East African Scholars Journal of Medical Sciences
Abbreviated Key Title: East African Scholars J Med Sci
ISSN: 2617-4421 (Print) & ISSN: 2617-7188 (Online)
Published By East African Scholars Publisher, Kenya

OPEN ACCESS

Volume-5 | Issue-2 | Feb-2022 | DOI: 10.36349/easms.2022.v05i02.009

Case Report

Prolymphocyte Leukemia: A Case Report

Ghita Elghouat[1, 3*], Abderrahim Raissi[2, 3], Hicham Yahyaoui[1, 3], Raja Nakhli[1, 3], Mohammed Chakour[1, 3]

[1]Haematology Laboratory, Avicenne Military Hospital, Marrakesh, Morocco
[2]Haematology Department, Avicenne Military Hospital, Marrakesh, Morocco
[3]Faculty of Medicine and Pharmacy, Cadi Ayyad University, Marrakesh, Morocco

Article History
Received: 16.01.2022
Accepted: 21.02.2022
Published: 28.02.2022

Journal homepage:
https://www.easpublisher.com

Quick Response Code

Abstract: Prolymphocyte leukemia is a very rare, complex, and often aggressive, mature lymphoid hemopathy. The mean age of onset is 65 years with a predominance of males. We report here the case of a patient with splenomegaly and severe lymphocytosis in whom the smear showed an invasion of 90% of prolymphocytes suggesting Prolymphocyte leukemia confirmed by immunophenotyping. Both purine analogues and monoclonal antibodies have shown promoting results, however, allogeneic hematopoietic stem cell transplantation remains the only therapeutic means allowing a lasting response. However, it is reserved for young patients with compatible donors. A good understanding of the pathogenesis and a better integration of the molecular data of this hemopathy open the way to the use of new targeted therapies.

Keywords: B cell prolymphocytic leukemia, chronic lymphocytic leukemia, diagnosis, treatment, case report.

Copyright © 2022 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution **4.0 International License (CC BY-NC 4.0)** which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

Prolymphocytic leukaemia (PLL) is a very rare haemopathy constituting less than 1% of mature B lymphoid haemopathies, usually affecting the elderly and characterised by an aggressive clinical course [1]. Initially described as a variant of CLL, it was later individualised as a distinct entity with clinical, morphological, phenotypic and cytogenetic specificities [2].

Treatment is currently based on purine analogues and monoclonal antibodies, with promising results. Allogeneic haematopoietic stem cell transplantation remains the only curative treatment, but it is only indicated in younger patients [3].

We report here a case of a patient with LPL-B, illustrating the diagnostic, therapeutic and evolutionary aspects of this pathology.

PATIENT AND OBSERVATION

A 60 year old patient, chronic smoker and type 2 diabetic on metformin, referred for major hyperlymphocytosis with anemia and thrombocytopenia.

Clinical examination revealed mucocutaneous pallor and splenomegaly 8cm from the costal margin, without palpable peripheral adenopathy with a few subcutaneous nodules on the scalp.

The initial blood count revealed white blood cell count of 730 G/L with anaemia of 5.4g/dl normocytic aregenerative and thrombocytopenia of 26 G/L. The blood smear stained with May Grünwald Giemsa (MGG) showed 93% invasion by medium-sized cells with regular nuclei, dense chromatin, often nucleolated (large nucleoli), variable cytoplasm, moderately basophilic in favour of LPL (Figure 1) with 5% lymphocytes and 2% neutrophils. The myelogram showed a rich marrow, infiltrated by 90% of cells identical to those found in the peripheral blood.

***Corresponding Author:** Ghita Elghouat
Haematology Laboratory, Avicenne Military Hospital, Marrakesh, Morocco

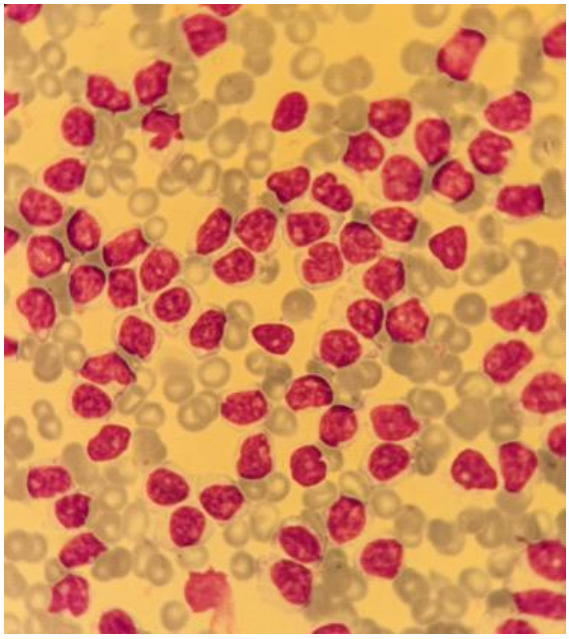

Figure 1: (x 100) MGG-stained blood smear: presence of medium-sized prolymphocytes with a high nucleo-cytoplasmic ratio, regular nucleus sometimes notched, with dense chromatin with prominent nucleolus, and low basophilic cytoplasm

Immunophenotyping revealed a monotypic B lymphoid population of CD19+, CD5+partial, CD23+, CD43+, FMC7+, CD79b+, CD20+ (high intensity), expressing a lambda light chain of moderate intensity in favour of LPL-B.

Cytogenetic analysis revealed a complex karyotype with clonal chromosomal abnormalities in number including: monosomy of chromosome 10, monosomy of chromosome 15, monosomy 20, and in structure including: a derivative of chromosome Y, a derivative of chromosome 9, a deletion of the long arm of chromosome 11 and a derivative of chromosome 12. Fluorescence in situ hybridisation (FISH) showed a deletion of the P53 locus on the short arm of chromosome 17 at 17p13 and of the ATM2 locus on the long arm of chromosome 11 at 11q22.3. The P53 mutation tested positive by PCR.

The thoracic-abdominal-pelvic CT scan revealed supra- and subdiaphragmatic polyadenopathy and a nodular splenomegaly of 18 cm. The rest of the work-up was unremarkable (renal and hepatic functions, viral serologies for hepatitis B, C and HIV, TPHA-VDRL).

The patient was initially started on obinutuzumab and bendamustine, with an initial decrease of more than 50% in WBCs. However, there was a rapid re-escalation of WBCs at week 3 of treatment. The patient was then given ibrutinib at a dose of 420mg/d.

The course was marked by a moderate decrease in WBC but also in platelets. During the second cycle of ibrutinib, the patient developed a progression of lymphocytosis with profound thrombocytopenia and massive brain haemorrhage. Unfortunately, he died a few days later.

DISCUSSION

B-cell leukaemia was originally described by Catovsky *et al*., and Galton *et al*., in the 1970s as a variant of chronic lymphocytic leukaemia [4]. It is a rare disease, accounting for less than 1% of chronic lymphoproliferative syndromes (cLPS) [1]. The average age of onset is 65 years with a male predominance [5].

Signs of the disease are often not pathognomonic. Confirmation of the diagnosis requires a multidisciplinary approach including clinical, cytological, immunophenotypic, cytogenetic and molecular data.

Patients typically present with enormous splenomegaly (more than 80% of cases), with little or no adenopathy [6]. A frank hyperleukocytosis (>100 G/L) is almost constant, associated with a massive lymphocytosis. Anemia and thrombocytopenia are not uncommon, especially in cases of extensive bone marrow invasion [7, 8]. The blood smear is an important element in orienting the diagnosis. According to the British-French-American (FAB) classification and the World Health Organization (WHO) 2016, the smear shows more than 55% (usually >90%) involvement of circulating B-cells [9] with cytological features such as an enlarged cell volume up to twice the size of a mature lymphocyte, a rounded nucleus, a prominent nucleolus, a condensed chromatin and a low basophilic cytoplasm. Unlike splenic marginal zone lymphoma and Hairy Cell Leukaemia, there are no cytoplasmic projections [6]. The myelogram shows significant bone marrow infiltration with the persistence of variable haematopoiesis, as in our patient [2].

Lymphocyte immunophenotyping is an essential diagnostic tool. It can differentiate B-PLL from other cPLS. Malignant B-cells strongly display the antigens CD19, CD20, CD22, CD79b and FMC7, as well as the surface immunoglobulin IgM +or- IgD. CD23 is usually absent and CD5 is only expressed in 30-65% of cases. The Matutes score is classically between 0 and 1, exceptionally 2 [2, 5, 6]. Cyclin D1-expressing tumour cells represent a variant of mantle cell lymphoma [10]. Cyclin D1 expression by tumour cells represents a variant of mantle cell lymphoma [10]. In our patient, immunophenotyping showed: CD19+, partial CD5, CD23+, strong FMC7+ and strong CD79b+. The Matutes score was 2, consistent with the literature.

BPL is often associated with a complex karyotype (>3 chromosomal abnormalities) [1, 10]. The

most recurrent chromosomal abnormalities include translocations involving the MYC gene (t(8;14)(q24; q32), t(2; 8)(p11; q24), t(8; 22) (q24; q11) and overexpression of C-MYC), suggesting a major role for this oncogene in the pathogenesis of B-PLL. More recently, fluorescent in situ hybridisation techniques have demonstrated deletions of the 11q23 (RB1), 17pl 3 (TP53) regions [1]. Exon sequencing has revealed recurrent mutations in TP53 genes. Immunoglobulin heavy chain variable regions (IGVH) are mutated in more than 50% of cases [1]. Our patient presented with a complex karyotype, a deletion of the 11q23, 17p13 regions and a mutation of the TP53 genes. Recently, a prognostic model has been proposed taking into account MYC and 17p status. This model identifies three risk groups: low risk (no MYC abnormality), intermediate risk (MYC abnormality without del17p) and high risk (MYC abnormality and del17p) [1].

Regarding therapeutic management, there is currently little published data on small case series studies. Results from randomised clinical trials are still lacking [5]. At present, there is little data on treatment management and outcomes. The published studies are small case series and there are no randomised clinical trials. Published data have shown that the use of rituximab immunotherapy in combination with fludarabine and cyclophosphamide or bendamustine chemotherapy in patients without TP53 abnormalities induces complete remissions of more than 5 years. For patients with the TP53 mutation, other treatments such as alemtuzumab are proposed, given the primary resistance they develop to standard therapy. Recently, the BTK inhibitor (ibrutinib) has shown promising results, especially in patients with del17p. Targeting MYC may be an additional option in the therapeutic arsenal [1, 3]. Other new molecules (venetoclax, silinexor, CART-Cell, new BTK inhibitors, etc.) are being evaluated in this disease. Currently, allogeneic hematopoietic stem cell transplantation remains the only promising therapeutic means to obtain a long-term response [5]. However, it is reserved for young patients with compatible donors.

CONCLUSION

The analysis of this case confirms the difficulty of the diagnosis of this pathology whose clinical evolution is aggressive and survival is estimated in months. Its diagnosis is based on a complete biological exploration using morphological, immunophenotypical, cytogenetic and molecular studies. Advances in the understanding of the pathogenesis of BPL have led to the development of promising new therapeutic agents.

Conflicts of interest: The authors declare no conflict of interest.

REFERENCES

1. Chapiro, E., Pramil, E., Roos-Weil, D., Dillard, C., Gabillaud, C., Maloum, K., ... & Nguyen-Khac, F. (2019). Genetic characterization of B-cell prolymphocytic leukemia: a prognostic model involving MYC and TP53. *blood*, *134*(21), 1821-1831.
2. Rabhi, S., Amrani, M., Khammar, Z., Khibri, H., Lamchachti, L., & Ouazzani M. (2011). Prolymphocytic leukemia of phenotype B with poor prognosis. *Maroc Méd*, 33(3), 212-215.
3. Collignon, A., Wanquet, A., Maitre, E., Cornet, E., Troussard, X., & Aurran-Schleinitz, T. (2017). Prolymphocytic leukemia: new insights in diagnosis and in treatment. *Current oncology reports*, *19*(4), 1-11.
4. Galton, D. A. G., Goldman, J. M., Wiltshaw, E., Catovsky, D., Henry, K., & Goldenberg, G. J. (1974). Prolymphocytic leukaemia. *British Journal of Haematology*, *27*(1), 7-23.
5. Bellal, M., & Damaj, G. (2019). Prolymphocytic leukemias. *Hematology*, (253), 163-168.
6. Nguyen-Khac, F. (2006). Prolymphocytaire B Leucemia. *Rev Franc des Lab*, 379, 45-47.
7. Krishnan, B., Matutes, E., & Dearden, C. (2006, April). Prolymphocytic leukemias. In *Seminars in oncology* (Vol. 33, No. 2, pp. 257-263). WB Saunders.
8. Dungarwalla, M., Matutes, E., & Dearden, C. E. (2008). Prolymphocytic leukaemia of B-and T-cell subtype: a state-of-the-art paper. *European journal of haematology*, *80*(6), 469-476.
9. Bennett, J. M., Catovsky, D., Daniel, M. T., Flandrin, G., Galton, D. A., Gralnick, H. R., & Sultan, C. (1989). Proposals for the classification of chronic (mature) B and T lymphoid leukaemias. French-American-British (FAB) Cooperative Group. *Journal of clinical pathology*, *42*(6), 567-584.
10. Ruchlemer, R., Parry-Jones, N., Brito-Babapulle, V., Attolico, I., Wotherspoon, A. C., Matutes, E., & Catovsky, D. (2004). B-prolymphocytic leukaemia with t (11; 14) revisited: a splenomegalic form of mantle cell lymphoma evolving with leukaemia. *British journal of haematology*, *125*(3), 330-336.

Cite This Article: Ghita Elghouat, Abderrahim Raissi, Hicham Yahyaoui, Raja Nakhli, Mohammed Chakour (2022). Prolymphocyte Leukemia: A Case Report. *East African Scholars J Med Sci*, *5*(2), 77-79.