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Epidemiological, Diagnostic, Therapeutic and Evolutionary Profile of Patients with Follicular Lymphoma from 2012 to 2015 in Casablanca (Morocco)

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Abstract: *Background:* Follicular lymphomas are indolent lymphomas of low incidence in Africa. They are considered incurable, but recent progress has led to a significant increase in survival. The aim of our work is to describe the epidemiological, diagnostic, therapeutic and evolutionary profile of patients followed for follicular lymphoma in Casablanca, Morocco. *Patients and methods:* During the period of January 1, 2012 to December 31, 2015, were included, all patients diagnosed of follicular lymphoma on a histological and immunohistochemical study of the ganglion or the affected tumor tissue. The treatment was either a therapeutic abstention or chemotherapy with or without Rituximab. *Results:* 53 (6.4%) of the 841 patients followed-up for non-Hodgkin's lymphoma had follicular lymphoma, only 35 were included in this study. The median age of diagnosed patients was 56.1 years [27; 87] and the sex ratio 2. The primary site was the ganglion in 28 (80%) patients and 71.5% of the patients were at stage III and IV of Ann Arbor at diagnosis. According to the FLIPI score 1 about 1/3 of the patients were classified as low risk, intermediate risk and high risk, respectively. 3 (9.4%) patients were under supervision/observation, 1 patient under CVP, 13 (40.6%) patients on CHOP, 1 patient on R-chloraminophen, 14 (43.6%) on R-CHOP. In the R-CHOP group, 85.7% of the patients were on CR with a median remission of 25.8 months. 3 patients in the R-CHOP group had/received maintenance with rituximab. *Discussion and conclusion:* Follicular lymphoma is of low frequency and is often revealed by lymphadenopathy. The patients are diagnosed at an advanced stage. The R-CHOP protocol with rituximab maintenance is the most used and best protocol for our patients.

Keywords: Follicular Lymphoma, Frequency, Rituximab, Survival

1. Introduction

Follicular lymphoma (FL) is a non-Hodgkin lymphoma (NHL) of the B lymphoid lineage derived from germinal center cells: centroblasts and centrocytes [1, 2]. They represent 70% of indolent lymphomas [3]. In contrast to developed countries where its incidence is 20 to 25% of lymphomas [4, 5], in developing countries and particularly in Africa it is low: 13.2% in Algeria, 13.8% in Egypt [6]. The therapeutic progress of the latter has significantly improved the prognosis with an increase in life expectancy [2].

In Morocco, the management of lymphomas and in particular follicular lymphomas has been improved in recent years, but their incidence is not known due to a lack of registry.

The aim of our work is to describe the epidemiological, clinical, biological and evolutionary profile of patients diagnosed with follicular lymphoma in Casablanca, Morocco.

2. Patients and Methods

During the period of January 1, 2012 to December 31, 2015, were included, all patients diagnosed of follicular lymphoma on a histological and immunohistochemical study of the ganglion or the affected tumor tissue. The panel used for immunophenotyping is CD20, CD10, bcl2, bcl6 and CD5. Extension assessment consisted of clinical examination, cervico-thoraco-abdomino-pelvic CT scan, chest X-ray, abdominal ultrasound, osteomedullary biopsy, blood count, and LDH assay. The pre-treatment assessment was based on cardiac ultrasound and hepatitis B, C and HIV viral serologies. The prognostic stratification was based on the FLIPI score 1. Only patients who had a high tumor mass were put on treatment. These patients had one of the following criteria: lymph node or extra ganglionic location > 7 cm; at least three lymph node locations in 3 different areas, each with a diameter > 3 cm; troubling localization (pleural or peritoneal effusion, ureteral compression, epidural localization...); splenomegaly beyond the umbilical line; blood cytopenia. The treatment was heterogeneous, either therapeutic abstention or chemotherapy (CHOP (Cyclophosphamide-Adriamycin-Oncovin-Prednisone), CVP (Cyclophosphamide-Vincristine-Prednisone), with or without immunotherapy (R-chloraminophen, R-CHOP) and sometimes a maintenance with Rituximab.

The data were collected retrospectively on a pre-established form containing the epidemiological, diagnostic, extension and pretreatment components. The analysis of the results was by SPSS 20.0 type software. Descriptive statistics were used to summarize the data. The qualitative variables were expressed as frequency, while the quantitative variables were expressed as median and their standard deviations. Correlations between the variables were tested by the chick test. The materiality threshold was set at 0.05.

3. Results

Epidemiological aspects

During the study period, 841 cases of NHL were identified, 53 (6.3%) of which were of follicular lymphomas. The median age at diagnosis was 56.1 years with extremes ranging from 27 to 87 years. There was a male predominance of 33 men for 20 women with a sex ratio of 1.65.

Of the 18 patients who exercised a professional activity, 10 worked in the agricultural sector, 3 were laborers, 2 in the industrial sector and 3 in the tertiary sector (trade, services).

After the first consultation, we lost sight of 18 patients and only the remaining 35 patients were included for the study of diagnostic, therapeutic and progressive (evolutionary) aspects.

Diagnostic aspects

The median time from the onset of symptoms to the first visit was 9 months with extremes of 2 months to 17 months, and that between the first visit and diagnosis was 9 days with extremes of 1 day to 30 days.

The majority of patients, 22 (65.75%) had a performance status (PS) WHO score between 1 and 2, 4. 11.4% of the patients had a WHO PS at 0, 6. 17.1 patients were at a WHO PS at 3 and 3 (8.6%) patients were at WHO PS at 4.

The primary site was the lymph node in 80% of cases, followed by digestive localization in 8.6% of cases, the spleen and the bone in 5.7% of cases each.

According to the classification of Ann Arbor 25 (71.5%) patients were at stage III and IV and 10 (28.5%) patients were at stage I and II (table 1).

Table 1. *Case Distribution at Diagnosis by Ann Arbor Extension Stage.*

Stratification Ann Arbor	Number of cases	%
I	4	11.4
II	6	17.1
III	17	48.6
IV	8	22.9
Total	35	100

Histologically, the 35 cases of FL were confirmed by anatomy pathology and immunohistochemistry, but only in 20 cases were the histological grades specified, 12 cases, that is to say 60% were grade 1, 7 cases (35%) grade 2 and 1 case (5%) grade 3A.

The prognostic stratification according to the FLIPI 1 score was established in 32 patients, i.e. approximately 91.4% and 12 (37.5%) patients were classified as high risk (Table 2).

Table 2. *Distribution of cases by FLIPI score 1.*

Prognosticgroup	Number of cases	%
Low risk	11	34.4
Intermediate risk	9	28.1
High risk	12	37.5
Total	32	100

Therapeutic and evolutionary aspects

The median time from diagnosis to treatment was 4 days with extremes of 0 to 22 days.

Of the 35 patients, 6 (17.1%) were abstaining from therapy, 14 (40%) had benefited from R-CHOP, 13 (37.1%) were on CHOP, 1 (2.9%) on CVP and R-chloraminophen for only one patient.

Of the 14 patients who received R-CHOP, 12 (85.7%) were in complete remission (CR) with a median CR duration of 25.8 months, only 3 patients (21.4%) received rituximab for maintenance (Table 3).

Table 3. *Therapeutic Results.*

Therapeutic regimen	Number of cases	CR	median CR (mois)	Relapse	Death	Lost of sight
Abstention	3					
R-CHOP	14	12 (85.7%)	25.8	2 (14.3%)	0	3
CHOP	13	11 (84.6%)	16.5	1	0	1
CVP	1	1	26	1	0	1
R-chloramin	1	1	21	1	0	0

Of the 13 patients on CHOP, 11 (84.6%) were on CR with a median CR duration of 16.5 months, and 1 patient was relapsed after 18 months of CR.

The event-free survival patients regardless of the treatment regime at 40 months were 84% (figure 1).

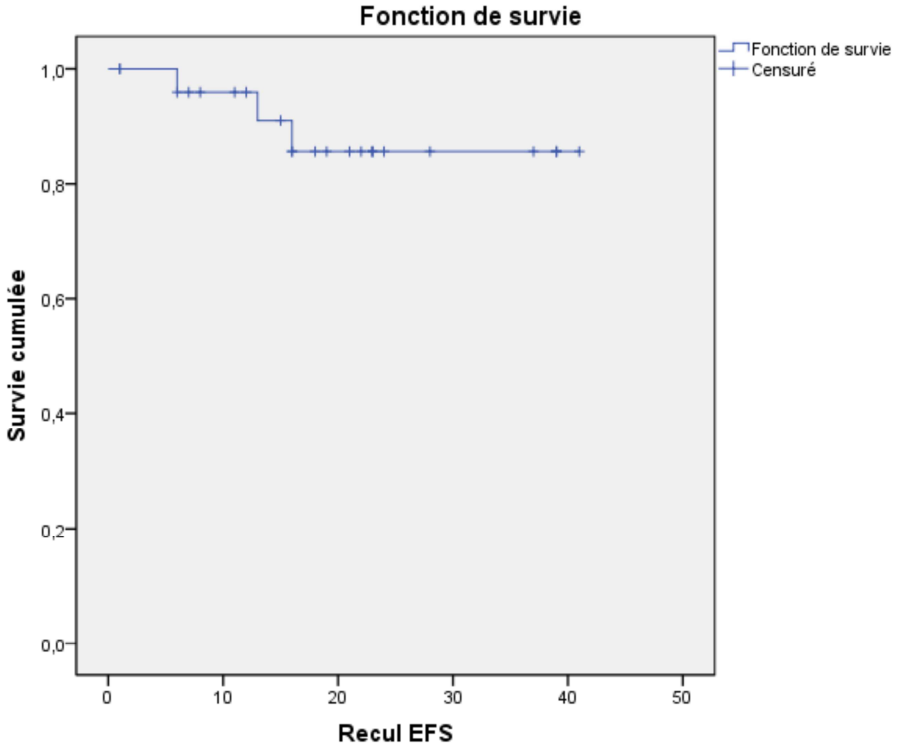

Figure 1. *Event-free survival of patients followed for follicular lymphoma.*

4. Discussion

In our 841 NHL series, FL represents 6.4%. This frequency is that of the largest clinical hematology center in Casablanca, Morocco. There are several other public and private centers for lymphoma management in Morocco; the availability of the registry would permit to have an incidence of lymphoma in general and particularly that of FL. The incidence of FL reported in southern countries is 13.2% in Algeria, 13.8% in Egypt [6], 13.3% in Nigeria [7], 6.3% in Taiwan [8], 8.1% in Pakistan [9], 8% in the Philippines [10] and 1.5% in Gabon [11]. The incidence is 6.2% in Korea [8] and 6.4% in Hong Kong [9]. These different rates contrast with higher rates in the industrialized countries of North America and Western Europe, which vary between 20% and 33% [14]. These similarities of frequencies found in Asia and Africa despite their different ethnic origins and geographical locations are more in agreement with a dominant effect of the environment rather than genetic influences. This is also consistent with data derived from Asian emigrants in the United States and their descendants, in which emigrants in the United States appeared to maintain the risk of disease of their country of birth, whereas the incidence of children born in the United States has approached those of whites born in the United States [15, 16].

The median age at diagnosis which is 56.1 years is lower than that reported by the team of Sebban C. in 2014, which is 63 years old [17]. The Kane EV team in 2012 found in their study of menstrual and reproductive factors and the use of hormonal contraception in association with non-Hodgkin's lymphoma a slight female predominance sex ratio H/F: 1/1.7 in FL [18] contrary to the male predominance found in our study.

The median time between the first consultation and the diagnosis which is 9 days with extremes of 1 day to 30 days is better than the 30 days with the extremes of 8 days to 72 days found by the team of Dakar in 2002 [19]. On the other hand, as in their study, our patients are diagnosed at an advanced stage since 71.5% are at stage III and IV of Ann Arbor. This large proportion of patients with advanced FL is justified by the delay between the onset of symptoms and the first consultation, which is 2 months to 19 months.

The histological stratification finds grade 1 and 2 in 95% of cases, which is superimposable to what is reported in the literature [17].

The positron emission tomography (PET) scanner which is now recommended for the initial assessment of extension and evaluation [20, 21] is done in our department only for evaluation of patients in whom the tomodensitometry does not allow a good estimate of the response to therapy.

For the prognostic group classification, the choice of FLIPI 1 was made because not all patients had the β2 microglobulin at diagnosis. The low risk group in our study which is 34.4% is close to the standards which are 36% [22].

The intermediate group that is 28.1% is less than 37% reported in the literature [22]. The 37.5% of the high risk group is more than the standards which are 27% [22].

The majority of our patients were without social coverage, which makes it difficult to use rituximab because the molecule was expensive; but since 2016 in Morocco, all patients routinely benefit from rituximab. The starting of treatment is based on the presence of criteria of high tumor mass. Patients on R-CHOP have an 85.7% remission and a median CR duration of approximately 26 months, better than other chemotherapy regimens. It is now the only diet used in our center for FL. Maintenance with rituximab is now a routine.

The survival of patients of all treatment regimens at 40 months is 84% comparable to international standards [17].

5. Conclusion

FL is of low frequency and is often revealed by lymphadenopathy. The patients are diagnosed at an advanced stage. The R-CHOP protocol with rituximab maintenance is the most used and the best protocol for our patients. The establishment of the register will enable us to know the incidence of NHL and particularly that of the FL.

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