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Case Report

A rare case of bone marrow infiltration by T-cell/histiocyte-rich large B-cell lymphoma masquerading as hemophagocytic lymphohistiocytosis

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ABSTRACT

T-cell/histiocyte-rich large B-cell lymphoma (THRLBCL) is an uncommon B-cell non-Hodgkin lymphoma with an aggressive course. Here, we report a case of a 55-year-old lady presenting with fever for 1 month duration with no localizing signs, who underwent bone marrow (BM) examination with the suspicion of hemophagocytic lymphohistiocytosis (HLH). BM examination showed evidence of hemophagocytosis satisfying the criteria for HLH. In addition, there was infiltration by discrete large atypical cells in the BM immunohistochemically compatible with involvement by THRLBCL. The case is presented due to the rarity of the pattern of presentation of an uncommon B-NHL which posed challenges to an accurate diagnosis.

Keywords: Bone marrow, Hemophagocytosis, Infiltration, T-cell/histiocyte-rich large B-cell lymphoma

INTRODUCTION

T-cell/histiocyte-rich large B-cell lymphoma (THRLBCL) is a rare non-Hodgkin lymphoma (NHL) characterized by malignant B-cells with an infiltrative reactive T-cell population in the background.[1] It accounts for <10% of diffuse large B-cell lymphoma.[2] Hemophagocytic lymphohistiocytosis (HLH) is an uncommon acute hyperinflammatory condition that is often fatal when treatment is delayed. HLH can be familial or acquired due to infections, malignancy, or autoimmune conditions. Hematological malignancies account for the vast majority of a secondary form of HLH.[3] Herein, we present an intriguing case of THRLBCL with diffuse marrow involvement that presented as HLH.

CASE REPORT

A 55-year-old lady presented with fever for a 1-month duration with no other localizing symptoms. She had pallor, pedal edema, and hepatosplenomegaly. Complete blood count showed bicytopenia with a hemoglobin of 6 gm/dl, total leukocyte count of 6820 cells/mm^3, and platelet count of 38,000/mm^3. Peripheral smear showed microcytic hypochromic RBCs with polychromatophils and 04 nRBCs/100 WBCs. Reticulocyte count was 04%. Liver function tests were within normal range. Triglyceride level was 372 mg/dl. Serum procalcitonin was elevated (8.61 ng/ml) and serum ferritin was very high (1100 mg/dl). The direct Coombs test was negative. The acute febrile panel of investigations for malaria, toxoplasmosis, scrub typhus, and

typhoid was negative. Blood cultures were sterile. HBsAg and HCV serology were negative. CECT of thorax and abdomen showed multiple retroperitoneal and pelvic lymph nodes. Bone marrow (BM) aspiration and biopsy were done with the suspicion of HLH/lymphoma.

BM aspirate was cellular and active with a good number of discrete, large atypical cells with open chromatin, prominent nucleoli with a moderate amount of intensely basophilic cytoplasm, and punched out vacuolations [Figure 1a]. There was also evidence of hemophagocytosis [Figure 1b], satisfying the criteria for HLH. Some of these atypical cells were reminiscent of erythroid precursors [Figure 1c], and hence, there was a dilemma as to the nature of these cells. However, there was no dyspoiesis in other lineages and late erythroid precursors were normal. E-cadherin immunostain did not highlight these large atypical cells but CD20 [Figure1d] did, suggesting infiltration by B-cell lymphoma into the marrow. BM biopsy was hypercellular and showed small clusters of large cells with open chromatin and conspicuous nucleoli [Figure 2a] but these turned out to be erythroid precursors, as highlighted by E-cadherin immunostain [Figure 2b]. However, CD20 [Figure 2c] highlighted the subtle interstitial infiltration by discrete, large atypical cells with a high N: C ratio, vesicular nuclei, and scant cytoplasm. These were also highlighted by CD79a, PAX5 [Figure 2c inset] but negative for CD10, CD30, and CD34. The background reactive cells were more T lymphocytes [Figure 2d] than B lymphocytes and the proportion of CD8 was more than CD4 [Figure 2d inset]. CD68 stained the background histiocytes. There were no nodular aggregates or sheets of atypical cells seen. These features were compatible with the involvement of B-NHL possibly THRLBCL. The patient succumbed to the underlying condition shortly before any definitive treatment could be started. No lymph node biopsy was done.

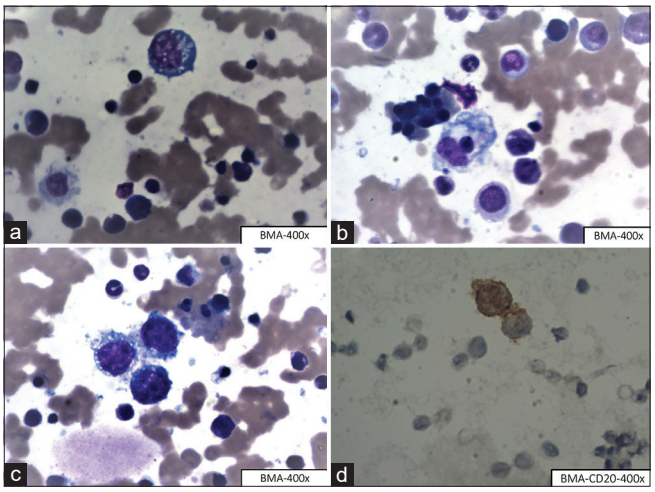

Figure 1: A 55-year-old lady with THRLBCL presenting as HLH. Bone marrow aspirate (BMA) showing (a) large atypical cells with macrophages and hematopoietic cells (Giemsa ×400); (b) erythroid hyperplasia with evidence of hemophagocytosis (Giemsa ×400), (c) large atypical cells resembling erythroid precursors (Giemsa ×400), (d) immunocytochemistry showed CD20 positivity in atypical cells (ICC ×400). THRLBCL: T-cell/histiocyte-rich large B-cell lymphoma, HLH: Hemophagocytic lymphohistiocytosis.

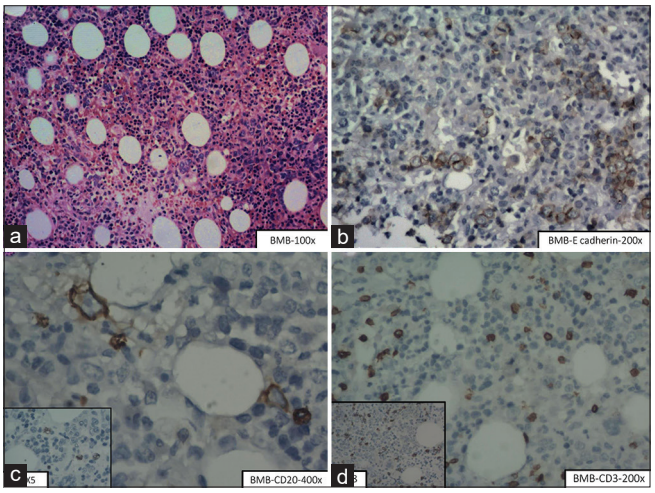

Figure 2: Bone marrow biopsy (BMB) showing (a) erythroid hyperplasia with scattered atypical cells (H&E ×100), (b) immunohistochemistry with E-cadherin highlighting erythroid hyperplasia (IHC ×200), (c) IHC with CD20 highlighting scattered large atypical lymphoid cells (IHC ×400) and inset showing PAX5 positivity, (d) CD3 IHC highlighting the reactive cells (IHC ×200) which are CD8 positive (inset).

DISCUSSION

THRLBCL is a rare type of B-NHL. Histologically, it is characterized by large malignant B-cells (typically accounts for <10% of the population) in the background of reactive T-cells and histiocytes which are the unique feature of the diagnosis of THRLBCL. It is an aggressive type of lymphoma presenting with extranodal involvement in about 60% of the cases.[4] Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL) typically mirrors the disease as it has large abnormal cells with T-cell and histiocyte rich background.[5] However, THRLBCL has an aggressive course with a presentation at a later stage of the disease and a poor prognosis as compared to NLPHL.[6] Histologically, the differences between the two are nodular patterns in NLPHL and not in THRLBCL and absence of small B-cells, and a dominant presence of CD8 positive cells favoring THRLBCL over NLPHL.[2]

HLH is an immune-mediated disorder that is characterized by fever, splenomegaly, and cytopenias. The laboratory features include hypertriglyceridemia, hyperferritinemia, hypofibrinogenemia, hemophagocytosis, low or absent NK cell activity, and elevated soluble CD25. The pathophysiology of HLH includes a defect in the cytotoxic and NK cells in

clearing the antigenic stimuli which result in uncontrolled activation of T cells and histiocytes. This leads to the overproduction of inflammatory cytokines, resulting in cytokine storm ultimately resulting in multiorgan damage.[3] HLH can be due to primary or familial disorder or it can be secondary to a triggering agent, of which the most common include infections and malignancy. HLH due to lymphoma is one of the most common triggering agents.[7,8] It is very rare for THRLBCL presenting as HLH and there are only around five cases described in the literature.[1]

CONCLUSION

Aggressive lymphomas such as THRLBCL can have subtle BM infiltration with HLH as the only presenting feature which can be diagnostically challenging.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Nil.

Conflicts of interest

Author Dr. Rakhee Kar is the Associate Editor of the journal.

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