideration, patient record numbers instead of patient names were used to protect and safeguard the identities of the patients involved in this study.

Results

During the year 2009, the frequency of DLBCL in Al-Amal Oncology Unit in Aden was 35% (14 out of 40 NHL patients) (Fig. 1). The percentage of males affected with DLBCL was 78.6%, while that of other subtypes was 46.2%. The male to female ratio for patients with

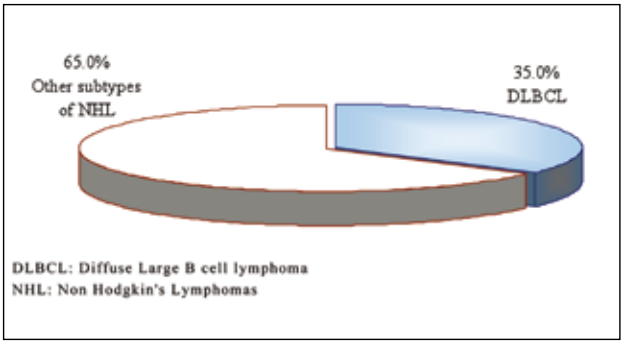

Fig. 1: The frequency of DLBCL in relation to other subtypes of NHL, Al-Amal Oncology Unit, Aden, Yemen, 2009

DLBCL was 3.67: 1; it is significantly different from the ratio of other subtypes of NHL (Table 1). In DLBCL, patient age ranged from 18 to 70 years with a median age of 51.5 years. This was not found significantly differing from the median age of other subtypes of NHL (50 years) (Table 1).

Patients with DLBCL were residents of Aden (35.7%), Lahj (28.6%), Abyan and Shabwa governorates (14.3% for each). All the other subtypes of NHL were also distributed in similar manner in the same governorates (Table 2).

Clinically, most of the patients were primary nodal whereas 2 (14.3%) patients presented with primary extranodal DLBCL in the gastric and intestinal sites. B symptoms were reported by 64.3%, weight loss by 50% and sweating by 35.7%. They were reported more than in other subtypes of NHL (Table 3). Patients with DLBCL presented with higher percentage of splenomegaly and hepatomegaly when compared with the other subtypes of NHL. But statistically, none of the reported presentations showed significant association to DLBCL or the other subtypes of NHL ($p > 0.05$) (Table 3).

Investigations at diagnosis showed that 64.3% of patients with DLBCL were anemic according to WHO classification, 35.7% with high ESR and β2 microglobulin, 21.4% with low albumin and high uric acid and 14.3% with high LDH. All these percentages in patients with DLBCL are higher than that of other subtypes of NHL (Table 4).

Half of patients with DLBCL presented at

stage III and IV disease (50%), while in the other subtypes of NHL it was 42.3% (Table 5). According to the IPI scoring, 64.3% of them presented with high intermediate to high risk disease, while in the other subtypes of NHL, only 7.6% presented with high intermediate to high risk disease (Table 6).

Discussion

NHL encompasses several unique malignant lymphoid disease entities that vary in clinical behavior, morphologic appearance,

Sex	DLBCL (n=14)		Other subtypes of NHL (n=26)		*p*-value
	№	%	№	%	
Males	11	78.6	12	46.2	0.99*
Females	3	21.4	14	53.8	
Male: female ratio	3.67 : 1		0.86 : 1		0.001**
Median age (years)	51.5		50.0		0.84***

DLBCL: diffuse large B cell lymphoma NHL: Non Hodgkin's Lymphoma
*Calculated by Fisher Exact test *p*-value > 0.05 is statistically insignificant
Calculated by hypothesis test (Z-test) for the difference between two proportions from one group (mutually exclusive). * Calculated by the student t-test for two means.

Table 1. Sex and age distribution of patients with DLBCL compared to other subtypes of NHL

Residence	DLBCL (n=14)		Other subtypes of NHL (n=26)	
	№	%	№	%
Aden	5	35.7	8	30.8
Lahj	4	28.6	7	26.9
Abyan	2	14.3	6	23.1
Shabwa	2	14.3	2	7.7
Other governorates	1*	7.1	3**	11.5

DLBCL: diffuse large B cell lymphoma NHL: Non Hodgkin's Lymphoma
Chi square test(χ^2 = 1.0, *p*=0.91) statistically insignificant
* From Ibb governorate.
** From Taiz, Al-Dhala'a and Ibb governorates.

Table 2. Residence of patients with DLBCL compared to other subtypes of NHL

Clinical presentation	DLBCL (n=14)		Other subtypes of NHL (n=26)		*Statistics*
	№	%	№	%	*p*
Primary nodal	12	85.7	19	73.1	0.31
Primary extranodal**	2	14.3	7	26.9	
B symptoms§	9	64.3	17	65.4	0.61*
Fever	4	28.6	14	53.8	0.23
Weight loss	7	50.0	11	42.3	0.64*
Sweating	5	35.7	5	19.2	0.25*
Splenomegaly	4	28.6	6	23.1	0.49
Hepatomegaly	5	35.7	4	15.4	0.14

DLBCL: diffuse large B cell lymphoma NHL: Non Hodgkin's Lymphoma
*Calculated by the Chi square test, while others by the Fisher exact test.
** Include primary gastric and intestinal NHL.
§ Refers to the presence of at least one of: fever, weight loss and sweating
p-value > 0.05 is statistically insignificant

Table 3. Clinical presentation in patients with DLBCL compared to other subtypes of NHL

Lab findings	DLBCL (n=14)		Other subtypes (n=26)		*Statistics*
	№	%	№	%	*p*
Anemia§	9	64.3	14	53.8	0.52*
High ESR (> 50 mm/hr)	5	35.7	7	26.9	0.56*
Low albumin (< 3.5 g/dl)	3	21.4	1	3.8	0.11
High β_2 microglobulin**	5	35.7	8	30.8	0.51*
High LDH (>450 iu/L)	2	14.3	3	11.5	0.58
High uric acid (>7 mg/dL in females) (>8.5 mg/dL in males)	3	21.4	2	7.7	0.22

DLBCL: diffuse large B cell lymphoma NHL: Non Hodgkin's Lymphoma
§According to WHO definition: < 12g/dl in adult non-pregnant women and < 13 g/dl in men[10]
*Calculated by the Chi square test, while others by the Fisher exact test.
**In regard to the reference value of Kit *p*-value > 0.05 is statistically insignificant

Table 4. Lab findings at presentation of patients with DLBCL compared to other subtypes of NHL

Stage*	DLBCL (n=14)		Other subtypes of NHL (n=26)	
	№	%	№	%
I	2	14.3	7	26.9
II	5	35.7	8	30.8
III	4	28.6	6	23.1
IV	3	21.4	5	19.2

DLBCL: diffuse large B cell lymphoma NHL: Non Hodgkin's Lymphoma
Chi square test($\chi^2 = 0.85$, p=0.83) statistically insignificant
* According to the Ann Arbor staging of NHL (Cancer Staging Manual)[9]

Table 5. Clinical staging of patients with DLBCL compared to other subtypes of NHL

Risk according to the score of IPI	DLBCL (n=14)		Other subtypes of NHL (n=26)	
	№	%	№	%
Low risk (score 0 or 1)	1	7.1	15	57.7
Low intermediate risk (score 2)	4	28.6	9	34.6
High intermediate risk (score 3)	5	35.7	1	3.8
High risk (score 4 or 5)	4	28.6	1	3.8

IPI: International Prognostic Index[11]
DLBCL: diffuse large B cell lymphoma NHL: Non Hodgkin's Lymphoma
Chi square test($\chi^2 = 1.0$, p=0.91) statistically insignificant

Table 6. The International Prognostic Factor Index in patients with DLBCL compared to other subtypes of NHL

immunologic, and molecular phenotype. DLBCL is the frequent subtype of NHL and it is the most common malignant lymphoma all over the world.[12]

This study showed that DLBCL is a common subtype of NHL, represented 35% of all the studied NHLs. This percentage is similar to that reported in India,[13] where DLBCL was the most common subtype of all NHLs (34%), as well as in Denmark (33%).[14] However, higher frequencies of DLBCL were reported in other countries like Jordan (53%),[15] Pakistan (76.4%),[16] and Oman (83%).[17] Lower percentage was reported in the current study, in spite of the fact that Yemen is near the area of lymphoma belt. This is may be attributed to different factors as the lack of modern immunohistochemistry techniques in Yemen which could be the first contributory factor towards poor diagnosis of DLBCL, as well as the lower percentage of congenital and acquired immunodeficiency states.

DLBCL in this series is more common in

males as compared to females with a male to female ratio of 3.67: 1. This ratio is slightly higher than that report in Pakistan (2.3: 1).[16] The median age of patients with DLBCL in this study was 51.5 years which is not far from that reported in Pakistan (47.2 years)[16], but higher than that reported among Jordanian patients with DLBCL (44 years).[15]

Studies showed that about 40% of cases presented with extranodal disease and the most common extranodal site was the GIT (stomach or ileocaecal region).[18] The most common site of origin of extranodal NHL in Pakistan was the GIT (representing 37.5% of all extranodal NHLs),[16] and a similar percentage (37.5%) was reported in Jordan.[15] The current study found extranodal DLBCL with lower percentage (14.3%).

Literature showed that about 15 – 20% of patients with DLBCL presented with localized disease defined as stage I or II.[18] In this series; 50% of DLBCL were in stage I and II (14.3% and 35.7% respectively). It is believed that clinical staging of NHL patients is subjected to variation due to demographic, socioeconomic and cultural variation. Some patients present in early stages while others in late stages due to the variable attitude toward health services, variable economic ability, and variable social beliefs.

This series revealed that DLBCL in our patients presented aggressively compared to other subtypes of NHL. This is clear from the higher percentages of anaemia, hypoalbuminaemia, hepatosplenomegaly, advanced clinical stage and high risk according to the IPI.

Laboratories in Yemen lack modern diagnostic equipments and techniques which led us to depend on clinical evaluation and the available histopathological techniques. Poor identification of the histopathological characteristics of lymphoma cells and the absence of immunophenotyping and cytogenetic analyses forced our pathologist to diagnose most NHL as unclassified. Because of that, all our NHL patients in Aden are sent abroad for immunophenotyping and cytogenetic studies for correct subtyping of lymphoma.

Conclusions

1. DLBCL is the frequent subtype of NHL in our patients, presented with an aggressive clinical and paraclinical presentation when compared with other subtypes of NHL.
2. Half of the patients presented with late stages of the disease at the time of diagnosis and 64.3% of them presented with high intermediate to high risk disease.
3. There is an underestimation by higher health authorities for the importance of subtyping lymphoma in the management and prognosis of the disease.

Recommendations

1. Higher health authorities should establish a specialized lab with immunophenotyping and cytogenetic studies, for subtyping NHL in Al-Gamhouria Modern General Hospital in Aden to decrease the economic and social burden on patients and the Ministry of Public Health and Population.
2. Further national studies are recommended to include all Yemeni patients with NHL (pediatrics and adults) and to follow their response to the commonly used therapeutic regimens.

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