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THE CONTRIBUTION OF THE LABORATORY IN THE DIAGNOSIS AND MONITORING OF CHRONIC LYMPHOPROLIFERATIVE SYNDROMES: THROUGH AN EXPERIENCE AT THE LABORATORY OF CHEIKH ZAID HOSPITAL

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SUMMARY

This retrospective study carried out at the Cheikh Zayed Hospital Laboratory in Rabat explores Chronic Lymphoproliferative Syndromes (CLLS), a group of diseases characterized by excessive proliferation of lymphoid cells. Based on the analysis of 79 patients between 2020 and 2022, the study shows that multiple myeloma is the most common type of SLPC (95%), followed by chronic lymphocytic leukemia and hairy cell leukemia (2.5% each). The patients, mainly elderly (63.6 years on average), often present bone pain as their main symptom. The study highlights the importance of a multidisciplinary approach and advances in laboratory techniques to improve the diagnosis and monitoring of these diseases.

KEYWORDS: SLPC, multiple myeloma, chronic lymphocytic leukemia, hairy cell leukemia, diagnosis, epidemiology, clinical characteristics.

INTRODUCTION

Chronic lymphoproliferative syndromes (CLLS) include a heterogeneous group of hematological disorders characterized by excessive and persistent proliferation of lymphocytes. These pathologies, ranging from benign forms to malignant conditions, include chronic lymphocytic leukemia, non-Hodgkin lymphomas and multiple myeloma.[1] Accurate diagnosis and ongoing monitoring of these diseases rely heavily on laboratory testing, including complete blood count (CBC), immunophenotyping, and protein electrophoresis. These tools not only confirm the diagnosis, but also monitor progress and guide therapeutic decisions.[2] In this context, our retrospective study carried out in the laboratory of Cheikh Zayed Hospital aims to evaluate the specific contribution of biological analyzes in the diagnosis and monitoring of SLPC, while taking into account regional particularities.

MATERIAL AND METHODS

Type and Duration of the Study: This retrospective study took place over a period of 3 years (January 2020 to December 2022), covering 79 cases of chronic lymphoproliferative syndromes (CLLS) documented in the laboratory of Cheikh Zayed Hospital.

Location of the Study: The analyzes were carried out in the Hematology and Immunology departments of the laboratory, equipped with advanced technologies such as cytohematology machines and equipment dedicated to hemostasis.

STUDY POPULATION

- **Inclusion criteria:** Patients with persistent hyperlymphocytosis ($\geq 5x10^9$/L for more than 3 months) with additional examinations validating a diagnosis of SLPC (hemogram, blood smears, myelogram, etc.).
- **Exclusion criteria:** Incomplete files or cases of reactive/transient hyperlymphocytosis.

DATA COLLECTION

The data were extracted from hospital archives and recorded on a form including.

- Epidemiological information (age, sex, origin).
- Clinical and paraclinical results (hematological and immunological).

Statistical Analysis: Data were compiled in Excel 2021 and analyzed via Jamovi (v2.3.24) for descriptive analyses. Qualitative variables are presented as percentages, while quantitative data are described by measures of central tendency (mean, median) according to their distribution.

Ethical Aspects: This study received approval from the ethics committee of the Abulcasis International University of Health Sciences, with strict respect for patient anonymity and confidentiality.

RESULTS

Epidemiological characteristics of the sample

- Our total sample included 79 patients.
- The sex ratio was 1.26 with a slight male predominance.
- The average age was 63.6 ± 11.4 years with age extremes of 18 and 87 years. More than half of the patients were adults under 63 years old.

Distribution according to the type of chronic lymphoproliferative syndrome

- Three major lymphoproliferative syndromes were diagnosed in our study.
- Multiple Myeloma was the majority syndrome, found in 95% of patients.
- The other two syndromes were Chronic Lymphocytic Leukemia and Hairy Cell Leukemia, diagnosed in 2.5% of the sample.

Distribution according to clinical signs: Among the 79 patients, 57.4% suffered from bone pain. Back pain and signs of weight loss each affect 7.4% of patients, while 4.4% have various fractures.

Table 1: Distribution of the population according to clinical signs (N=79)

Clinical signs	Percentage (in %)
Bone pain	57.4%
Back pain and weight loss	7.4%
Fractures	4.4%
Asthenia, Fever, hip and chest pain.	2.5%

Description according to the types of chronic lymphoproliferative syndromes

1 - Multiple myeloma

- 75 patients had Multiple Myeloma.
- The average age was 64 years, with a male predominance with a sex ratio of 1.21.
- **At the Blood Count**
- Anemia was found in 68.7% of cases.
- It was isolated in 52% of cases, associated with thrombocytopenia in 16.7% of cases, and absent in 30.8%.
- 66% of cases had red blood cells in rolls on the blood smear, and all patients had plasmacytosis on the myelogram.
- The Sedimentation Speed was accelerated in 68% of cases.
- On serum protein electrophoresis and immunofixation, monoclonal gammopathy was identified in all patients.
- Kappa type IgG in 68% of cases - Lambda type IgG in 11% of cases.
- Kappa type IgA in 7% of cases - Kappa type IgM 5% of cases.
- Kappa light chains in 9% of cases
- Lacunar bone lesions typical of multiple myeloma were found on bone imaging in 12.5% of cases.

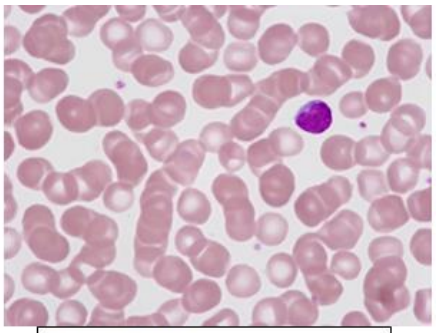

Figure 1 : Hématies en rouleaux

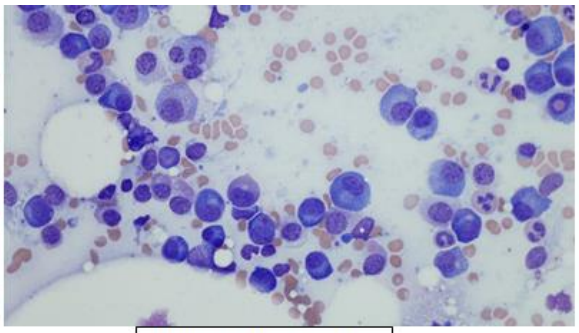

Figure 2 : Plasmocytes

2 - Chronic lymphocytic leukemia

- We found 2 cases of Chronic Lymphocytic Leukemia, a man and a woman, aged 62 and 58 years old.
- These two patients had the same clinical signs, namely peripheral lymphadenopathy and hepatosplenomegaly.
- On biological explorations, the results were significantly similar in the two cases, With hyperlymphocytosis associated with normochromic aregenerative anemia on the CBC, Small lymphoid cells on the blood smear, with a morphology reminiscent of Gumprecht's Shadows. As well as lymphocytic infiltration with a reduction in other lineages on the myelogram.

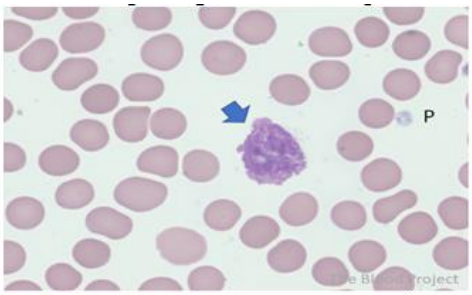

Figure 3 : Shadows of Gumprecht

3 - Hairy cell leukemia

- We found 2 cases of Hairy Cell Leukemia, a man and a woman, aged 62 and 75 years old.
- Patient 1 presented splenomegaly while patient 2 presented asthenia with palpitations.
- In the biological explorations, the results were significantly similar in the two cases, with.
- à non-regenerative normochromic normocytic anemia with associated thrombocytopenia,
- The presence of cells with hairy projections at the ends of the lymphocytes in the blood smear,
- As well as an infiltration of hairy cells on the myelogram.

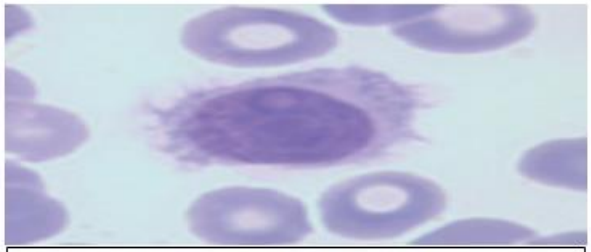

Figure 4: Hairy cells at the ends of lymphocytes

DISCUSSION

Prevalence of SLPC

- Global prevalence: 4% of cancers with 726,000 new cases in 2020 (Globocan 2020). SLPC mainly affects older men (median 70 years)[3] and is more common in high-income countries.[4]
- In Morocco: SLPC represents 26% of hematologic malignancies. Between 2004 and 2007, the incidence of hematological malignancies was 8.4/100,000 inhabitants (Casablanca register).[5]

Epidemiological aspect

- In Morocco, SLPC mainly affects the elderly, with a median age at diagnosis of 60 years, slightly lower than that of high-income countries.[5]
- A male predominance is observed, with a male/female ratio of 1.61.
- These epidemiological variations can be explained by differences in risk factors and access to diagnosis.[5]
- In this study, multiple myeloma represented 95% of cases, while chronic lymphocytic leukemia and hairy cell leukemia each constituted 2.5% of cases.

Socio-demographic characteristics

- In our study, the average age of patients was 63.6 years, with a balanced distribution between adults (53.3%) and elderly people (47%). This result is close to that observed in the United States, where the median age at diagnosis of multiple myeloma is 69 years.[6]
- A male predominance was noted (56% men versus 44% women), in contrast with a slight female predominance reported in Australia for SLPC.[7]
- The majority of patients were from Rabat (58.2%), a geographical distribution that would be interesting to compare with similar international studies.
- Bone pain was the most common symptom, affecting 57.4% of patients, consistent with studies showing that this symptom is common in multiple myeloma due to bone marrow infiltration and complications such as osteoporosis and fractures.[8]

Multiple myeloma

- Anemia: Present in 69% of patients, either isolated (52%) or associated with thrombocytopenia (16.7%). These figures are comparable to those of Kyle et al. (2003), who report a prevalence of 73% at diagnosis. In our study, the anemia was predominantly normochromic and normocytic (87%).[9]
- Blood smear: Rolled red blood cells were observed in 66% of patients, a typical feature of multiple myeloma due to the high concentration of monoclonal immunoglobulins. This is consistent

with the results of Kaur et al. (2017) in India (63%).[10]

- Myelogram: Medullary plasmacytosis varied from 2% to 90%. Medullary infiltration ≥10% remains a key criterion for diagnosis, in accordance with international recommendations.[11]

Table 2: Comparative table of the proportions of Immunoglobulins found in our patients with those found in the study by Kyle et al. (2003) in the United States.

Type d'Immunoglobulines	Proportions found in our patients	Proportions found in the study by Kyle et al. (2003)
IgG de type Kappa	68%	49%
IgG de type Lambda	11%	6%
IgA de type Kappa	7%	21%
IgM de type Kappa	5%	8%
Kappa light chains	9%	16%

- Monoclonal immunoglobulins and light chains: Multiple myeloma is marked by excessive production of monoclonal immunoglobulins, mainly of the IgG or IgA type, while IgM is rarely involved. A study by Kyle et al. (2003) on 1027 patients reported a distribution of 52% IgG, 21% IgA and 16% light chains only. Our results show an increased prevalence of Kappa type IgG (77%), consistent with the classic Kappa/Lambda ratio (2:1), but a lower proportion of light chains only.[9]
- Sedimentation rate (ESR): Accelerated ESR was observed in 68% of patients in our study, close to the 70% reported in India (2017). This marker, although not specific, often reflects hyperviscosity linked to increased production of monoclonal proteins.
- Radiological signs: In our study, 12.5% of patients presented bone gaps on imaging, compared to 40% reported in China (2019). This variation could be explained by differences in disease stages, imaging techniques or their interpretation.

Chronic lymphocytic leukemia

- **Clinical and biological characteristics:** CLL is manifested by persistent hyperlymphocytosis, defined by a diagnostic threshold ≥ 5 x 10^9/L. The values observed in our study (5.8 x 10^9/L and 6.6 x 10^9/L) confirm this characteristic.[5] Normocytic normochromic anemia and thrombocytopenia have also been noted, the latter being more common in advanced stages. These abnormalities are often due to marrow infiltration, hypersplenism or immunological destruction of blood cells.[12]

- **Comparison with the literature:** A study by Hallek et al. (2018) reported similar rates of anemia (10%) and thrombocytopenia (7%) at diagnosis. Furthermore, Gumprecht's shadows, although typical of CLL, are not specific and can appear in other lymphoproliferative diseases.[12]

- **Bone marrow infiltration:** More than 80% of patients with CLL in the study by Hallek et al. presented marrow lymphocytic infiltration, an important criterion also confirmed by our observations.)

Hairy cell leukemia (LT)

- **Clinical and biological characteristics:** Our two cases of LT presented typical symptoms: asthenia, palpitations, splenomegaly, and biological abnormalities such as normocytic normochromic anemia, thrombocytopenia, and bone marrow infiltration by hairy cells.[13,14]

- **Diagnostic specificities:** Hairy cells, characterized by cytoplasmic projections on the blood smear, are pathognomonic of this disease.[15]

- **Comparison with the literature:** A study by Dearden (2012) showed that the majority of patients with LT presented splenomegaly, and approximately 80% had anemia and 70% had thrombocytopenia at diagnosis, in agreement with our results. The proportions of bone marrow infiltration by hairy cells, although significant, vary between patients.[13,14]

Recommendations

- Improve the classification of SLPC: The 2016 classification should be revised to better integrate biological and genetic parameters, in order to better predict response to treatment.
- Prevention of risk factors: Raising public awareness of the risk factors of SLPC, such as chemical exposure and smoking, could reduce their incidence.
- Development of new therapies: Research into new therapeutic options is essential, particularly for patients resistant to current treatments.
- Optimization of existing treatments: Exploring optimal drug combinations, treatment sequence and doses can improve the effectiveness of treatments.
- Multidisciplinary approach: Care involving various specialists (oncologists, pharmacists, etc.) is necessary for comprehensive patient management.
- Improved screening and diagnosis: Develop new biomarkers and imaging techniques to improve screening and early diagnosis of SLPC.
- Longitudinal studies: Longitudinal studies would help to better understand the progression of SLPC and improve prevention strategies.

- Continuing training: Promote the continuing training of health professionals to guarantee optimal care of SLPC.

CONCLUSION

Our study highlights the importance of accurate diagnosis and prognosis in chronic lymphoproliferative disorders (CLLS). As hematologists, our essential role is to establish an accurate diagnosis, correct any previous misdiagnoses, and make appropriate treatment decisions. The laboratory also plays a crucial role in providing biological tools to complement diagnostic and prognostic examinations, such as immunohistochemistry and genetics. Our multidisciplinary approach optimizes patient care by integrating our clinical expertise and laboratory resources. This approach contributes to improving the understanding of SLPC and guiding therapeutic choices, which is essential in the field of hematology. Our research paves the way for future advances in the management of SLPC and has significant implications for clinical practice.

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