Article published online: 2021-08-09

CASE REPORT

Simultaneous hepatosplenic T-cell lymphoma and myelofibrosis

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Access this article online

Website: www.avicennajmed.com

DOI: 10.4103/2231-0770.130343

Quick Response Code:

ABSTRACT

Hepatosplenic T-cell lymphoma (HSTL) is a rare T-cell neoplasm of the lymphoid system. This type of lymphoma is characterized by sinusoidal infiltration of spleen, liver, bone marrow and lymph nodes by neoplastic lymphocytes. Here, we discuss a patient who had a left axillary lymph node biopsy with characteristic histological and immunohistochemical features of HSTL. In addition, infiltrating neoplastic T-cells and simultaneous characteristic features of myelofibrosis (MF) were also present in the bone marrow biopsy specimen. In contrast to secondary MF, primary MF is a progressive disease and may significantly affect the prognosis of coexisting HSTL. There are few reports in the literature talking about mild bone marrow fibrosis in association with T cell lymphoma, however marked increase in bone marrow fibrosis and HSTL never being reported. This case is shedding light on HSTL and marked increase in bone marrow fibrosis.

Key words: Bone marrow, CD3, Jak2, liver, T-cell

INTRODUCTION

Hepatosplenic T cell lymphoma is a rare and unique entity of peripheral T cell lymphoma that is characterized sinusoidal infiltration of liver, spleen and bone marrow by neoplastic cells. It affects young male individuals in most cases with an aggressive clinical course and a median survival rate of less than 2 year. The relationship between bone marrow fibrosis and lymphoma has been a subject of controversy and there are few reports in the literature talking about mild bone marrow fibrosis in association with T cell lymphoma. This case is shedding light on HSTL and marked increase in bone marrow fibrosis.

CASE REPORT

This was a case of a 37-year-old male patient who was admitted to the hospital because of a right sided abdominal mass. On examination, he had left axillary lymphadenopathy (1 cm) and hepatosplenomegaly. The complete blood count showed mild anemia and severe thrombocytopenia [Table 1]. The peripheral blood smear showed intermediate-sized atypical lymphocytes, immature granulocytes, nucleated red blood cells and tear-drop cells [Figure 1a]. Liver function tests were mildly impaired and screening for auto-antibody as well as viral serology for hepatitis A, B and C were negative. Computed tomography (CT) scan of the abdomen showed massive hepatosplenomegaly and minimal lymphadenopathy. He underwent left axillary lymph node biopsy followed 1 week later by bone marrow biopsy.

The patient was given two cycles of high dose dexamethasone, cytarabine and cisplatine followed by hyper-fractionated cyclophosphamide, doxorubicin, vincristine and dexamethasone chemotherapy regimen. There was an initial dramatic reduction in the size of spleen and liver which were confirmed by abdominal CT scan. However, 2 months later the spleen increased in size and he developed severe thrombocytopenia. At 5 months after completing radiotherapy for his enlarging spleen, the patient died of complications of septicemia. No post-mortem study was done on the patient.

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Table 1: Initial patient's CBC value

RBC $3.53x10^6/\mu L$
Hemoglobin 10.1 g/dL
Hct 30.9%
MCV 87.5 fL
MCH 28.6 pg
MCHC 32.7 g/dL
RDW-CV% 16.2
Platelet $27x10^3/\mu L$
WBC $3.91x10^3/\mu L$
Granulocyte $2.59x10^3/\mu L$
Lymphocyte $0.59x10^3/\mu L$
Monocyte $0.44x10^3/\mu L$
Eosinophil $0.24x10^3/\mu L$
Basophil $0.05x10^3/\mu L$

CBC: Complete blood count, RBC: Red blood cells Hct: Hematocrit, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RDW-CV: Red cell distribution width-coefficient of variation, WBC: White blood cell

RESULTS

The bone marrow biopsy showed increased cellularity and clusters of atypical megakaryocytes showing darkly stained and hypolobated nuclei [Figure 1b]. Cells of the neutrophilic granulocytic series showed normal maturation up to the metamyelocyte stage. Anti-CD34 staining of bone marrow showed marked intrasinusoidal hematopoiesis and the reticulin stain showed substantially increased reticulin throughout the specimen. There were several instances of bone marrow sinusoidal infiltration by neoplastic cells [Figure 2a] that stained positively for the CD3 T-cell marker [Figure 2b inset]. Since it is important to differentiate between primary and secondary forms of this lesion, in the current case we used melting curve analysis of polymerase chain reaction (PCR) amplified sample from paraffin fixed tissue, as described previously.[1] No JAK2 mutation was amplified in lymph node or bone marrow specimens.

Biopsy of the axillary lymph node revealed extensive sinusoidal infiltration by atypical lymphocytes [Figure 2b inset] with intact B- and paracortical T-zones [Figure 2b]. The cells were of T-cell cytotoxic lineage with positive CD3, CD57 and TIA1. Characteristically, the neoplastic cells were negative for CD5 expression. The differential diagnosis of this lesion included NK/T-cell lymphoma which was less likely as the neoplastic cells were negative for CD56 NK cell marker. Furthermore, the neoplastic cells were negative for both CD4 and CD8 and showed post-thymic maturation with the loss of CD1a and TdT expression. Genetic studies confirmed the presence of clonal rearrangement of the T-cell receptor delta gene. In addition, staining the neoplastic cells using a monoclonal antibody that binds to the TCR β-subunit (BF1) was negative. However, although beta and gamma T-cell receptor gene analysis is not done, both the clonal delta gene rearrangement and the negative anti-BF1 immunohistochemical stain support the γδ subtype of this lesion. Furthermore, flow cytometric analysis of the lymph node specimen demonstrated the presence of an abnormal T-cell population expressing CD3 and CD2 with CD5 deletion and low expression of CD7, CD4 and CD8.

DISCUSSION

Hepatosplenic T-cell lymphoma (HSTL) represents approximately less than 5% of all peripheral T-cell lymphomas.[2]

Histologically, the disease is characterized by T-cell neoplastic infiltration of the liver, spleen, bone marrow and lymph nodes.[3] In about 20% of the reported cases, mild peripheral lymphadenopathy was also present.[2] Liver biopsy was not performed in this case because of concern that the patient might bleed excessively due to thrombocytopenia. The clinical presentation of hepatosplenomegaly as well as the histological findings in bone marrow and lymph node specimen, including sinusoidal infiltration by neoplastic cytotoxic T-cell lineage that characteristically has CD5 deletion, are consistent with HSTL.[3-5] Furthermore, the initial regression of his hepatosplenomegaly after chemotherapy also supports the diagnosis of HSTL.

The bone marrow findings of increased reticulin, along with increased numbers of atypical appearing megakaryocytes, metamyelocyte/band stage and intrasinusoidal hematopoiesis support the coexistence of myelofibrosis (MF), which may significantly affect the prognosis of coexisting HSTL. The morphologic findings in the bone marrow as well as the clinical presentation of splenomegaly warrants a molecular testing for JAK2 mutation. Here we used melting curve analysis of PCR amplified sample from paraffin fixed lymph node and bone marrow tissues.[1,6,7] The results of JAK2 analysis in our case did not allow us to reach a final unequivocal decision since JAK2 mutation was not amplified. Thus, we could not exclude the diagnosis of primary MF since JAK2 mutation is only positive in 50% of the reported cases of primary MF.[8,9] However, considering the clinical presentation and the histological findings of both lymph node and bone marrow, secondary rather than Primary MF is more likely to be present in our case. Until date, no study has shown primary MF occurring simultaneously with HSTL and few reports have discussed the subsequent development of secondary MF in the background of peripheral T-cell lymphoma.[10] Our case illustrates that HSTL and MF can occur simultaneously at the time of diagnosis.

CONCLUSIONS

HSTL with concomitant MF presents a challenge for clinical and pathologic diagnosis. The diagnostic and prognostic

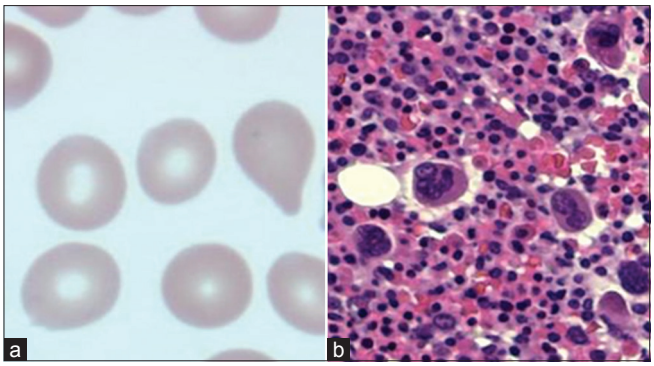

Figure 1: (a) Tear-drop red blood cell, original magnification ×100. (b) H and E stains of bone marrow biopsy specimen showing increased cellularity and atypical megakaryocytes with both large and small darkly stained nuclei, original magnification ×40

significance of the coexistence of the two diseases is important and we should be aware of these two different disease entities in an individual patient.

ACKNOWLEDGMENT

The authors of this manuscript are acknowledging full responsibility for the work.

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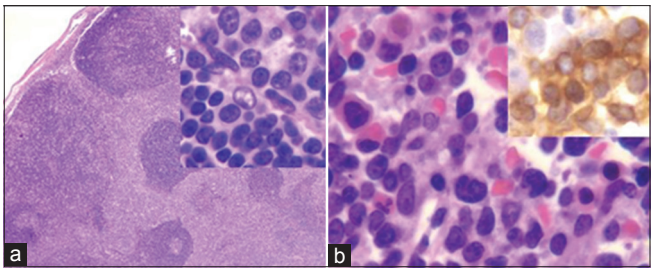

Figure 2: (a) Lymph node biopsy showing sinusoidal infiltration atypical lymphocytes. The infiltrating neoplastic cells are shown at higher magnification in the inset (b) H and E stains of bone marrow biopsy specimen showing sinusoidal infiltration of medium-sized atypical lymphocytes with irregular nuclei and a moderate amount of agranular cytoplasm that stain positive for anti-CD3 immunohistochemical stain (inset)

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Cite this article as: Gabali AM, Jazaerly T, Chang C, Cleveland R, Kass L. Simultaneous hepatosplenic T-cell lymphoma and myelofibrosis. Avicenna J Med 2014;4:34-6.

Source of Support: Nil, **Conflict of Interest:** None declared.