ORIGINAL ARTICLE

Diffuse Large B Cell Lymphoma in the University Hospital Centre of Batna (Algeria): A Retrospective Epidemiological Study

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ABSTRACT

Background: Diffuse large B cell lymphoma (DLBCL) is an aggressive lymphoma, results from the uncontrolled multiplication of abnormal B lymphocytes. In Algeria it represents 50 to 60% of all lymphomas. Great progress has been made in Algeria during these last years in terms of diagnosis and management of Non Hodgkin Lymphoma (NHL) and more specifically for DLBCL.
Aim: To study the epidemiological, anatomopathological, immunohistochemical, clinical, therapeutic and evolving characteristics of DLBCL in adults recruited from hematology department at the University Hospital Center (HUC) of Batna (Algeria).
Methods: This is a descriptive retrospective study on the records of 33 patients aged over 27 years with DLBCL, treated in the same department. The analysis revealed an average age of 54 years, men are more frequently affected than women (22 men/11 women), the sex-ratio is 2. A high prevalence of the disease was registered in Batna 45(45%) compared to other regions.
Results: The clinical and anatomopathological profile reveals that 54.54% of our patients had no specific antecedents and 45.45% of the patients were hypertensive, hepatic localizations are found in 24.24% of cases, a predominance of disseminated stages 63(63%) compared to localized stages 36(36%) was also recorded. The immunohistochemical analysis shows that the markers (CD20; CD45; CD3) are mainly expressed (90.90%, 39.39%, 21.21% respectively) in our patients. The therapeutic and evolutionary aspect affirms that the R-CHOP protocol (Rituximab+Cyclophosphamide, Doxorubicin, Vincristine, Prednisone) is the most adopted in our patients 54(54%), the evolution in our series was marked by a death rate of 33.33% of cases and complete remission was objectified in 21.21% of patients.
Conclusion: This study allowed us to establish an epidemiological profile of DLBCL and to study its characteristics within our region 'Batna'. The identification of characteristics with prognostic value could allow a better therapeutic adaptation for our patients.
Keywords: Diffuse large B cell lymphoma (DLBCL), retrospective epidemiological study, University Hospital Center (HUC) of Batna.

INTRODUCTION

Lymphomas are cancers of the lymphatic system, they can develop in any organ containing lymphoid tissue, especially where this lymphoid tissue is most dense, notably in the lymph nodes, the tonsils and the lining of the small intestine[1].
The Non Hodgkin Lymphomas (NHL) are hematological malignancies developing at the expense of B or T cells, but rarely from natural Killer (NK) cells[2,3]. Lymphomas result in clinical, morphological and biological diversity reflecting the complexity of modern histopathological classifications; their clinical evolutivity is variable, sometimes moderate (indolent lymphomas) and high (aggressive lymphomas) in other cases[4]. The particular interest in lymphomas is due to the increase of their incidence, better knowledge of their development and therapeutic progress allowing better healing in a certain number of cases[4]. The DLBCL is an aggressive lymphoma, it ranks first in NHL, in Algeria it represents 50 to 60% of all lymphomas[5]. The DLBCL is discreetly most common in men, it is classically diagnosed after the age of 60 years, but can occur in children and young adults[6]. To date, no study has been carried out on this type of lymphoma in our region "Batna". The present work aims to study the epidemiological, anatomopathological, clinical, therapeutic and evolving characteristics of DLBCL in the hematology department of Batna Hospital University Center (HUC).

METHODS

Patients and methods: This is a descriptive retrospective study on the files of 33 patients (archived from 2013, up to 2019) with DLBCL, treated by hematologists in the hematology department at the Batna University Hospital (Algeria).
In this study, we included all adult patients with DLBCL, diagnosed by specialist doctors in the hematology department, at different stages of the disease. Patients are aged betwen 27 and 89 years, of both genders and coming from different regions of eastern Algeria. We excluded from this study all patients with Burkitt's and Follicular Lymphomas.
Data collection: The data were collected by analysis of medical records in the hematology department. For each patient, several parameters (such as age, gender,

presence or absence of personal history, profession, immunophenotyping, chemotherapy protocol, etc.) were collected on an exploitation sheet. We have performed a descriptive statistical analysis of all the epidemiological and clinical characteristics of our patients.

RESULTS

In our study, the age varies from 27 to 89 (years) with an average age of 54 years, the group of 49 to 59 years is the most common age group in our patients, with a prevalence of 24(24%) (Figure 1). Age constitute a very important prognostic factor. We found in this survey a higher proportion of men; 22 cases or 67% with DLBCL, compared to the women; 11 cases or 33%.Therefore, we observe a male predominance with a sex ratio (male / female) of 2. Concerning the profession of our patients, 24.24% of them are manual workers, only 6.06% are farmers, however 45(45%) are unemployed (Table 1). This survey reveals that almost half of the DLBCL cases collected 45(45%) came from the Batna region or resided in this city (Table 1). According to our results, 54.54% of our patients had no particular antecedents and 45.45% of patients with a particular antecedents; it is mainly the hypertention HTN; 18(18%) of cases (Table 2). In the presence of a serious infection like HIV (human immunodeficiency viruses), it is necessary to carry out the treatment before starting the chemotherapy sessions. No carriers of retroviral infection (HIV) were reported in this study. Our findings show that there is a high incidence of patients with liver damage 24(24%) (Table 2), compared to those with neck (18.18%), gastric 12(12%) or intestinal damage 12(12%). According to the classification of Ann Arbor[7] and grace to the radiological, scannographic and endoscopic extension assessments carried out; we note a predominance of advanced clinical stages (III and IV) with 63.63%patients compared to localized clinical stages (I and II) which are of 36(36%) (Table 2). Signs of clinical evolutivity were present in all patients. In our series, immunohistochemistry analysis reveals that markers CD20, CD45 and CD3 are mainly expressed (90.90%, 39.39% and 21.21% respectively) (Figure 2). The CD20 marker was positive in all the cases studied (90.9%) and the CD30 marker was positive in only two cases. Among the 30 patients with DLBCL, 18 cases 54(54%) received an RCHOP protocol, 08 cases or 24(24%) received a CHOP protocol (cyclophosphamide, doxorubicin, vincristine, prednisone) and only 04 patients or 12(12%) of them received a COP (Cyclophosphamide, Oncovin, Prednisone) protocol (Table 2). However, we could not find the chemotherapy protocols for 3 patients (9.09%), either because they were lost to follow-up or died before receiving any treatment. The evolution of DLBCL is towards the extension, remission or even relapse. The evolution in our series was marked by a death rate of 33(33%) of cases (Table 2). Complete remission was objectified in 21(21%) of patients, partial remission was observed in 27(27%) of cases. In addition, 3 files (9.09% of patients) were being evaluated at the time of exploitation files. In our series, 3 patients (9.09%) were not treated.

Table1: Socio-demographic characteristics of DLBCL patients

Parameters	**Frequency**	**%age**
Profession		
Manual workers	**08**	**24,24**%
Farmers	02	6,06%
Merchant	03	9,09%
Employee	02	6,06%
Senior manager	03	9,09%
Unemployed	**15**	**45,45**%
Locality		
Batna	**15**	**45.45**%
Biskra	03	9.09%
Tbessa	04	12.12%
Khenchla	03	9.09%
Eloued	02	6.06%
Oum Elbouaki	04	12.12%
Ain oualméne	01	3.03%
Boumardes	01	3.03%

Table 2: Clinical and physiopathological characteristics of DLBCL patient

Parameters	**Frequency**	**%age**
Antecedents		
HTN	**06**	**18,18**%
Diabetes	03	9,09%
Asthma	02	6,06%
Sinusitis	01	3,03%
HCV + Hepatic cirrhosis	01	3,03%
Distal hernia L5 / L1	01	3,03%
Anemia	01	3,03%
HIV	00	00%
Nothing to report	**18**	**54,54**%
Localization of the DLBCL		
Gastric	04	12.12%
Intestinal	04	12.12%
Hepatic	**08**	**24.24**%
osseous	02	6.06%
Thyroid	02	6.06%
Lymph node parenchyma	01	3.03%
Muscular	01	3.03%
Neck	06	18.18%
Ethmoid sinus	01	3.03%
Pulmonary	04	12.12%
Stages		
Stage I	06	18,18%
Stage II	06	18,18%
Stage III	08	24,24%
Stage IV	**13**	**39,39**%
Chemotherapy protocol		
RCHOP	**18**	**54,54**%
CHOP	08	24,24%
COP	04	12,12%
Untreated	03	09,09%
Remission		
Complete remission	07	21.21%
Partial remission	09	27.27%
Deceaded	**11**	**33.33**%

Figure 1: Distribution of patients by age group. Numbers on top of histograms indicate the exact percentage value in each age range

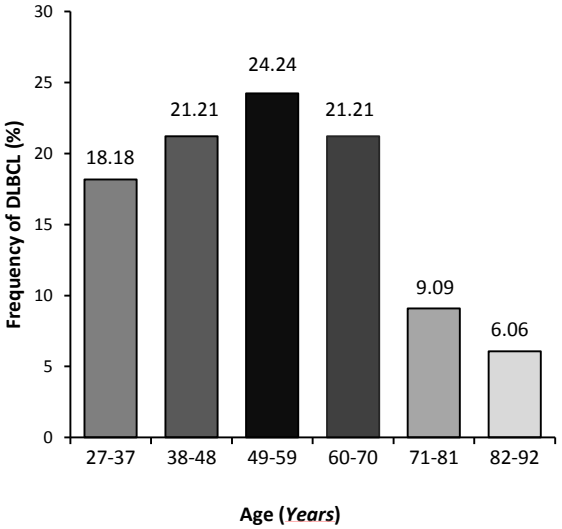
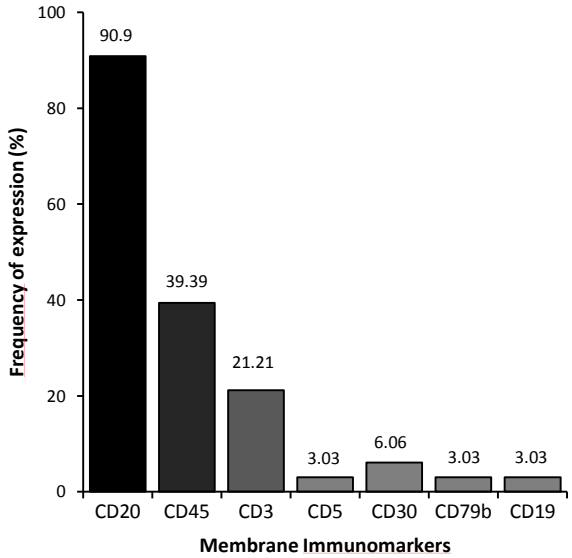


Figure 2: Percentage of positive CD for each marker in the DLBCL



DISCUSSION

In this study we investigated the epidemiological, anatomopathological, clinical, therapeutic and evolving characteristics of DLBCL in the hematology department of Batna Hospital University Center (HUC). We mainly report here a high prevalence of DLBCL in elder population, predominance in males, hepatic localization of DLBCL, high advanced stages of the disease and low remission of patients after chemotherapy.

In previous study, Boudjerra et al[8] recorded in a descriptive study of non-Hodgkin's lymphoma in adults, a median age of 52 years of patients with NHL with extremes: 16 - 95 years, a peak frequency for the 50 to 70 years age group was also observed during this investigation. The DLBCL represents 61% of all lymphomas [**8**]. Our results are close to those obtained by Boudjerra et al[5] who examined files concerning the age of patients with DLBCL, they then found a median age of 55 years (15-96) for Algeria and 52 years (15-92) for Tunisia. The frequency peak is observed on the age group [51 -70 years] for Algeria and [51 to 60 years] for Tunisia[5]. The population of patients with lymphoma is younger in our countries (Algeria and Tunisia) compared to the European series[9]. Regarding gender, our results are close to the findings found in the literature where the sex ratio is between 1.3 to 2 depending on the studies, Bouchama et al[10] also, noticed a male predominance of patients with DLBCL; (M/F 265/202) with a sexe ratio of 1.3. Similarly, men are more frequently affected than women in Europe, with a sex ratio of 1.5, the sex ratio of 2 found in our series is higher than that found in Europe 1.5[11,12]. The majority (45,45%) of our patients were without profession. Similarly Hamdi et *al*[13] found on 809 files examined; 16% are manual workers and 7% are farmers, however 52% are unemployed. The professional risk has been incriminated in several studies, the risk seems to be higher in people who come in contact with pesticides, particularly agricultural workers, a high risk was also found in teachers and workers in the wood industry[11].

We have noted in our study that the majority of patients had no specific antecedent (54.54%) and only 18.18% of patients had an HTN. Renard et *al*[14] found in their study an HIV-associated comorbidity in 2 cases with an NHL on 18 patients (11%). Patients with immune deficiency, such as transplant patients or those with HIV, may be at higher risk of developing NHL[15]. During this survey, 24.24% of the patients presented liver damage. According to data from Bosly et *al*[16] carried out on patients with DLBCL, the lymphoma had an extra-nodal extension in 12% of cases. The head and neck region is the second most affected site after the gastrointestinal tract[14]. Thus, the oral cavity and the maxilla represent 2 to 3% of the extranodal sites[17,18]. Similarly to our results, Bouchama et *al*[10] found that clinical stages III and IV are the most frequent stages of DLBCL disease in Algeria (61%). These frequencies seem to be higher in comparison with European countries[19]. The immunohistochemical methods[20] used for immunophenotyping are based on the specific recognition of antigenic determinants (epitopes) by antibodies coupled to revelation systems[21]. They make possible the microscopic detection of identifying molecules within cells (differentiation markers) or of molecules linked to a functional state (proliferation markers or expression of various oncoproteins)[21]. Immunohistochemistry therefore provides elements of diagnostic orientation which must be confronted with the reality of clinical expression. Clusters of Differentiation (CD or differentiation classes) are membrane marker, it considered positive if it is expressed by most of the cells analyzed (CD20, CD45, CD3, CD5, CD30, CD79b, CD19).The immunohistochemical study has a major interest in making the diagnosis and eliminating other lymphoid tumors. DLBCL is the most common lymphoma, it represents (35%) of NHL[22]. It expresses CD 20, CD 22, CD 79b, FMC7 [22] and CD 19[23]. CD20 is expressed on the surface of DLBCL intensively and it is also expressed on normal B lymphocytes[24]. It is not expressed on stem cells

of the B cell- line or on plasma cells[24]. The exact role of the CD20 is still debated; it appears to exert its action as a calcium channel when the cell is activated[24].The majority of these tumors express the CD45 antigen, which is an antigen common to leukocytes[23].This marker is very useful in practice for differentiating a malignant lymphoma (CD45 +) from non-lymphoid tumors of undifferentiated aspect, CD45–: carcinomas, melanomas, sarcomas[23]. The CD5 and CD10 antigens are occasionally found in DLBCL[23]. Our results obtained are therefore consistent with those published in literature. It is useful to note that lymphomas of anaplastic morphology which express the CD30 activating antigen, but which are phenotype B, are classified in diffuse large B cell lymphomas and not in anaplastic large cell lymphoma[23].

Regarding the treatment, the majority of our patients received the R-CHOP protocol. Some prospective studies have shown that adding Rituximab to the CHOP protocol results in a better therapeutic response and a better survival rate[25]. A German group compared R-CHOP to CHOP protocol, both administered every 14 days and also showed clearly the superiority of R-CHOP 14[26]. In addition, studies carried out in Canada[27] or in Czech Republic[28] showed also the superiority of R-CHOP over CHOP. These studies have clearly demonstrated the superiority of Rituximab + CHOP over CHOP alone, both in terms of complete response and objective response as well as failure and relapse rates. Our results therefore confirm the data from the literature. By comparing the response to treatment of our patients with the results of other studies, we find that the complete remission rate in our patients (21.21%) is lower than the complete remission rate of others series. Thus, in 469 patients with histologically confirmed DLBCL, 83% have achieved complete remission and 58 % of them were found with partial remission on 5-year of overall survival[29]. In another cohort of patients, 304 (86%) of 355 patients who assigned chemotherapy and rituximab had complete remission or unconfirmed complete remission 155 days after starting treatment, also, 27 deaths were noted in this study (19 lymphomaassociated, six treatment-related, and two due to concomitant disease), 3-year overall survival was (93%) for these patients[30]. One of the most important conditions for prolonged survival is achieving complete remission from initial treatment. Once the remission has been obtained, clinical and radiographic surveillance must allow early detection of a possible recurrence.

CONCLUSION

Diffuse large B-cell lymphoma (DLBCL) is an aggressive lymphoma, it ranks first among non-Hodgkin lymphomas, in Algeria it represents 50 to 60% of all lymphomas. The average age of onset is 63 years, with a predominance of men. Our study on diffuse large B cell lymphoma in University Hospital Center is the first in our region 'Batna' that allowed us to establish an epidemiological, anatomopathological, immunohistochemical, clinical, therapeutic and evolutionary profile of this aggressive lymphoma and to study their characteristics. This study confirms the anatomoclinical heterogeneity of LDGCB lymphomas. Indeed, the clinical presentation is very polymorphic depending on the location and the histological type.

The therapeutic strategy is based first of all on a very precise initial assessment, this work, which complements several national epidemiological studies, could assist in the development of new treatment and prevention strategies in order to improve the medical care of DLBCL patients in the Batna region (Algeria).

Competing interests: The authors declare no competing interest.

Authors' contributions: All authors have equally contributed to the manuscript content and to the management of this work. All the authors have read and agreed to the final manuscript.

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