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Research Article

PROGNOSTIC FACTORS OF NON-HODGKIN LYMPHOMA: RETROSPECTIVE STUDY IN UNIT BLOOD SERVICE OF THE INTERNAL MEDICINE DANTEC IN DAKAR (SENEGAL)

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ABSTRACT

INTRODUCTION: The non-Hodgkin's lymphoma is the monoclonal proliferation of B and T lymphocyte cells, responsible for the development of tumors in lymphoid organs. The objective of this study was to describe the prognostic factors for NHL and their impact in the care of patients

METHODOLOGY: This is a descriptive retrospective study on patients hospitalized files Medical Clinic I of the Aristide Le Dantec Hospital from January 2005 to December 2009. Were included in the study, patients for whom diagnosis of non-Hodgkin lymphoma was made on the basis of the results of histological and / or immuno-phenotypic examination of the biopsy specimen. Prognostic factors were studied and classified according to the prognostic scores in order to assess their impact on patient survival. Data analysis was done thanks to the IPSS software and the significance level was set at $p \leq 5\%$.

RESULTS: NHL 44 cases represented on all patients hospitalized for haematological malignancies during this period, a prevalence of 45.4%. We have noted an increase in the incidence of NHL 2005 to 2009. The sex ratio was 2.6 / 1 and the mean age was 46.77 years [17-78 years]. Among the general symptoms, fever and weight loss were in the forefront (61.4% of patients) and lymph nodes were the most frequent physical signs (75%) followed by splenomegaly (47.7%). anemia was found in 72.7% of cases, leukocytosis in 45.5% of cases and thrombocytopenia in 47.7% of patients. Thirty-seven point four percent of patients were classified stage IV Ann Arbor at diagnosis. The presence of general signs scalability B was observed in 70% of patients. Regarding the prognostic factors, the International Prognostic Index (IPI) was studied in 43.2% of patients (n = 19) patients showed that 16% (n = 3) were IPI 1; 37% (n = 7) had an intermediate risk (IPI 3 and 4) and the remaining 10% were high risk (IPI 4). The IPI adjusted for age (aaIPI), noted a correlation of the IPI with certain age groups (50 and 60 years, p = 0.00001, 60 and 70, p = 0.00001). All patients were classified LLC Binet stage C and FLIPI was low (1-2). Evolution were marked by a 100% survival for low-risk patients (with a statistically significant correlation between survival and IPI 1: p <0.00001) and a death rate of 100% for high-risk patients (p <0.00001). The evolution was marked by a prolonged clinical and laboratory remission in 61.3% of cases, 11.4% of patients lost to 27.4% of deceased patients.

CONCLUSION: Poor prognostic factors for lymphomas are mainly represented by the advanced Ann Arbor, international prognostic index (IPI) high and the presence of clinical signs of disease progression of the dice inclusion.

INTRODUCTION

Non-Hodgkin lymphomas represent a heterogeneous group of tumor entities of lymphoid origin, as distinguished from Hodgkin's disease. They bring together a large number of distinct morphological features, clinical presentation and outcome variables respond to treatment differently [1, 2].

Thus, in order to better clarify the characteristics of this disease in Senegal, we undertook this work which has for objective to describe all the epidemiological, clinical, therapeutic and prognostic NHA in the Internal Medicine Department and their impact prognostic.

PATIENTS AND METHOD

This was a descriptive retrospective study from January 2005 to December 2012, which had the framework, the Unit of Haematology Medicine Department of Internal Clinic of the University Hospital Aristide Le Dantec.

Was included in the study all patients with NHL, with assessment of the following prognostic factors:

- IPI (International Prognostic Index)
- FLIPI (Follicular Lymphoma International Prognostic Index)
- The classification Musshoff (gastric MALT)
- The classification Binet (LLC).

RESULTS

- **Epidemiological data:**

NHL 44 cases represented on all patients hospitalized for haematological malignancies during this period, a prevalence of 45.4%.

Our series consisted of 32 men, a percentage of 72.7% and 12 women, a percentage of 27.3%. The sex ratio was 2.6 / 1.

The average age of our patients was 46.77 +/- 19.39 years with a range from 17 to 78 years. The 60-69 age groups were the most representative, with a frequency of 25%, followed by the 20-29 age groups with a frequency of 18.2%.

- **Clinical Data:**

Fever and weight loss were the most frequent general signs up with 61.4% of cases. They were followed by asthenia with 52.3% and anorexia with 36.4% of cases.

Superficial lymph nodes were physical signs most frequently encountered in 75% of cases (n = 33), followed by splenomegaly, with a percentage of 47.7% (n = 21). Hepatomegaly was found in 6.8% of cases (n = 3).

The bilateral nature of lymphadenopathy (60.61%) was more frequent compared to the unilateral nature. The cervical area was the most affected with a percentage of 93.9% (n = 31), followed by the inguinal area with 60.6% (n = 20) and the axillary area with 48.5% (n = 16).

- **Biological data:**
  - Anemia was found in 72.7% of cases (n = 32); she was microcytic in 18.2% of cases (n = 8).
  - The leukocytosis was noted in 45.5% of patients (n = 20). The presence of lymphoblasts was noted in 11 patients, a percentage of 25%. Lymphocytosis was observed in 40.9% of cases (n = 18); likewise, neutrophilia was present in 11.4% of cases (n = 5).
    Furthermore, the presence of shadows of Gumprecht was noted in three holders CLL patients (30%).
  - Thrombocytopenia was present in 47.7% of cases (n = 21).
- The chest X-ray found a widened mediastinum with the presence of deep lymph nodes in 6.8% of patients. Abdominal ultrasound highlighted the deep lymph nodes in 18.2% of patients and epigastric mass in 4.5% of patients.
- Bone marrow biopsy moving towards a LLC in 20.4% of patients with spinal extension lymphoma in 11.4% and a reaction marrow in 6.8% of patients.
- The lymph node biopsy was performed in 52.3% of patients and, linked or not to immunophenotyping allowed to classify patients.

Histologically and according to the WHO classification 2001:
- Chronic lymphocytic leukemia was the most common NHL with 31.3%. Leukocytosis was

noted in 90% of cases with constant lymphocytosis and shadows of Gumprecht were present in 30% of cases with a statistically significant correlation (p = 0.005).

- Lymphoma diffuse large B cell lymphoma was the second in the WHO classification with 28.1
- Lymphoma T represented 9.1% of all lymphomas
  According to the working use classification (WF = Working Formulation)
- Intermediate grade lymphomas were the most common, 16% of cases.

• On the evolutionarily, 37.4% were classified as stage IV Ann Arbor at diagnosis. The presence of general signs scalability B was observed in 70% of patients.

• Regarding prognostic factors, the International Prognostic Index (IPI) was studied in 43.2% of patients (n = 19) patients. Of these patients, 16% (n = 3) had a lower risk index, or IPI 1; 37% (n = 7) had intermediate risk (IPI 3 and 4) and the remaining 10% were at high risk (IPI 4).

These prognostic index had no statistically significant correlation with age (p = 0.216), nor with sex (p = 0.381). Low-risk and intermediate - low (IPI 1 and 2) were present mainly in subjects under 50, while the intermediate risk - high (IPI 3) was more frequently found in patients over 60 years. This reflects the role of age in the evolution of lymphoma prognosis, hence the concept of IPI adjusted for age (aaIPI), especially as we noted a correlation with certain IPI age groups (50 and 60 years, p = 0.00001, 60 and 70, p = 0.00001).

- The FLIPI was applied to two patients with follicular lymphoma that also at low risk (FLIPI 1 and 2).
- The Binet score was used for all patients with CLL. These patients were all at an advanced stage, so classified Binet stage C. There was no correlation between score Binet, epidemiology and general signs.
- The evolutionary terms were marked by a 100% survival for low-risk patients (with a statistically significant correlation between survival and IPI 1: p <0.00001) and a death rate of 100% for high-risk patients (with statistically significant correlation between 4 and IPI death: p <0.00001); while the

results were intermediate for stages 2 and 3. The outcome was favorable in 40% of patients with Binet C score no statistically significant correlation.

- With regard to the therapeutic aspects, CHOP was most used (36.4%), followed by the COP protocol (11.4%). Rituximab has been used in 2.3% of patients and 4.5% of patients received radiotherapy. General side effects were found in 15.9% of patients; gastrointestinal side effects in 16% of cases and biological complications 29.5% of patients, including two cases of chemotherapy-induced suppression.

The evolution was marked by a regression of symptoms in 61.3% of cases, while 11.4% were lost to follow and 27.4% had died.

DISCUSSION

Lymphoma Low grade was the most representative with a frequency of 41.7% lymphomas classified by WF. In the study of Tolo [3] however, it was less frequent with only 29.8% of cases, behind the 34% intermediate grade and high-grade lymphoma was more frequent with 36.2%. A male predominance was noted statistically significant (p = 0.001). The average age of onset was 37 years. The most representative age group in the study of Tolo was that of 40-49 years and the most common clinical signs were superficial lymph nodes, followed by impaired general condition, stage III / IV were the most frequent, significant number of patients lost to but clear regression of tumor syndrome after one to two treatments.

Plan on prognosis, patients with diffuse large cell lymphoma B, with the same histological appearance and the same evolutionary stage, and does not have the same clinical course, has led to develop the concept of prognostic factors [4]. This led to the development of the International Prognostic Index (IPI), based on age, life stage of the disease, lactic dehydrogenase rate, performance status of WHO and the number of extranodal site.

Of the 44 patients, nineteen (19) patients have benefited from the IPI classification, two (02) of the FLIPI classification, and ten (10) of the Binet classification [5].

In our study, patients with IPF 1 numbered

3, a percentage of 16%, while patients with IPI 2 or 3 were an equal number of patients, a percentage of 37% and IPI score 4 was noted in two patients (10%).

This data is discordant with those noted in several Western studies, including that of Todeschini [6] who found a clear predominance of low-risk patients (IPI 1) with 59.4%, followed by intermediate risk with 18.1% 16.6% (stage 2 and 3, respectively) and 5.7% with stage 4. Chung et al. [4] found results similar to those of Todeschini with IPI 1 in 46.8% of patients, a score 2-3 in 45.6%, and a score 4 to 7.6% of patients; patients with spinal cord lesions had a higher prognostic index. This difference in distribution to our study, where the score 1 is not found can be explained by delayed diagnosis noted the consultation delays and delays when the diagnosis is made by histopathology.

The study of Blay [7], covering the cerebral localization of lymphoma, was, in turn, rates varying between 20% (IPI 1) and 28% (IPI 4), to 28 and 24% (respectively IPI 2 and 3).

Regarding the distribution by age, 1 to prognostic index was found mainly in the 30-40 age group; intermediate risk (IPI 2 and 3) in subjects under 50, while the high-risk (IPI 4) was noted in older subjects, more than 60 years. This reflects the important role of age in the prognosis of patients with NHL, as reported Hasselblom [8] in a study conducted in Sweden, where the average age at diagnosis was 72 years, was at high risk IPI in 34% of cases.

The influence of age on the IPI led to the simplification IPI adjusted for age (adjusted IPI age: aaIPI). It then has three risk factors: clinical stage, general condition and LDH. In France, in subjects under 60 years without risk-adjusted IPI factor, the overall 5-year survival is 80%. In patients less than 60 years of age with 2 or 3 factors aaIPI, overall survival at 8 years was 64%. [9].

In our study, there was a death rate of 100% in patients with an IPI to 4 and a 100% survival rate in patients with an IPI to 1; patients with IPI between 2 and 3 had intermediate results (71.45% survival for IPI 2 and 83% for patients IPI 3). Thus, we find an excellent prognosis for IPF 1, intermediate forecasts for the IPI 2-3 and a poor prognosis for the IPI 4. These results are broadly similar to those found by Shipp et al. [10]; Indeed it was the percentage of 5-year survival ranging from 26% for IPI 4-73% for IPI 1, to 51% for IPI 2 and 43% for IPI 3, the latter two being considered intermediate stages. Note that the workforce was relatively high in 2031 with patients from diverse backgrounds. The complete remission rate in the study of Blay [7] varied between 51.1% and 83.7% for patients with a score between 1 and 2 and 50% to 66.6% for patients with a score between 3 and 4. The Chung et al. [4] found results similar to those of Todeschini with IPI 1 in 46.8% of patients (5-year survival of 64.7%), a score 2-3 in 45.6% (5-year survival between 38.2 and 24.3%) and a score 4 to 7.6% of patients (5-year survival 26.7%).

The trend in conventional treatment of patients with follicular lymphoma was almost always fatal. These treatments altered little natural history of the disease, with morbidity and variable costs. Thus, the influence of various prognostic factors was investigated in follicular lymphoma. Based on five parameters, the FLIPI can separate patients into homogeneous risk groups, with very significant differences in survival between the three groups. Patients with follicular lymphoma, FLIPI with between 1 and 2, and a statistically significant correlation (p = 0.0001), had a 100% survival rate. This is comparable with the data reported in the literature, including Tilly [11], which yields a survival rate of 80% at 10 years. Solal-Céligny [12] in the first study on the validity of FLIPI percentage was 49% for patients with a low risk, with a survival rate at 5 years of 88.1% and 67.3% 10 years.

The classification used in this study for prognostic factors for CLL is that of Binet [5] with its three stages. The advantage of this classification is to determine whether the disease will remain stable or, conversely, grow. However, it should be noted that in our study, all patients were at an advanced stage, so classified stage C.

The multicenter study Sarfati et al. [13] carried out in several centers found a clear predominance of stages A (68%) while stage C was only 15%. In Ivory Coast [3] , 24% in stage B and stage C was less representative with 16%. Also, Step A was more frequent (52%), but the stadium was more C found that the stage B with 28%.

This delay in diagnosis noted in our regions could be due to the fact that the LLC is an indolent

disease, progressive evolution over several years, resulting in a delay in the consultation and in the orientation of the patient. Difficult access to laboratory tests (blood count, bone marrow biopsy, immunophenotyping) may also explain this diagnostic delay.

The survival rate was 40%. This poor prognosis in advanced stages of the disease is confirmed by Sarfati [13], in which the survival rate was 37%, with a statistically significant correlation (p <0.00001). The death rate was 46% in the IvoryCoast [3].

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CONCLUSION

Bad prognostic factors for lymphomas are mostly represented by the advanced stage Ann Arbor, international prognostic index (IPI) high and the presence of clinical signs of disease progression of the dice inclusion. Through our study, we noted an evolution marked by a 100% survival for low-risk patients, and a death rate of 100% for high-risk patients.

CONFLICT OF INTEREST

None.

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