Case Report

Dual kappa and lambda expressing in mature B-cell neoplasm: An unusual case

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ABSTRACT

A 57 years old male presented with transfusion dependent anemia for last 2 months with mild weight loss and on and off fever. On examination he was found to have small axillary lymph nodes with moderate splenomegaly. Flow cytometry revealed 63.2% cells in the lymphocyte window in cluster of differentiation (CD) 45 versus side scatter plot. Further analysis on CD-19 gated cells showed that - 75.9% of these cells expressed CD-19 plus the expression of CD23, CD25, CD43, CD20 and CD22. The entire cluster showed dual expression of kappa and lambda light chains. Final diagnosis of low-grade B non-Hodgkin lymphoma was made. Given that dual kappa and lambda expressing in mature B cell neoplasm has been described in literature, it is important to differentiate such cases from reactive lymphoid proliferations.

Key words: Dual, kappa, lambda, mature B-cell neoplasm, non-Hodgkin lymphoma.

INTRODUCTION

Lymphoid malignancies are heterogeneous group of disorders which may be difficult to differentiate from reactive proliferations. Mature B lymphocytes exhibit allelic exclusion in which only a single class of immunoglobulin heavy chain (IgH) and a single class of light chain, either kappa or lambda, are expressed.[1] One of the ways to prove clonality in B lymphoproliferative disorders (LPD) is by restriction to either kappa or lambda light chain by flow cytometry or immunohistochemistry or by IgH gene rearrangement by PCR.

CASE REPORT

A 57 years old male presented with transfusion dependent anemia for 2 months with mild weight loss and on and off fever. On examination he was found to have small bilateral axillary lymph nodes with moderate splenomegaly. The hematological investigations showed the following: Hemoglobin-5.3 g/dl, Total leucocyte count-1700/ul, differential count-neutrophils-21%, lymphocytes-79% and platelet count-30000/ul. Peripheral blood smear showed marked rouleaux formation with pancytopenia. Lactate dehydrogenase levels was 390 mg/dl. Bone marrow aspirate examination showed hypercellular marrow with diffused infiltration by atypical lymphoid cells (76%). The atypical lymphoid cells were small to intermediate in size, with irregular nuclear contours and with condensed chromatin.

Flow cytometry revealed 63.2% cells in lymphocyte window in cluster of differentiation (CD)-45 versus side scatter (SSC) plot. On CD-19 gating and further analysis showed that 75.9% of these cells expressed CD-19 with expression of CD23, CD25, CD43, CD20 and CD22. CD10, CD117, CD5, CD34, CD11c, FMC7, sIgM and CD-103 were negative. There was dual expression of Kappa and Lambda light chains (as shown in Figures 1 and 2; the red population) in which 98% cells expressed kappa light chain and 99.1% cells expressed lambda light chain weakly. Bone marrow aspirate [Figure 3] and bone marrow trephine biopsy [Figures 4 and 5] showed a diffused interstitial infiltration by atypical lymphoid cells. Bone marrow karyotype showed no clonal abnormalities. Patient has fever on and off and transfusion dependent anemia for at least 2 months. He was diagnosed previously clinically as acute leukemia with reports stating a marrow blast of around 20%.

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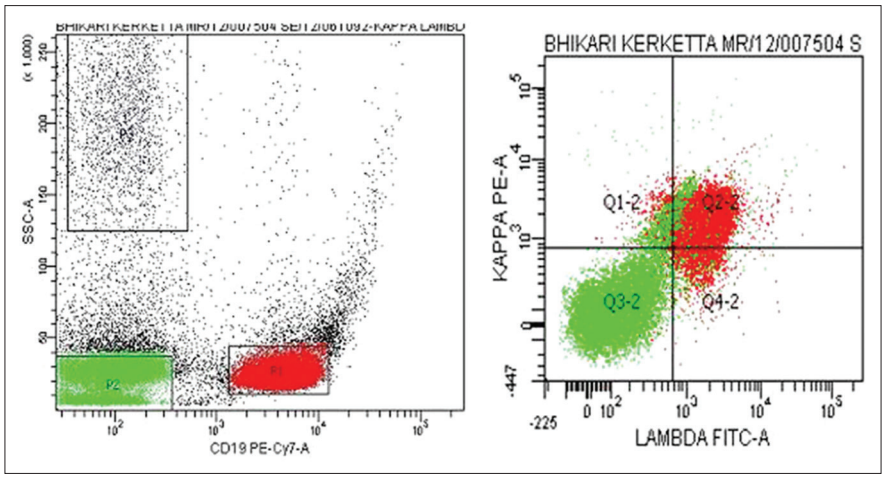

Figure 1: Immunophenotyping by flow cytometry which showed dual expression of kappa and lambda by the CD19 gated (the red population) cells. Negative control (the green population) stained with isotype is also shown which is absolutely negatively stained thus ruling out the issue of non-specific binding

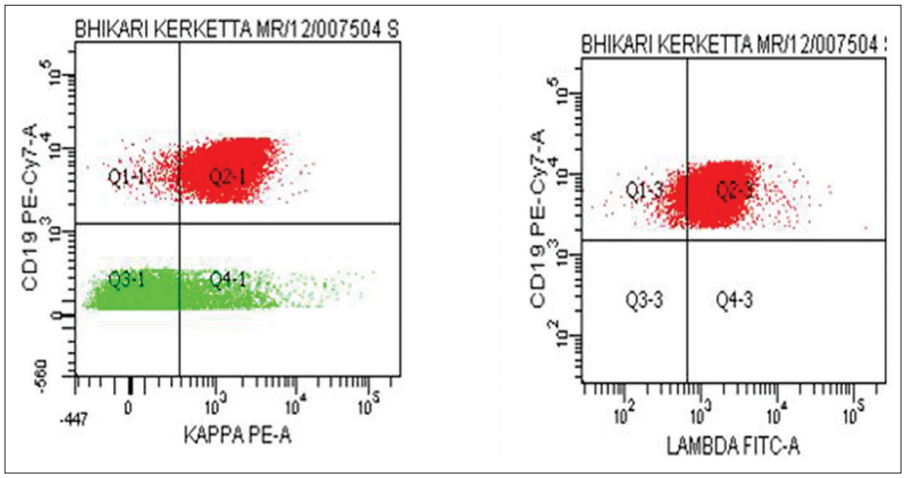

Figure 2: Immunophenotyping by flow cytometry which showed equal expression of kappa and lambda by the CD-19 gated (the red population) cells

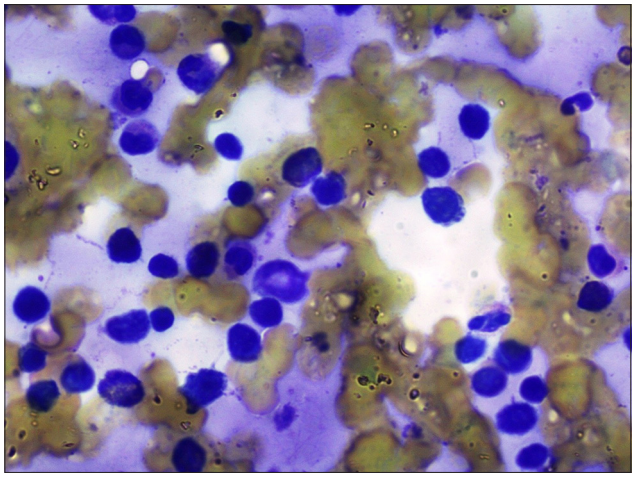

Figure 3: Giemsa stained bone marrow aspirate smear (X40) showed infiltration by atypical lymphoid cells

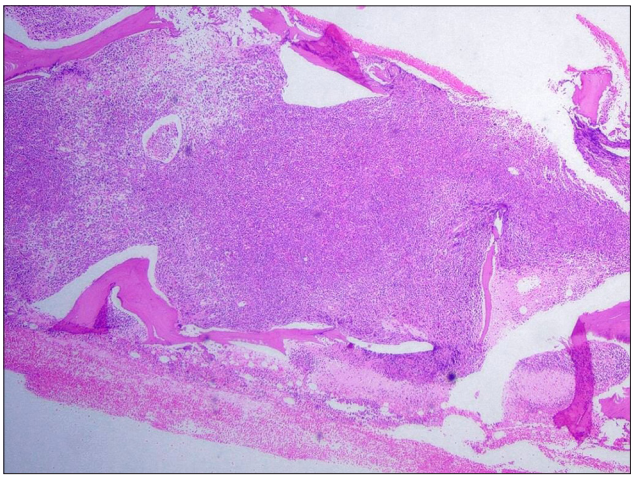

Figure 4: H and E section of bone marrow trephine biopsy (X10) showed hypercellular marrow with diffuse infiltration by atypical lymphoid cells

DISCUSSION

During the normal ontogeny of B cells it has been demonstrated that dual isotype expressing B- cells arise in the bone marrow and populate both the spleen and peritoneal cavity of nontransgenic mice.[2] Furthermore, receptor editing may play a role in the generation of a significant fraction of dual isotype expressing B cells which

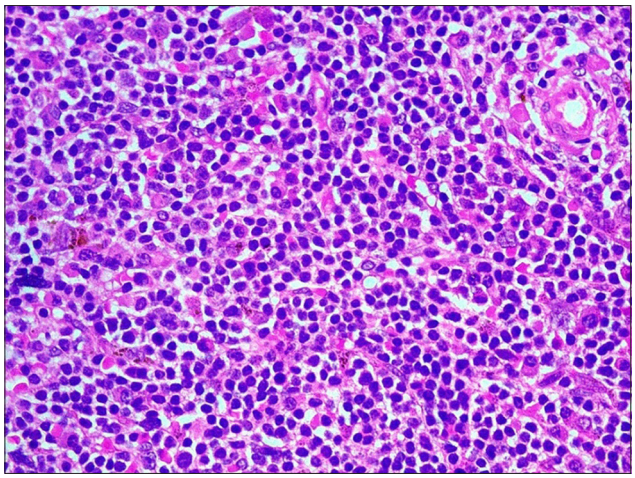

Figure 5: H and E section of bone marrow trephine biopsy (X40) with hypercellular marrow with diffuse infiltration by atypical lymphoid cells

has been seen during single cell analysis of the expressed immunoglobulin light chains.[2] IgH gene rearrangement by polymerase chain reaction (PCR) have been used successfully to investigate the clonality and cell lineage of various B-cell lymphoid malignancies.[3] B-LPD disorders derived from pre-germinal center (naive B cells) express unmutated IgH variable region (VH) genes and show a high detection rate of clonal IgH gene rearrangement while B -LPDs derived from GC-germinal center (memory B cells) have somatically hypermutated VH genes (GC and post-GC memory B-cells), and have a lower rate of clonality detection.[3]

Low grade B LPDs can present as pancytopenia specifically if they have infiltrated the bone marrow. Dual expression of Kappa and Lambda by B LPDs has been described in literature[4] and are quite rare. The index case showed a dual kappa and lambda light chain expression by flow cytometry. The challenge is always to differentiate it from reactive lymphoid proliferations. But the clinical profile of the patient, atypical morphology of lymphoid cells in bone marrow aspirate along with bcl-2 expression by cells on immunostaining led to a strong suspicion of a clonal disorder in this patient. Hence a final diagnosis of low-grade B LPD was offered. Patient was started on chemotherapy (on single agent Rituximab) for low-grade B LPD to which he responded well. The existence of normal human B-cells expressing cell surface kappa and lambda refutes the widely accepted concept that expression of a single light chain isotype is immutable.[5] The kappa positive/lambda positive cells may represent transients undergoing light chain isotype switching.[5]

CONCLUSION

Currently, it is a common notion in which demonstration of light-chain restriction in a B-cell population is generally considered proof of mono-clonality and indicates malignancy. Dual kappa/lambda light-chain expressing B-cell LPD does exist. Recognition of the dual kappa/lambda light-chain expression on B cells has diagnostic implication in LPD immunophenotyping.[1]

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