**Uncommon IgA lymphoplasmacytic lymphoma: Case report**

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**Introduction**

Lymphoplasmacytic lymphoma (LPL) is a rare neoplasm of small B lymphocytes with varying degrees of plasmacytic differentiation, usually comprising clonal plasmacytoid lymphocytes and plasma cells, which does not fulfill the criteria for any of the other small B-cell lymphoid neoplasms that can also have plasmacytic differentiation [1]. The immunophenotype usually resembles the normal lymphocytes and plasma cells, except for clonal restriction and CD25+/- and CD138+/- expression, differing from the profile of neoplastic myeloma plasma cells, that usually lose CD19 and abnormally express CD56, along with loss of CD45 and CD81, and expression of CD117 [2]. If both bone marrow infiltration and IgM monoclonal gammopathy are present, the disease is called Waldenström Macroglobulinemia (WM), accounting for up to 2% of all cases of non-Hodgkin lymphoma in the United States and Europe [4]. Non-IgM lymphoplasmacytic lymphoma (LPL) is very rare, comprising less than 5% of LPLs [5] with no clinical or pathological differences when compared to the more common IgM LPL [6]. Differential diagnosis should include multiple myeloma (MM), chronic lymphocytic leukemia and other non-Hodgkin lymphomas such as splenic or nodal marginal zone lymphomas, as different treatment approaches are recommended.

**Case Report**

A previously healthy 74-year-old Chinese female patient living in Northern Brazil had a broken right femur after a moderate trauma, with no other clinical symptoms. Medical examination revealed no lymphadenopathies, or organomegalies. Her hemoglobin was 9 g/dL, white blood count 16.5x10^9/L (neutrophils 15.2x10^9/L; lymphocytes 0.66 x10^9/L) and platelet count 497x10^9/L. Protein electrophoresis showed the typical L265P mutation.

**Immunophenotyping** by 8-color flow cytometry of the BM showed 28% of clonal lymphocytes and 3.5% of clonal plasma cells. Lymphocytes expressed CD19, CD20, FMC-7, heterogeneous CD38, surface IgA, and lambda light chain; they were negative for CD5, CD10 and CD11c. Plasma cells showed a “normal” phenotype, expressing CD38, CD138, CD19, CD45, cytoplasmic IgA, cytoplasmic lambda and no expression of CD56, CD117, CD81, or CD27.

**Discussion**

In the present case, an expressive monoclonal peak of more than 3g/dL, in a patient with mild anemia and no other MM clinical features raised the suspicion of a non-IgM LPL. Bone marrow immunophenotyping and the presence of MYD88 L265P mutation confirmed the diagnosis.

Non-IgM LPL is a rare disease and the precise diagnosis could be challenging. While IgM gammopathy is associated with LPL, IgA or IgG are more common in MM [9]. However, clinical presentation is similar to MM, with bone lesions, hypercalcemia and renal insufficiency, rarely observed in LPL [10]. Less frequently, IgA or IgG gammopathy might be associated with other non-Hodgkin lymphoma such as splenic or
nodal marginal zone lymphomas, and chronic lymphocytic leukemia. For a definite diagnosis, it is essential to perform a thorough analysis of the morphology and the immunophenotype, as well as the confirmation of clonality [4].

There are no specific chromosomal aberrations in LPL but 6q deletion is the most common, present in 30% of patients, and may be associated with worse prognosis [11]. MYD88 L265P mutation is present in about 90% of WM and has become a new tool for diagnosis. In non-IgM LPL, the mutation is less common, occurring in about 40% of patients in two case series [5,6]. Besides, it is rarely present in marginal-zone lymphomas and is absent in MM [12].

Conclusion

In conclusion, our case illustrates that the presence of IgA paraprotein should be carefully investigated, and the differential diagnosis should include LPL. The lack of MM features, such as bone lytic lesions or hypercalcemia, the specific immunophenotype along with MYD88 L265P mutation favored LPL. MYD88 L265P mutation is a very helpful tool to a more precise diagnosis of WM.

References

1. Swerdlow SH, Berger F, Pileri SA (2008) Lymphoplasmacytic lymphoma. In: Swerdlow SH, Campo E, Harris NL (Eds). WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. (4th Edn) IARC: Lyon, France, pp. 194-195.
2. Konoplev S, Medeiros LJ, Bueso-Ramos CE, Jorgensen JL, Lin P (2005) Immunophenotypic profile of lymphoplasmacytic lymphoma/Waldenström macroglobulinemia. Am J Clin Pathol 124: 414-420. [Crossref]
3. Björkholm M, Johansson E, Papamichael D (2003) Patterns of clinical presentation, treatment, and outcome in patients with Waldenström's macroglobulinemia: a two-institution study. Semin Oncol 30: 226-230.
4. Castillo JJ, Garcia-Sanz R, Hajjiharris E (2016) Recommendations for the diagnosis and initial evaluation of patients with Waldenström Macroglobulinaemia: A Task Force from the 8th International Workshop on Waldenström Macroglobulinaemia Br J Haematol 175: 77-86.
5. Cao X, Medeiros LJ, Xia Y, Wang X, Thomas SK, et al. (2016) Clinicopathologic features and outcomes of lymphoplasmacytic lymphoma patients with monoclonal IgG or IgA paraprotein expression. Leuk Lymphoma 57: 1104-1113. [Crossref]
6. King RL, Gonsalves WI, Amelio SM, Greipp PT, Frederick LA, et al. (2016) Lymphoplasmacytic Lymphoma With a Non-IgM Paraprotein Shows Clinical and Pathologic Heterogeneity and May Harbor MYD88 L265P Mutations. Am J Clin Pathol 145: 843-851. [Crossref]
7. Morel P, Duhamel A, Gobbi P (2009) International prognostic scoring system for Waldenström Macroglobulinemia. Blood 113: 4163-4170.
8. Leblond V, Kaldis E, Advani R (2016) Treatment recommendations from the Eighth International Workshop on Waldenström's Macroglobulinemia. Blood 128: 1321-1328.
9. Kyle RA, Larson DR, Therneau TM, Dispenzieri A, Kumar S, et al. (2018) Long-Term Follow-up of Monoclonal Gammopathy of Undetermined Significance. N Engl J Med 378: 241-249. [Crossref]
10. Schuster SR, Rajkumar SV, Dispenzieri A, Morice W, Aspirita AM, et al. (2010) IgM multiple myeloma: disease definition, prognosis, and differentiation from Waldenstrom's macroglobulinemia. Am J Hematol 85: 853-855. [Crossref]
11. Nguyen-Khac F, Lambert J, Chapire E (2013) Chromosomal aberrations and their prognostic value in a series of 174 untreated patients with Waldenström's macroglobulinemia. Haematologica 98: 649-654.
12. Treon SP, Xu L, Yang G, Zhou Y, Liu X, et al. (2012) MYD88 L265P somatic mutation in Waldenström's macroglobulinemia. N Engl J Med 367: 826-833. [Crossref]

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