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Characteristiccs of malignant non hogdkins lymphoma recieved in the onco-haematological unit of Douala General Hospital: Retrospective study over 5 years (2008-2012)

Ngouadjeu Dongho TE[1,2], Tomowiak C[3], Effa G[2], Banos A[4], Araujo C[4], Sume GE[5], Andong A[6], Mouelle Sone A[1,2], Bauduer F[7]

1 *Internal Medicine Service of Douala General Hospital, Douala, Cameroon*
2 *Faculty of Medicine and Pharmaceutical Sciences, University of Douala, Douala, Cameroon*
3 *Hematology Department, Poitiers Teaching Hospital, Poitiers, France*
4 *Hematology Department, Centre Hospitalier de la Côte Basque, Bayonne, France*
5 *World Health Organization (WHO), Yaounde, Cameroon*
6 *Faculty of Health Sciences, University of Buea, Buea, Cameroon*
7 *UFR des Sciences Médicales, Université Bordeaux Segalen, Bordeaux, France*

Abstract

Malignant Non Hodgkins lymphoma (MNHL) is defined as a malignant tumorale disease of lymphoid tissue, characterised by the proliferation of one or two abnormal lymphocyte clones. In Cameroon it is cited among the cancers whose incidence are rising in an alarming manner. It's frequency is estimated in men at 22 % and in women at 13 %. This retrospective and descriptive study had as aim to describe the epidemiological, clinical and therapeutic profile of malignant non Hodgkins lymphoma in the onco-haematological unit of Douala General Hospital over a period of five years. Our selection criteria permitted us to collect 86 cases. The mean age was 42 ±20 years. We noted a male predominance with a sex ratio of 1 ;6. This population came mainly from a low social class (42 cases that is 48.84%). The tumoral syndrome was the most frequent physical sign present (69 cases that is 80.23%). The mean delay in cosultation was about 233.271±251,511 days. At the time of diagnosis, 41 patients that is 47.7% of cases had an activity index ≥ 2. Nodular localisation was predominant 22 cases (25.58%). Among the Extra Nodular localisatio, bone marrow localisation was at the first place 16 cases that is 18.60%). The majority of patients were diagnosed at stage IV of Ann Arbor classification that is 30 cases (34.88%) followed by stage III with 29 cas (33.72%). The predominant histological type was type histologique was that of large cell lymphomas, found in 16 patients (18.60%). Immunohistology was realised in 11 patients (that is 13%). The CHOP protocol was done on CHOP 52 patients that is in 60.50% of cases, followed by RCHOP in 9,30 % of cases. The patients recieved between 1 and 8 cycles. Complete remission was obtained in 32.5% of cases and partial remission in 65,1 % of cases. Half of the patients are alive, 36 % are lost and 14 % are dead. We noted a predominance of these cases having an elevated activity index, a large tumoral syndrome, an Ann Arbor stage of IV and III. The majority of patients are classified as intermediate high risk or high risk. A better knowledge of the clinical presentation will permit us to carry out sensitization actions and better structure our treatment.

Keywords: Non Hodgkins lymphoma, Epidemiology, Africa.

INTRODUCTION

Malignant non Hodgkins lymphomas (MNHLs) represents a heterogenous group of diseases defined by an abnormal proliferation of lymphoid cells [1]. Even though they present with common characteristics, they regroup numerous different entities, particularly in the clinical, biological, histological and prognostic plan. Few studies on MNHLs are available in Cameroon. In order better understand the profile of theses affections and to improve on the management in our country, we carried out a retrospective study of the cases recieved in our centre over a period of 5 years.

PATIENTS AND METHODS

Study area

This study was carried out in the onco-haematological unit of the internal medicine service of Douala General Hospital, Cameroon. This units recieves patients from four big regions of the country : Littoral, South-west, West and North West (figure 1) [2]. According to the 2010 report of the 3rd general census of the population and the habitats of Cameroon, population per region was estimated at 2865795 for Littoral, 1384286 for South-west, 1785285 west and 1804695 at the North-west [3]. The total therfore constitutes a target population of 7840061 inhabitants with a mean age of 22.1 ans [3].

***Corresponding author:**
Dr. Ngouadjeu Dongho TE
Internal Medicine Service of Douala General Hospital, BP 4856 Douala, Cameroon
Email: ngouadjeue[at]yahoo.fr

FIGURE 1 : Cameroonian map with it's different regions

The under 25 population represents 64.2% and elderly people of 60 years and above represent 5% of the population [3]. The internal medicine service has set aside a unit destined for the treatement of malignant hemopathies since 2011 with the help of the ON-HEM association Cameroun, Bayonne, France. This service comprises of 40 beds of which 2 isolated rooms for management of patients with neutropenia. The patients are being managed by a haematologist, a general practitioner and twp nurses specialised in oncology.the diagnosis of MNHL is done either in the anatomo-pathological laboratory of our hospital, either at l'Institut Pasteur du Cameroun (national refference laboratorty) or at Cerba laboratory. Immunohistology is done at Pasteur institute of Yaoundé or at Cerba laboratory (11 Rue de l'Equerre ,95310 Saint-Ouen -l'Aumône, France). The karyotype is not been done for financial reasons. Routine biological examinations are done at the level of our hospital laboratory. Standard radiography, echography and and CTScan imaging are equally been done in our centre. PET scanning is not been done because its abscrnt in our country.

Type of study

This descriptive, retrospective study was done over a period of 5 years going fro. January 1st 2008 to December 31st 2012. It is based on file analysis of patients who were being hospitalised in the unit during this period. étude descriptive,.

Study population

It involves patients of all age carrier of a MNHL documented by anatomo-pathological examinations of a biopsy sample obtained at Douala general hospital from January 2008 to December 2012.

Data collected

For every patient were recorded the following characteristics:

Sociod-ermographical: age, sex, occupation, socioeconomical level. This last parameter was defined according to three levels: 1/ low = absence of a fixed revenue and inability to respect the planned care, 2/ medium = presence of a fixed revenu permitting to follow the treatement or 3/ high = presence of a permanent health insurance and choice of treatment without any financial constraints.

Clinical: delay in consultation (period in between appearance of symptoms and the first consultation at the haematologist), circumstances of discovery, eventual presence of of general signes known as B signs (fever, weight loss, sweating), performance status according to ECOG, localisation of the lymphoma and tumoral extension according to d'Ann Arbor classification.

Biological: haemoglobin concentration, Lactate dehydrogenase (LDH), HIV, hepatitis B and C serology and d'Epstein Barr virus serology.

Radiology: Thoraco abdominal CT Scan results, sometimes just a chest x-ray with and abdominal ultrasound permit to classify according to Ann Arbor.

Anatomo-pathology: histologic type according to the international classification of a tumour localisation. Analysis of the bone marrow biopsy is not systematic.

Therapeutic: the type of treatment chosed, the number of times the treatment was done, the results ; the degree of response (complete, partial ou abscent), follow-up.

Data analysis

The sofwares Epi info version 3.5 and Excel were used to analyse the data.

Ethical considerations

This study was done after ethical approval from the ethical committee of the Douala General Hospital.

RESULTS

Sociodermographical characteristics

Over a total of 120 files censused during the study period, 85 we're retained by our study that is 86 cases of NHML confirmed by anatomo-pathological over a period of 5 years. This corresponds to a mean of about 24 cases/year and equivilent to an incidence of 0.306 cases per year per 100000 inhabitants.

The patients ages varied between 4 and 78 years with a mean of 42 ±20 years. The sex ratio was at 1.6 in favor of women. The classification with respect to Sociodermographical data is presented in table 1. The age range the most involved was that of 50 to 59 ans (20 cases that is 23.35%. Secondary, high school and university students were in majority (22 cases, 25.58%). The socioeconomical level was mostly low (42 cases, 48.84%).

Clinical characteristics

The time range before consultation varied between 20 and 1118 days (37.26 months) with a mean of 233 2±251.511 days (about 7.7 months).

The principal discovery circumstance was the tumoral syndrome (69 casse, 80.23%). Lymphadenopathies were found in 22 cases (25.58%).

Table 1: Distribution of the patients according to socio Dermographical data

Variables	Categories	Frequency	Percentage %
Age range	0-9	6	6.97
	10-19	10	11.62
	20-29	11	12.80
	30-39	9	10.50
	40-49	13	15.11
	50-59	**20**	**23.25**
	60-69	12	13.95
	70-79	5	5.80
Sex	Female	33	38.37
	Male	**53**	**61.63**
Occupation	Administration	12	13.95
	Farming	5	5.81
	Secondary and tertiary students	**22**	**25.58**
	Housewives	20	23.26
	Industrial sector	18	20.93
	Others	9	10.47
Socio-economical status	High	12	13.95
	Moderate	32	37.21
	Low	**42**	**48.84**

Table 2: Distribution of patients according to clinical data

Variables	Categories		Frequency	Percentages %
Delay in consultation	**0-200**		**54**	62.79
	201-400		20	23.26
	401-600		2	2.33
	601-800		7	8.14
	801-1000		1	1.16
	1001-1200		2	2.33
Circumstances of discovery	Lymphadenopathy(ies)		**22**	**25.58**
	Alteration in the general status		19	22.09
	Masse/ tumefaction		**47**	**54.65**
	Long term fever		6	6.98
	Leucocytosis		3	3.49
	Pancytopenia		5	5.81
	compression Syndrome of the urogenital pathway		2	2.33
	*Others		15	17.44
B signs of evolution	Weight loss		**53**	**61.63**
	Hyperhydrosis / Night sweats		52	60.47
	Fever		50	58.14
	Puritus		20	23.26
Performans Status	0		23	26.7
	1		22	25.6
	2		20	23.3
	3		11	12.8
	4		10	11.6
Tumoral syndrome	Lymphadenopathy localisation	Sub maxillary	12	13.95
		Cervical	29	33.72
		Subclavicular	5	5.81

	Axillary	11	12.79
	Inguinal	18	20.93
Hepatomegaly		19	22.09
Splenomegaly		25/86	29.1

*others: Anaemia, epistaxis, dyspnoea, convulsion, disturbances in the conscious state, haematuria, pathological fractures, bi cytopenia, bone marrow and media's tindal compression syndromes.

Table 3: Distribution of patients according to Ann Arbor classification and lymphoma localisation

Variables	Categories	Frequency	Percentages %
Ann Arbor Classification	1	9	10.47
	2	18	20.93
	3	29	33.72
	4	**30**	**34.88**
Localisations	Abdominal	13	15.12
	Tonsilar	4	4.65
	Cavum	7	8.14
	Cerebral	3	3.49
	Ganglion	**26**	**30.23**
	Hepatosplenic	2	2.33
	Maxillofacial	4	4.65
	Bone marrow	16	18.60
	Bony	2	2,33
	Splenic	5	5.81
	*others	4	4.65

*Others: mammary, pleural localisation

Table 4: Classification of patients with respect to histological type

Histological type	Frequency	Percentage %
NHML not precised	9	10.47
T cell NHML	1	1.16
Large cell diffuse NHML	16	18.60
Small cell NHML	14	16.28
Burkitt NHML	7	8.14
Centroblastic NHML	10	11.63
Centroblastic and immunoblastic NHML	1	1.16
Centrocytique NHML	1	1.16
folliculaire B NHML	3	3.49
Immunoblastic NHML	3	3.49
Lymphoblastic NHML	12	13.95
Lymphocytic NHML	1	1.16
Lymphocytic NHML	4	4.65
Pleomorphic NHML	1	1.16
T lymphoblastique NHML	1	1.16
Marginal zone NHML	1	1.16
B monocytoide Marginal zone NHML	1	1.16
Total	86	100

Their sizes varied between 1 to 22cm. Splenomegaly and hepatomegaly we found respectively in 29.1 and 22.01 % of cases. Weight loss was found in 53 patients, hyperhydrosis in 52 and fever in 50 cases as shown in table 2. We noticed *performans status* of 0 and 1 in 23 and 22 cases respectively (that is 26.7% and 25.6%) and great her than on equal to 2 in 41 patients (47.7%). Stages III and IV of Ann Arbor were predominant respectively in 33.7% and 34,88%.

Anatomopathological complications

The most biopsy organ was lymph nodes followed by bone marrow and abdominal masses. Only 11 patients benefited from an immunohistological study on the biopsy piece.

Histology permited to notice the most frequent type was Large celle NHML followed by small cell NHML and lymphoblastic NHML (see table 3). We counted just three cases of follicular lymphoma (3.49 % of cases).

Biological Characteristics

The hemoglobin concentration varied between 3.1 à 16.40 g /dl with a mean of une 10.0 ± 2.4 g /dl. The majority of patients had an LDH greater than the normal value (54 cas, 62.7 %). Amongst the 86 patients recruited, 21 patients had a positive HIV, hepatitis (B and C) or Epstein Barr virus serology, screened either before diagnosis or during a pretherapeutic workup. The prevalence of HIV in our study population was 16.27%, that of Hepatis B at 1.16 %, that of Hepatitis C 5.81 %, and that of Epstein Barr Virus 1.16 %.

Therapeutic characteristics

Before chemotherapy, the minimal pre therapeutic workup consist of the renal and liver function tests, virology (HIV, Hepatitis B and C), blood sugar and heart ultrasound scan.

In 33% of cases the patient had recieved first COP chemotherapy to reduce the tumor mass and reduce lysis syndrome.

The CHOP 21 protocol (cyclophosphamide : 750 mg/m² at d 1, adriamycine : 50 mg/m² at d1, vincristine : 1.4 mg/m² at d 1 and prednisone : 60 mg/m² at d1 to d5 ; d1 = d21) was done in 52 patients that is in 60.5 % of cases as represented in table 4. Only eight patients had recieved the R protocole (rituximab : 375 mg/m² at D1) -CHOP (9.3%). The CHOP-Bléomycine protocol was done in 8.1% of cases and the COP in 17.4% of cases. The number of chemotherapy treatments varied in between one and eight cycles (the objective being to do atleast 6 treatments over the 8 requested). The number of patients having 1, 2, 3, 4,5 and more than 6 treatments were respectively of 23, 9,10, 7, 8, 16 et 13 on 86.

A total of 56 patients, that is 65.1% recieved between one and five chemotherapy treatments and were in partial remission. Complete remission was observed in 28 patients (32.6%) having recieved atleast 5 treatments. In 2.3 % of cases (2 cases) there was a progression on treatment. A blood transfusion was neccessary during the treatment of 38% of patients.

Growth factors (G CSF) were neccessary in 23.3% of cases to correct chemotherapy induced aplasia. Alopecia was observed in half of the cases.

Thier Becoming

Half of the patients were alive after a mean survival of 318.417 ± 313.209 days that is 10.6 months ; 36% were lost and 14% dead of the disease. We counted amongst the 12 dead cases 7 deaths in the first 300 days of management and four deaths in between day 301 and day 600 of management.

The performance status was associated to death ($p < 0.0001$) as well as the number of disease localisation ($p = 0.0016$).

DISCUSSION

We have described here the different aspects of NHMLs recieved in our centre in order to optimise in future the management and to make known the realities of the management of this disease in a Central African country.

On 120 files of lymphoma 86 we retained for our study as they were documented.

The ages of the patients varied between 4 and 78 years with a peak frequency in between 50 and 59 years ; this age range represented 23.25% of cases, that is 20 patients. The mean age was 42.09± 20.14 years, with a median of 45 years.

This mean is a little higher than that described in African literature: notably Sawadogo et al in Ivory Coast found a median age of 37 years [4].

Our results are different from those of malignant hemopathies registrars of Gironde (France) which gave a mean age of 66 years and a median of 69 years [5]. In the same manner the national cancer institution of France present a median age at diagnosis of à 64 years in males and 70 years in females [1]. This youthful presentation of patients with MNHL could be explained by secondary immunodepression to HIV frequently found in African countries [4].

The male sex was predominant in our series. Hence 62% of our patients were of the male sex, with a male/female ratio of 1.6/1. The male predominance has equally been found by other African authors, Tolo *et al* [6] in Ivory Coast. In France a mild male predominance has been found in adults (54 % of cas) [1]. Our data consists mainly of secondary and tertiary school students, followed by housewives, and industrial workers with respective proportions of 25.58 %, 23.26%, 20.90%.

A low socio-economical status was found in 48,84% in our context, which is supreimposible to that reported by Sawadogo in Ivory Coast (51%) [4].

The mean delay in management was of 233.371±251.511 days (about 7.77 months), with extremes in between 20 and 1118 days. This long delay raises the problem of late diagnosis of MNHL which is often brought up only as a last resort, after failure in anti-tuberculosis treatment or after a long stay at « traditional doctors ».

In this our series, in more than 50% of the disease cases, was revealed by a tumoral syndrome, either as superficial lymphdenopathies in, 25.58% of cases (22 patients), or in the form of organ involvement (54.65%).

Our results are comparable to those of Tolo *et al* [6] who found equally as first circumstance of discovery the tumoral syndrome (superficial and deep lymphadenopathies). Nevertheless wih a frequency of 39.53%. But for Sawadogo *et al* [4], the lymphadenopathies revealed lymphoma in 93.3% of cases.

Weight loss was the B sign the most represented with a frequency of 61.6%, followed by hyperhydrosis and fever found respectively 60.5% and 58.1% of cases. Purity was found only in 23.3% of cases (20 patients). This correspond to the results of Sawadogo *et al* [4] in 2001, where weight loss represented the first sign of evolution (61,63% of cases). Toloen 1999 on the other hand, found weight loss in 6,89% and fever in 13.79% [6].

Almost half of the patients had and activity index according to ECOG greater or equal to 2 (47.7 %), during the first consultation. This could be justified by the fact that the patients are generally seen at an advance stage of the disease.

In our series, we found splenomegaly in 29.1% of cases, and hepatomegaly in 22.1% of cases. Sawadogo had noted a higher proportion than ours, respectively 42.2% and 26.7% for splenomegaly and hepatomegaly [4].

Lymph node localisation was predominant (2.58%). As far as extra lymphatic Localisations are concerned, bone marrow localisation was at the fore front (18.6%) (stage IV) followed by abdominal localisations (15.1%).

These results are quite close to those of Diop et al, for whom lymphoma localisation was exclusively in the lymph nodes in 30.8 % of cases, extra ganglionic in 31.7 % of cases and mixed in 37.3% of cases [7]. The Ivorian study found values higher than ours respectively 64% and 36% for lymph node localisation and extra ganglionic. Bhatia in Inde observed bone marrow localisation in 21 patients on 137 cases having an extra ganglionic MNHL that is 15.3% [8].

The majority of patients were at an advanced stage of Ann Arbor classification that is 33.7% of patients recieved at stage III and 34.88% of patients at stade IV. This predominance of advanced stages was equally described by Tolo and Sawadogo [4,6].

This could be explained by a low socio-economical status in general in Africa and especially lateness in diagnosis with respect to the practice of traditional medicine.

The histological types the most found we're diffuse large cell lymphoma (18.60%), followed by diffuse small cell lymphoma (16.28%) and of the lymphoblastic type (13.95%). Our results are similar to those described in literature : Molina and Thoraya cite large cell diffuse lymphoma as being the most frequent type of lymphoma [9,10]. Tolo in his series observed a superposable value to ours (17.20%) [6].

On the other hand Diomande found a predominance of lymphoblastic lymphoma in (56.43 %) [11]. Folicular lymphomas represented only 3,5% of Lymphomas in our study whereas Solal-Celigny [12] in France and Sandeep [13] in the United States estimated that it represented 20 to 25 % of non hodgkins. Lymphoma

Immunohistology was done only in 13% of cases that is 11 patients on 86. This exam is rarely used in our region in comparison with the Maghreb [14]. The technical and financial accessibility remains a limitation to the exploitation of this exam even though it permits us improve on the management of lymphomas and increases survival notably with the uses of the monoclonal antibody (Rituximab) [15-17].

The prevalence of HIV was of 16.27%. Mwamba *et al* [18], in Uganda found an HIV serology positive in 71% of adult patients having Burkitt lymphoma and large B cell lymphoma.

The CHOP protocol was done 52 patients that is in 60.50 % of caes. We convey with Tolo Diebkilé that the CHOP is done in our economically limited context [19].

Only eight patients recieved the R CHOP protocol (9.30%), this could be explained by the low income of the population and abscence of social security.

The number of chemotherapy sessions varied in between one and eight cycles and complete remission was obtained in 32.5% of cases. Tolo Diebkilé obtained in their series 43 % of complete rémission in the treatment of diffused large cells B lymphoma [19]. On the other hand Thoraya in Egypte obtained 79.5% of complete response with 3-8 cycles in diffuse large cell lymphomasles lymphomes [10].

Limitations

It is a retrospective study. Lack of certains information did not permit us explore some variables such as follow up.

Complete remission corresponds to abscence of clinical signs, normalisation of biological and radiological (CTSCAN) exams. There is no TEP scan. Nevertheless these informations presented are useful as they give orientation for a better management of lymphomas in our context.

CONCLUSION

Non Hogkins lymphomas involves mostly men. The age range the most involved in our sample is that of 50 to 59 years with a median age of 45 years. The socio-economical level is low for almost half of the patients. The delay in treatement is was long with a mean 233.271 days (that is 7.77 months). The B evolution sign are found in more than half of the cassette as well as an important tumoral syndrome. The majority of patients have an activity index of equal to or greater than 2. The most present histological types are large cell lymphomas, small cell lymphomas and lymphoblastic lymphomas. Lymph node localisation was prédominant, but among the extra nodal localisation, bone marrow localisation was the most present. The rate of incomplete rémission was high due to the fact that the treatment was often incomplete.

In light of the increasing number of cases of NHML in the young subject, it will be important to turn towards the realities of the hemato-oncological practises in a difficult context on the infrastuctural and resource plan

Conflict of Interest

Authors declare no conflict of interest.

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