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Case Report

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Pure Biclonal Hairy Cell Leukemia–Apt Diagnosis with Multicolor Flow Cytometry

Shanza Adnan, Saba Farrukh, Arsalan Ahmed, Muhammad Shariq Shaikh

Department of Pathology and Laboratory Medicine, Aga Khan University, Karachi, Pakistan

Corresponding Author: Muhammad Shariq Shaikh**,** Department of Pathology and Laboratory Medicine, Aga Khan University, Karachi, Pakistan
E-mail: muhammad.shariq@aku.edu

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ABSTRACT

Hairy cell leukemia (HCL) is a rare B-cell neoplasm that constitutes around 2 percent of all lymphoid leukemias and occurs more frequently in elderly males. The usual triad of HCL includes pancytopenia, splenomegaly, and hairy cells in the bone marrow. This is a case of an atypical presentation of biclonal HCL diagnosed on flow cytometry; the existence of biclonal HCL is extremely rare with very few case reports. Pure biclonal HCL should be regarded as an extraordinary finding among the so-called composite lymphomas.

Keywords: Biclonal; Hairy cell; Leukemia; Flow cytometry

INTRODUCTION

Rare indolent B-cell cancers include hairy cell leukaemia (HCL), hairy cell leukaemia variation (HCL-V), and splenic diffuse red pulp lymphoma. While the overall symptoms (splenomegaly, tiredness, and pancytopenia) are somewhat vague, HCL cells have a distinctive immunophenotypic, morphologic, and mutational profile that is crucial to the diagnosis. Oval nuclei, a lot of cytoplasm, and typical cytoplasmic extensions are characteristics of malignant cells. The diagnosis can be suggested by identifying typical hairy cells in peripheral blood and bone marrow films. However, because there are typically few hairy cells in blood, a high level of suspicion is needed to make the diagnosis, and ultimately a bone marrow test is required. Key antigens that are prominently expressed in flow cytometric immunophenotyping, besides usual antigens used for B cell lymphoproliferative disorders, include CD11c, CD25, CD103, and CD123[1]. Additionally, a recurrent V600E BRAF mutation has recently been found in HCL but not in its imitators, and is now thought to constitute the disease's molecular signature[2].

Most B-cell malignancies are monoclonal. In B-cell lymphoproliferative disorders (LPDs), biclonality is a rare occurrence. It can manifest as a composite lymphoma or as the expansion of two or more concurrent subclones over the course of intra-clonal evolution within the same illness, as is frequently documented in B-CLL[3]. Due to its high sensitivity and specificity, multi-color flow cytometry (MFC) is essential in the detection of such composite cases. Despite the well-known association of HCL with other lymphomas including Hodgkin's, pure biclonal HCL should be regarded as an extraordinary finding among the so-called composite lymphomas. Here we present a case of pure biclonal HCL diagnosed using multicolor flow cytometry.

Case presentation

A 59-year-old male with no prior significant history presented with two months history of fever, fatigue, weakness and weight loss. Initial investigation included baseline CBC, routine biochemistry, blood culture, and chest X-ray. Blood examination showed

haemoglobin of 9.5 g/dl, total leukocyte count (TLC): $10x10^9$/L, and platelets $83x10^9$/L. Biochemistry results were within reference limits and there was no growth in blood culture. Bone marrow biopsy and CT chest & whole abdomen were done for further workup. CT scan revealed hepatosplenomegaly and some paraaortic lymph nodes. Bone marrow aspirate was a hemodiluted specimen however showed prominent atypical lymphoid cells with abundant cytoplasm and irregular cytoplasmic projections (Hairy cells, Figure 1A). Bone trephine (H & E) sections showed hypercellularity for age due to infiltration by atypical lymphoid infiltrate exhibiting cytoplasmic clearing (fried egg appearance, Figure 1B).

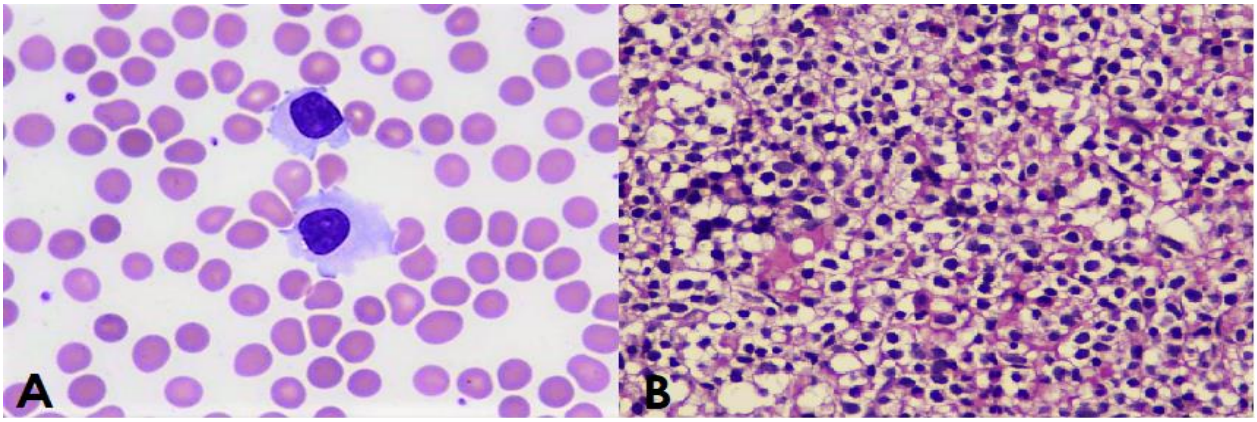

Figure 1. Bone marrow aspirate showing typical hairy cells (A); Fried-egg appearance on bone trephine H & E sections (B)

Immunophenotyping by multicolor flow cytometry using a comprehensive panel of antibodies was performed. Gating was done on target population exhibiting bright CD45 positivity with relatively increased side scatter than normal lymphocytes.

In addition to Pan-B-markers i.e. CD19, CD20, CD22 and cCD79a, this population specifically showed positivity to hairy cell markers including CD103, CD25, CD11c and CD123. Most significantly both kappa and lambda light chain were positive on malignant clone (Figure 2).

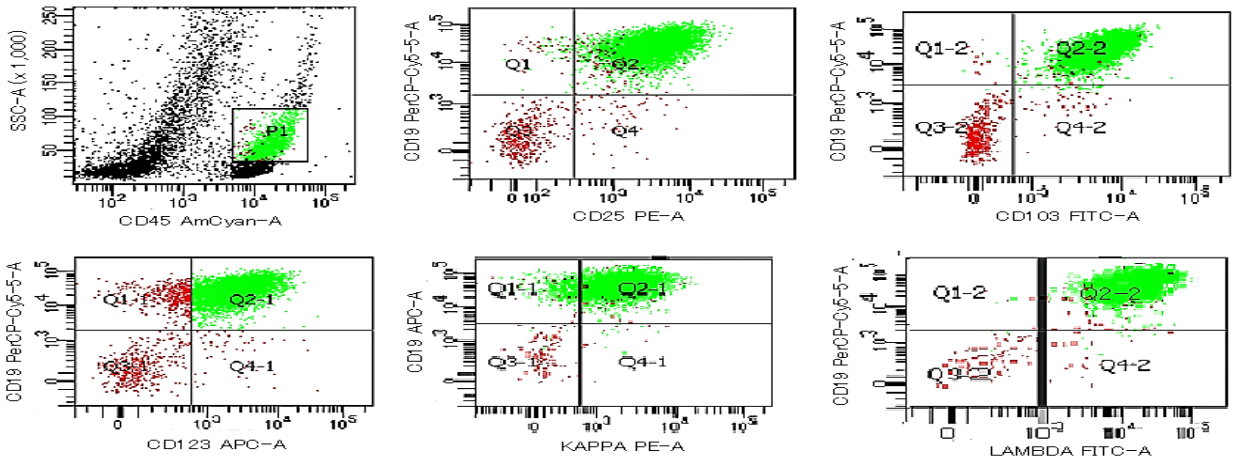

Figure 2. Dot plots showing malignant B-cell cluster in green color. CD19 (Pan-B cell marker) is co-expressing with typical HCL markers (CD25, CD103 and CD125). Distinctively, both kappa and lambda light chains are positive on malignant clone.

DISCUSSION

In this report, we have described a case of gentleman with biclonal hairy cell leukemia. In the context of composite lymphoma, HCL has generally been infrequently found, and to our knowledge, pure HCL with two concurrent subclones is a very uncommon finding.

Our case further highlights the fundamental role of MFC in discovering a rare biclonal HCL. MFC is the most eminent available method for detecting bi-clonal LPDs.The existing literature further testifies to the rarity of this disease. In a sample of 1090 newly diagnosed B-LPD cases examined over a ten-year period, bi- or multi clonality was found in 4.7% of the cases. Only one bi-clonal HCL was found out of total 26 HCL cases[4]. Since biclonal HCL is extremely rare, it clinical significance is yet to be proven. Raghavachar described two coexisting kappa and lambda clones in HCL, one of which was resistant to interferon alpha[5].

The final piece of such a fascinating diagnosis could have been supported further by the BRAF mutation and monitoring response to treatment including interferon alpha. Regretfully, our patient lost to follow up as he belonged to another city. Nevertheless, this case report will help in building up scientific database and expanding knowledge of hematological malignancies.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

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