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Alternative Phenotypic Profile for B-Cell Abnormality in a Case at Zinder National Hospital

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Abstract

Introduction: Since it is impossible to establish a diagnosis in the presence of hyperlymphocytosis not secondary to lymphocytic hyperactivation, we considered a B-lymphoid hematopathy with a non-specific phenotypic profile. We report one case of this. **Observation:** This is a forty-eight (48) year old patient with hyperlymphocytosis at 139,000 elements per cubic millimeter, heterogeneous splenomegaly at 25.6 cm in diameter on abdominal ultrasound without detectable deep or peripheral lymphadenopathy. Peripheral blood cytology shows lymphocyte cell proliferation suggestive of the circulating phase of chronic lymphoproliferative B syndrome. The expression profile of cell membrane markers did not allow for the definition of a specific phenotypic profile. Faced with this immunophenotyping result, we considered a B-lymphoid hemopathy with a non-specific phenotypic profile. After three courses, the MINICHOP treatment was used to achieve partial remission with wasting of more than 80% of the evaluable masses. **Conclusion:** Despite the contribution of immunophenotyping in the diagnosis of lymphoproliferative syndromes, it is possible to consider the diagnosis of a B-lymphoid hemopathy with a phenotypic non-specific profile of CD45+, monotypic kappa, CD19+, FMC7+, CD22+, CD5−, CD79b−, CD23−, CD43−, CD38−, CD200−.

Keywords

Hyperlymphocytosis, CLL, Immunophenotyping, MINICHOP

1. Introduction

In the presence of a lymphoproliferative syndrome, immunophenotyping provides precise information about the lymphocyte phenotype. The expression of certain cluster of differentiation (CD) markers [1] confirms the diagnosis. The absence of specific CD markers reduces diagnostic accuracy and consequently, the quality of patient care [2]. The addition of the additional markers should have led us to a more accurate diagnosis [3]. This is not the case in our context. According to the Strasbourg experience, in the context of hyperlymphocytosis, diagnosis can be difficult in about 20% of cases [2]. This is especially due to the lack of a specific marker [4] [5]. Only chronic lymphocytic leukemia (CLL) has a score that can be used to make a definitive diagnosis through immunophenotyping. Apart from the Matutes/Moreau score (RMH) for CLL, there are no other scores for other lymphoproliferative B syndromes (SLP-B) [2]. The absence of specific cytometric markers decreases diagnostic accuracy. This hinders the quality of management of these lymphoproliferative syndromes. This is why, since it is impossible to establish a diagnosis in the presence of hyperlymphocytosis not secondary to lymphocyte hyperactivation, we considered a B-lymphoid hematopathy with a non-specific phenotypic profile. It is for this reason that we report a clinical case in the Zinder region (Niger).

2. Case Report

We present, with his informed consent, the case of a forty-eight (48) year old patient with no significant medical history who was admitted to our department with left hypochondrium discomfort, lymphocytosis of 139,000 cells/mm^3, and accompanying infectious symptoms. The symptomatology began approximately 8 weeks ago with generalized fatigue, digestive discomfort, and left hypochondrium discomfort. The clinical course was marked by persistent fatigue, fever, increased abdominal swelling in the left hypochondrium, and cramping sensation in the thoracic limbs. Due to the persistence of these symptoms, the patient sought medical attention at the referral center of the Zinder National Hospital (HNZ), from where he was referred to the clinical hematology department for further management.

- The physical examination revealed:
  - General deterioration of the patient's condition, with a World Health Organization performance status of III.
  - Persistent fever higher than 38˚C for an extended period (more than 4 weeks).
  - Conjunctival paleness.
  - Significant splenomegaly at stage IV, with no peripheral lymphadenopathy.
- Regarding the laboratory findings: The blood count at diagnosis showed:
  - Hyperleukocytosis with a count of 175,000 cells/mm^3.
  - Lymphocytosis with a count of 139,000 cells/mm^3.

- Thrombocytopenia with a count of 96,000 cells/mm^3.
- Normocytic anemia with a hemoglobin level of 7.5 g/dL.
- Blood smear analysis revealed a proliferation of lymphoid cells suggestive of the circulating phase of a B lymphoproliferative syndrome.
- The results are summarized in Table 1.

Blood smear analysis revealed a proliferation of lymphoid cells suggestive of the circulating phase of a B lymphoproliferative syndrome, Figure 1.

Abdominal ultrasound reveals a heterogeneous splenomegaly measuring 25.6 cm in the longest axis, without deep lymphadenopathy, Figure 2.

Immunophenotyping analysis of the studied cells shows that 85% of these cells express surface immunoglobulin (IgS) with kappa light chains, CD19+, and CD45+. A high expression of FMC7+ (100%), CD22+ (99%), and CD11c+ (98%) is observed.

A low expression of CD10+ (4%) and CD5+ (14%) is also detected. The diagnostic aspects of lymphocyte immunophenotyping are summarized in Table 2.

Lymphoproliferative syndromes can be classified into four groups based on the expression of CD5 and CD10 [3]:

-CD5+/CD10+: Rare co-expression.

-CD5+/CD10−: Mainly represented by chronic lymphocytic leukemia (CLL) and mantle cell lymphoma (MCL).

Table 1. Distribution of blood count results at diagnosis.

Laboratory Findings		Values (international units)
Hemogram	Leukocyte	175,000 éléments/mm^3
	Lymphocyte	139,000 éléments/mm^3
	Thrombocyte	96,000 éléments/mm^3
	Hemoglobin Level	7.5 g/dl
	MGV (Mean Blood Cell Volume)	84 fl
Blood Smear		Proliferation of lymphoid cells

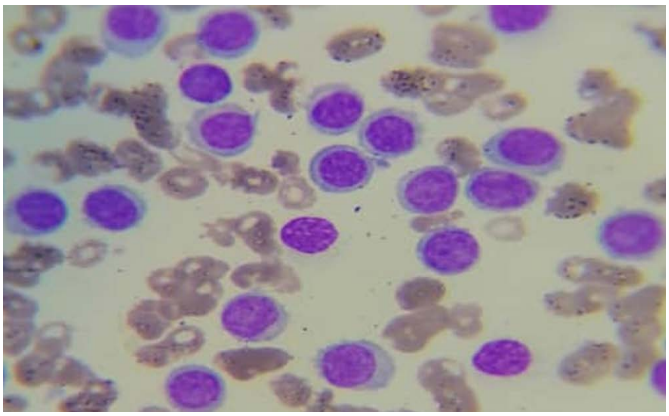

Figure 1. Proliferation of lymphoid cells on blood smear stained with May-Grünwald Giemsa (Image at immersion magnification: 100×).

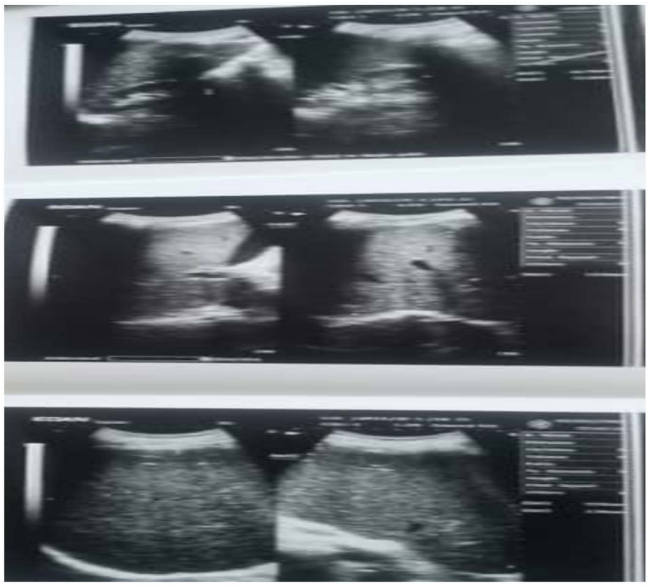

Figure 2. Splenic ultrasound at diagnosis.

Table 2. Distribution of lymphocytes by lymphoid markers.

Lymphoid Markers		**Percentage (%)**
Fenestration on lymphocytes	Proportion des cellules étudiées	85
T cells	CD3+	0
	CD3+ CD4+	0
	CD3+CD8+	0
	CD3+ CD5+	14
	CD3+CD4+CD8+	0
	CD3+CD4− CD8−	0
	CD3+CD4+CD7-	0
	CD3+ CD56+	0
	CD4/CD8	0,00
Lymphocytes NK	CD3− CD56+	0
Lymphocytes B	CD19+	97
	CD19+ CD10+	4
	CD19+ CD20+	96
Surface immunoglobulins	CD19+ Chaînes kappa	100
	CD19+ Chaînes lambda	0
B-cell markers (vs. B-cells)	CD19+ CD5+	3
	CD19+ CD23+	4
	CD19+ FMC7	100
	CD19+ CD79b+	5

Continued

	CD19+ CD22+	99
	CD19+ CD25+	3
	CD19+ CD103+	4
	CD19+ CD11c+	98
	CD19+ CD38+	4
	CD19+ CD43+	3
	CD19+ CD200+	0

Table 3. Immunophenotyping of chronic B lymphoproliferative syndromes [6] [7].

Markers	LLC	LPL	HCL	HCL-V	SLVL	MCL	FL	MZL
Surface Ig intensity	weak	Strong	Strong	Strong	Medium	Strong	Medium/Strong	Medium/Strong
CD19	+	+	+	+	+	+	+	+
CD22	−	+	+	+	+	+	+	+
CD23	+	−	−	−	+/−	−	+/−	−
FMC7	−	+	+	+	+	+	+	+
CD5	+	+/−	−	−	+/−	+	−	−
CD10	−	+/−	−	−	−	−	+/−	−
CD25	+/−	−	+	−	−	−	+/−	+/−
CD11c	+/−	−	+	+	+	−	+/−	+/−
CD103	−	−	+	+	−	−	−	−
CD79b	−	+	+	+	+	+	+	+

Legend: CLL: chronic lymphocytic leukemia; LPL: prolymphocytic leukemia; HCL (−V): hairy cell leukemia; SLVL: splenic lymphoma with villous lymphocytes; MCL: mantle cell lymphoma; FL: follicular lymphoma; MZL: marginal zone lymphoma.

-CD5−/CD10+: Usually associated with follicular lymphoma (FL).

-CD5−/CD10−: Predominantly represented by marginal zone lymphoma (MZL) and hairy cell leukemia (HCL).

In our case, this classification brings us closer to HCL, HCL-V, and MZL. The addition of additional markers should have led to a more precise diagnosis. However, this is not the case in our context. According to the experience of Strasbourg, diagnosis can be difficult in approximately 20% of cases of hyperlymphocytosis due to the lack of specific or discriminatory markers [3]. The addition of the additional markers would have led to an accurate diagnosis. In the context of hyperlymphocytosis, diagnosis can sometimes be difficult, due to the lack of a specific or non-discriminating marker [4] [5]. Some of these markers of chronic lymphoproliferative syndromes are summarized in **Table 3**.

- Therapeutically: We considered MINICHOP treatment. After 3 cycles:
  - Improvement in general condition (WHO 0).
  - White blood cell count (WBC): 10.8 G/L, hemoglobin level (Hb): 9.8

g/dL, and platelet count (Plt): 108 G/L. The results are summarized in Table 4.

– Abdominal ultrasound shows a homogeneous spleen measuring 15 cm in the longest axis (Partial remission, with approximately 80% reduction in evaluable masses), Figure 3.

3 Comments

Since CD20 was the first molecule described and used in the characterization of B lymphocytes, its expression at 96% in our patient suggests B lymphocyte proliferation. The discovery of several pan-B antigens such as CD19+, CD22+, and expression of kappa light chain of IgS has helped to better understand the population of B lymphocytes in this patient. However, the presence of additional markers such as FMC7+ (100%), CD22+ (99%), and CD11c+ (98%), and the absence of expression of markers such as CD79b− (5%), CD23− (4%), CD43− (3%), CD38− (4%), CD200− (0%) suggests a non-specific phenotypic profile of B lymphoid hematopathy. Our patient's Matutes score was 1/5 with no expression of CD5. This is a non-CLL lymphoid hematopathy, which represents only 12% (8) of B-cell lymphomas in adults, with CD5 being almost always expressed (approximately 95%) [9] [10] [11] [12] [13]. Cases of CLL with atypical immunologic

Table 4. Distribution of blood count results after CHOP chemotherapy.

Laboratory Findings		Values (international units)
Hemogram	Leukocyte	10,800 éléments/mm^3
	Thrombocyte	108,000 éléments/mm^3
	Hemoglobin level	9.8 g/dl
	MGV (Mean Blood Cell Volume)	81.7 fl

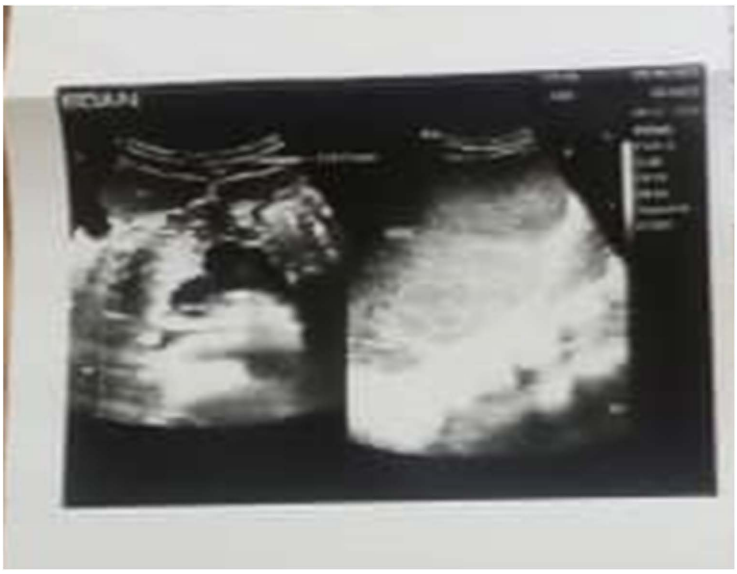

Figure 3. Splenic ultrasound after CHOP chemotherapy.

profile (score ≤ 3) frequently have strong FMC7 expression, but very rarely loss of CD5 [14] [15] [16]. Mantle cell lymphoma (MCL) represents 3% - 10% of non-Hodgkin's lymphomas [8] [9] and the cells are positive for CD5 (90%) [10] and strongly express CD79b. This result is different from our patient, who does not express CD5 or CD79b. Marginal zone lymphoma (MZL) represents approximately 15% of non-Hodgkin's lymphomas [17]. The negative variant is characterized by negative CD5 (80%), CD10, CD23, and strongly positive CD79b. In our case, CD79b is not expressed at all. Hairy cell leukemia (HCL) is generally an indolent hematopathy [8]. According to the original publication by Matutes *et al.* 98% of HCL have a score (HCL marker score) (18) of 3 to 4. Our patient's score is less than 3 with no expression of CD25 and CD79b, which is not compatible with HCL, let alone the variant that strongly expresses CD79b. Follicular lymphoma represents 20% of lymphomas [19] and has expression of CD23 and CD79b. B-cell prolymphocytic leukemia (B-LPL) is a very rare condition [8]. Expression of CD79b and light chains are the most discriminatory markers [20]. Lymphoplasmacytic lymphoma is distinguished from other CD5+ B-cell lymphoproliferative syndromes [1].

4. Conclusion

Despite the contribution of immunophenotyping in the diagnosis of lymphoproliferative syndromes, it is possible to consider the diagnosis of a non-specific phenotypic profile B lymphoid hematopathy with CD45+, monotypic kappa, CD19+, FMC7+, CD22+, CD5–, CD79b–, CD23–, CD43–, CD38–, CD200–. The search for new diagnostic markers plays an important role in confirming the diagnosis of non-CLL lymphoproliferative syndromes. Therefore, it is necessary to validate other diagnostic scores in non-CLL hematolymphoid pathologies.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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