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Case Report

A case of lymphoplasmacytic lymphoma mimicking as chronic lymphocytic leukemia

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ABSTRACT

Lymphoplasmacytic lymphoma (LPL) is a B-cell non-Hodgkins lymphoma (B-NHL) that has small lymphocytes, plasmacytoid lymphocytes and plasma cells in varying proportions. It commonly involves the bone marrow, lymph nodes, spleen and rarely other extra-medullary sites. LPL tends to have a varied morphology and immunophenotype (IPT). Though it is characterized by the presence of monoclonal IgM protein in serum, it can also be seen in other B-NHL. Thus, it may impose a diagnostic challenge by morphology and IPT in some cases. Chronic lymphocytic leukaemia (CLL) is another small B cell NHL, which has a more typical morphology and characteristic IPT. IPT is done by flow cytometry (FCM), which is a rapid and efficient tool in the diagnosis of NHL involving blood and marrow. We present a case of LPL which mimicked CLL by morphology and IPT.

Keywords: Lymphoma, Lymphoplasmacytic, B-NHL, Small B cell, FCM

INTRODUCTION

B cell non-Hodgkin lymphoma (B-NHL) is one of the most common neoplasms of the lymph nodes. Morphologically, it is divided into small, medium, and large cell lymphomas, and each category includes different entities. IPT is required to differentiate lymphomas, which is done by FCM when blood and bone marrow are involved and immunohistochemistry (IHC) when extramedullary sites are involved. LPL involves the bone marrow, lymph nodes, and spleen, and it is small B lymphocyte neoplasm that has plasmacytoid lymphocytes, small lymphocytes, and plasma cells.[1] Waldenstrom macroglobulinemia is defined as bone marrow involvement by LPL and monoclonal IgM proteins in serum of any concentration.[2] LPL expresses surface immunoglobulin, which is usually IgM, followed by IgG, and IgA rarely. LPL expresses B cell markers like CD19, CD20, CD22, and CD79a, but CD5, CD10, and CD23 are frequently negative. It may show expression of CD25 and CD38. A subset of plasma cells that are CD138, CD19, and CD45 positive with/without light chain restriction are also seen. Studies shown that B cell antigens CD19 and CD45 are generally expressed on LPL plasma cells as opposed to plasma cell malignancies which lack expression of these antigens. These imply that FCM would be useful in differentiating these entities, especially considering that FCM unintentionally assesses B cell antigen expression simultaneously.[3] Commonest B-NHL involving blood and marrow is CLL, which presents with lymphocytosis and indolent clinical course. The neoplastic B cells show expression of CD5, CD23, CD43 and CD200, along with characteristic dim expression of CD20, CD79b and surface IgM.[4] Herewith, we present a case of LPL that simulated CLL in morphology and IHC but was diagnosed by FCM.

CASE REPORT

A 64-year-old male presents with a history of fever for 25 days, associated with headache, and shortness of breath, and was evaluated for pyrexia of unknown origin. A complete blood count showed pancytopenia and was evaluated further. Ultrasound of the abdomen revealed

mild hepatosplenomegaly. No lymphadenopathy was identified clinically. A bone marrow aspiration and bone marrow biopsy were done. Bone marrow aspirate slides were aparticulate and blood diluted exhibiting lymphocytosis with predominance of small mature lymphocytes. Bone marrow biopsy showed hypercellular marrow with suppression of erythroid, myeloid, and diffuse proliferation of atypical small lymphoid cells, and IHC was suggested. IHC was positive for CD20, CD5, Bcl2 (diffuse), MUM1 (rare cells), and PAX5 with a Ki index of 20-25%. CD23, CD30, BCL6, C-MYC, Cyclin D1, Sox 11, CD21, and CD43 were negative. With these markers, diagnosis of low-grade small B-NHL lymphoma was suggested with the possibility of CLL. An EDTA bone marrow sample was sent to our laboratory for FCM. IPT was done on a Navios Ex flow cytometer (Beckman Coulter U.S.A.), which is 10-colour, three-laser instrument. Machine is subjected to strict QC protocols. FCM showed clonal neoplastic B cell population expressing CD19 (moderate), CD20 (dim to moderate), surface IgM (moderate), CD5 (dim), CD23 (variable), CD43 (dim), CD200 (dim expression) and kappa light chain restricted. CD10, CD11c, surface lambda, CD38, CD2, CD3, CD4, CD8, CD7, CD16+56, and FMC7 were negative. Though the cells showed expression of CD5, CD23, CD43, dim CD20 and CD200, they were showing moderate surface IgM expression, which is unlikely in CLL. Moreover, though CD200 was positive, it was dim in intensity, which is again not consistent with CLL. We then gated the plasma cells (CD38 bright population) and checked for kappa and lambda expression, which were predominantly kappa light chain positive (Figure 1).

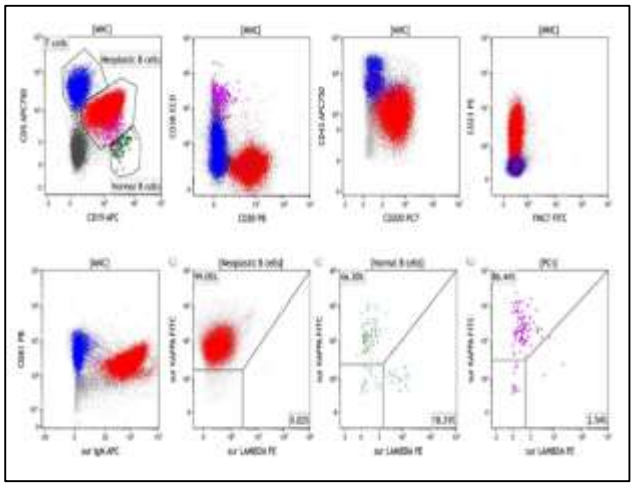

Figure 1: All events are checked with time plot for stable acquisition. Viable events are selected using FSC-A vs. SSC-A plot, which is then gated on FSC-A vs. FSC-H to discriminate singlets. Singlets are gated on SSCvsCD38, to isolate mononuclear cells (MNC). MNC population is gated on many bivariant dot plots with different combinations of markers. The most representative plots are shown here.

Blue-Kappa restricted neoplastic B cells; blue-normal T cells, green-normal polyclonal B cells; pink-plasma cell population which show predominantly Kappa light chain expression.

Since there was a clonal plasma cell population and a B cell population, a diagnosis of LPL was made. The peripheral smear and BMA slides were reviewed, which showed rouleaux formation and very occasional lymphoplasmacytoid cells. Serum protein electrophoresis was done, which showed a sharp monoclonal protein peak in the gamma globulin region and M protein measuring 1.40 g/dL. Immunotyping showed IgM kappa monoclonal gammopathy. The patient was started on chemotherapy and is currently under follow-up.

DISCUSSION

We have reported a case of LPL that mimicked CLL in morphology and immunohistochemistry. Even in flow cytometric analysis, the neoplastic B cells imitated the CLL phenotype with expression of CD5, CD23, CD200 and CD43. However, the intensity of the markers CD200, and IgM were not consistent with CLL, which shows bright CD200 and dim IgM. We checked the clonality of plasma cells, which were predominantly kappa light chain restricted and this favoured the diagnosis of LPL. FCM plays a significant role in the diagnosis of haematological neoplasms and allows quick multiparametric evaluation of single cells. It also measures the intensity of antigen expression in the target cells in contrast to IHC.

Small B cell lymphomas could not be sub-classified in some cases due to phenotypic overlap, and the final diagnosis should be made after a constellation of clinical, morphology, IPT and molecular findings. LPL is often described as a B-cell lymphoma with plasmacytoid differentiation, and the distinction between LPL and other small B-cell lymphomas is not always obvious.[2] Marginal zone lymphoma can also show plasmacytic differentiation. Though LPL shows lymphocytes, plasma cells, and plasmacytoid lymphocytes in morphology, the degree of plasmacytic differentiation and pattern of infiltration vary in the bone marrow.[1] Morice et al showed that their LPL cases had a varied distribution of lymphoid infiltrates associated with plasma cells, and they also had cases that had difficulty identifying lymphoid infiltrates among the plasma cell component. Thus, LPL had a wide diversity in morphological presentation. Generally, the IPT of LPL was defined as positive for CD25, CD27, SmIgM, CD22 (low) and negative for CD23 which is distinct from B-NHL by negative expression of CD10, CD5, CD11c, CD103. Yet LPL has also expressed CD5 and CD23 positivity at varied frequencies demonstrating its varied IPT.[1] The B cell population in LPL shows heterogenous CD38 expression.[5] Moreover, 40% of all LPL patients had clonal B cells which are lymphoplasmacytoid cells having intermediate **s**catter properties between those of small B lymphocytes and plasma cells. This population exhibits high levels of CD38 expressions; however, it lacks CD138 on the surface and is distinguished by CD19, CD20, and FMC7 expression.[6] In the case of CLL, Matutes et al proposed a scoring system for CLL that

includes CD5, CD23, FMC7, surface IgM, and CD22. Later, it was modified by Moreau et al. by substituting CD79b instead of CD22.[7,8] Various studies have been done to improve CLL IPT by adding CD43 and CD200.[9] Recent studies have shown that in CLL, CD43 and CD200 show significant expression, while CD45 and CD20 are downregulated.[10] In our case, FCM showed dim CD43 and CD200 expression, which is in favour of non-CLL lymphoma according to the other studies.[10] Konoplev et al did a study on the immunophenotypic profile of 77 known cases of LPL in which they described cases with CD23, CD5 and CD10 positivity and concluded that IPT of LPL is variable and overlaps with other B cell NHL.[11] The plasma cell population should be checked for clonality in all cases exhibiting bright IgM, as Kappa and lambda are an integrated part of the CLPD panel. This approach may help in diagnosing LPL cases with atypical phenotypes.

CONCLUSION

The majority of LPL cases have the characteristic morphology and IPT to distinguish them from other small and mature B-cell neoplasms. A subset of cases may have varied morphological and immunophenotypic expression, which may be difficult to distinguish or mislead to a diagnosis of different B cell neoplasms. Hence, an integrated and careful approach with clinical history, biochemical, morphology, IPT, and molecular studies, helps in making the correct diagnosis. This is significant because the course of the disease, treatment regimen, and prognosis are different for various B-cell lymphomas.

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