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Case Report

A rare case of leukemic presentation of blastoid variant of mantle cell lymphoma with isolated splenic involvement: Flowcytometric revelation

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ARTICLE INFO

Article history:

Received 29 May 2012

Accepted 24 September 2013

Available online 21 November 2013

Keywords:

Blastoid mantle cell lymphoma

Leukemic presentation

Flowcytometry

Introduction

Mantle cell lymphoma (MCL) is a B-cell neoplasm generally composed of monomorphic, small to medium-sized lymphoid cells with irregular nuclear contours and a CCND1 translocation. It comprises approximately 3–10% of non-Hodgkin lymphomas and occurs in middle-aged to older individuals

with a median age of about 60 years and a variably marked male predominance (about 2:1 or greater). Lymph nodes are the most commonly involved site; spleen and bone marrow (BM), with or without peripheral blood (PBS) are the other frequently involved extranodal sites.¹

Classical MCL is a monomorphic lymphoid proliferation with a vaguely nodular, diffuse, mantle zone or rarely follicular growth pattern. One of the variant is blastoid variant which is considered to be more aggressive and characterized by the cells which resemble lymphoblasts with dispersed chromatin and a high mitotic rate.¹

The peripheral spill with massive spleen is frequently seen in the classical MCL and splenic marginal zone lymphoma where differential diagnosis is splenic lymphoma with villous lymphocytes, Hairy cell leukemia and Small lymphocytic lymphoma (SLL)/Chronic lymphocytic Leukemia (CLL). The differentiation is done on the basis of flowcytometry.

They are usually positive for CD5, FMC-7 and CD 43, but negative for CD10 and BCL6. These cells express relatively intense surface IgM/IgD, more frequently with lambda than kappa restriction. CD23 is negative or weakly positive. Aberrant phenotypes have been described, sometimes in

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<http://dx.doi.org/10.1016/j.mjafi.2013.09.014>

Fig. 1 – Massive splenomegaly measuring 8 cm below the left costal margin.

association with blastoid/pleomorphic variants, including absence of CD5 and expression of CD43 and BCL6.

All cases are BCL2 protein positive and almost all express cyclin D1, including the minority of cases that are CD5 negative. Leukemic presentation of B-MCL is an exceedingly uncommon event. Largest case series of 23 cases is published so far however, from India there is only one case which has been reported to best of our knowledge.^{2,3}

Case report

A 68-year-old male patient with no known co morbidities presented with complaints of easy fatigability and generalized weakness of one month duration in a private hospital. There was no history of weight loss, fever, night sweats and bone pain. Hemogram showed: Hemoglobin (Hb)-2.4 g/dl, Total Leukocyte Count (TLC) – 2,42,000/cumm, Platelets – 33,000/cumm. He was diagnosed as a case of ALL on the basis of peripheral blood smear and bone marrow examination.

With presumptive diagnosis of ALL he was admitted to our hospital. At the time of admission, he was afebrile and his vitals were stable. Patient had severe pallor, splenomegaly measuring 8 cm below the left costal margin (Fig. 1), mild hepatomegaly (3 cm from right costal margin). No icterus, lymphadenopathy, bony tenderness, subcutaneous nodules was present.

Peripheral blood smear was examined by senior haematopathologist. Hemogram revealed-Hb – 2.9 g/dl, TLC – 3,36,860/cumm, Platelet – 20,000/cumm. Peripheral blood smears showed atypical cells forming 90% of all the White blood cells (WBCs). Morphologically, these atypical cells are of large size, with high N:C ratio with indented, irregular nuclear contour and dispersed chromatin with prominent nucleoli in few cells (Fig. 2). These cells were negative for Myeloperoxidase and Non Specific Esterase. Based on the above-mentioned findings diagnosis of high grade lymphoma with peripheral spill was given and Flowcytometric was done on the peripheral blood in our laboratory. In the flowcytometry, 92.13% of all WBCs were gated. Gating strategy used was FSC vs SSC. Initial panel of markers used included CD19,

CD20, CD34, CD3, CD10, CD5 and CD7. These cells were positive for CD19, CD20 and CD5 and negative for CD3, CD10, CD34 and CD7. Based on these findings second panel of antibodies was used which showed, these atypical cells were positive for CD45, CD19, CD20, CD79a, CD5, Bcl-2, Lambda, Anti-IgM, Anti-IgD and cyclin D1 and negative for CD10, CD4, CD8, kappa, CD25, CD38, CD23, CD3, CD34, TdT, Anti-MPO and CD7 (Fig. 3).

Kappa to Lambda ratio was 1:128, thereby showing lambda restriction. Flowcytometric pattern was of mantle cell lymphoma with leukemic phase.

Based on the clinical, peripheral blood morphology and flowcytometric findings final diagnosis of blastoid variant of mantle cell lymphoma with leukemic presentation was given. Combination chemotherapy using R-CHOP (Rituximab and anthracycline based regimen) was planned. But our patient had a very rapid and aggressive clinical course and died within one month of the diagnosis.

Discussion

Mantle cell lymphoma (MCL) is typically disseminated at presentation, with a leukemic component in 20%–30% of patients. Classic and blastoid variants are recognized, the latter associated with inferior clinical outcome. Distinction of mantle cell lymphoma (MCL) from other mimickers often can be a diagnostic challenge. Although morphologic criteria have been well established, a wide range of histological and cytological patterns can be seen in MCL, some of which may mimic CLL/SLL.⁴

CD23 expression is widely used to differentiate MCL from CLL/SLL. Various studies have shown that the flowcytometric analysis of CD23 is a useful tool for differentiating MCL from CLL/SLL only when CD23 expression is negative as it was in our case.⁵

Blastoid mantle cell lymphoma (B-MCL) is a rare and clinically more aggressive variant than typical mantle cell lymphoma (MCL). In case of leukemic blastoid variant of MCL

Fig. 2 – Peripheral blood smear showing large sized atypical lymphoid cells with scant basophilic cytoplasm, high N:C ratio, indented nuclei, irregular nuclear contour, dispersed chromatin and prominent nucleoli. (Leishman's stain, ×1000).

Fig. 3 – (a) Gated cells express CD5 and CD20, (b) Gated cells are negative for CD34 and CD10, (c) Gated cells express Cyclin D1 and negative for CD23, (d) Gated cells express Bcl-2 and negative for TdT. *Other positive and negative markers are not shown in this figure.

(B-MCL), the differentiation from acute lymphoblastic leukemia, B cell prolymphocytic leukemia (B-PLL) and leukemic phase of large cell lymphoma is required. Cells of acute lymphoblastic leukemia lack SIg and cyclin D1 expression and express TdT, while those of B-MCL express SIg but not TdT.

Large cell lymphoma cells can rarely express CD5 in 10% of cases.⁶ These can be distinguished from B-MCL by the absence of Cyclin D1 expression. B-PLL may be very difficult to differentiate from B-MCL on the morphological grounds and immunophenotyping, however t(11;14) translocation and cyclin D1 expression is not seen in B-PLL.⁷

Hence it is really difficult to diagnose patients with B-MCL correctly without immunophenotyping. Immunophenotypic analysis is really required to characterize the lymphoid proliferation which has got both therapeutic and prognostic implications. Immuno-histochemistry and cytogenetic analysis can substantiate the diagnosis.

MCL and B-MCL is incurable with standard chemotherapy. Response rates to single-agent and combination chemotherapy range from 40% to 70% but generally are short-lived, with progression in 6–18 months.⁸ Rituximab plus thalidomide is found to be beneficial in few patients.⁹

Conflicts of interest

All authors have none to declare.

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