Hepatosplenic T-cell Lymphoma Presenting with Severe Hemolytic Anemia

Shahreen Billah, MD, Wei Feng, MD, Anthony Padula, MD, N. D. Nguyen, MD, Margaret Uthman, MD[a]

a: Department of Pathology, University of Texas Medical School at Houston, Houston TX, 77030

Introduction:

Hepatosplenic T-cell lymphoma is a rare extra-nodal systemic neoplasm first described by Gaulard in 1986. It is derived from cytotoxic T-• •• • • • ••• • •• • • • • cell receptor gene rearrangement. It typically occurs in young adult men presenting with hepatosplenomegaly, marked thrombocytopenia and bone marrow involvement. We report a case with a review of literature.

Case Report:

This is a 30-year-old African American man who presented with severe hemolytic anemia. His laboratory findings included severe anemia with hemoglobin of 6.2 g/dL, 12% reticulocytes, platelet count of 193K/uL and microspherocytes identified on peripheral blood smear. Furthermore, the direct antiglobulin test (DAT) was negative and there was an elevated LDH (1609 U/L), decreased haptoglobin (<42.1 mg/dL), jaundice (total bilirubin: 2.7 mg/dL), elevated liver enzymes (ALT: 531U/L; AST: 262U/L) and hepatosplenomegaly with dilated portal vein as identified on imaging. Serology was negative for hepatitis A, B and C viruses and positive for CMV IgG and EBV IgG (titer of 1280).

Material and Methods:

Fixed and paraffin embedded sections were stained with hematoxylin and eosin. Immunohistochemistry was performed on a representative section using the following antibodies: CD3, TdT, CD79a, and MPO. Positive controls and negative internal controls were performed with each antibody. Flow cytometry was performed on the liver biopsy and bone marrow aspirate. Cytogenetic studies were also performed on the bone marrow aspirate.

Fig. 1

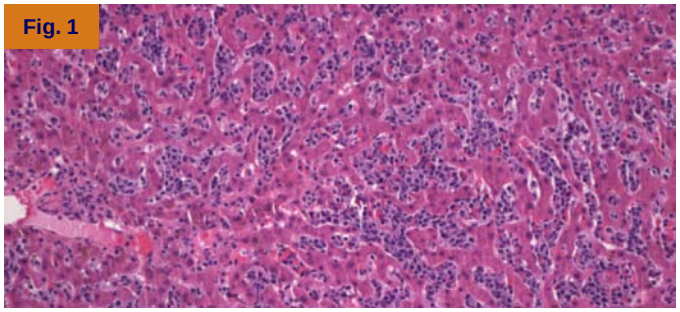


Fig. 2

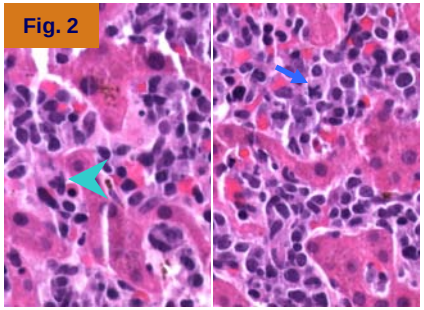


Fig. 3

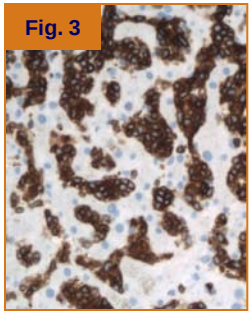


Fig. 4

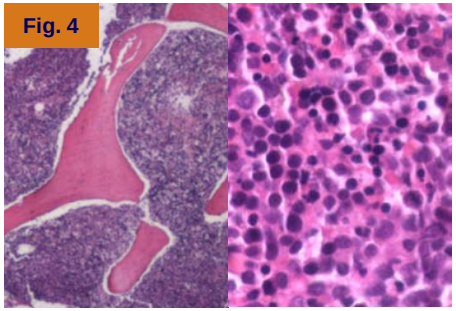
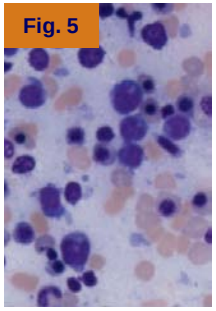


Fig. 5



Pathological Findings:

The liver biopsy showed a sinusoidal infiltration of medium-sized lymphocytes with scant to moderate cytoplasm and moderately condensed chromatin without prominent nucleoli (Fig 1-2). Immunohistochemistry and flow cytometry studies of the liver biospy revealed the following immunophenotype: positive for CD3, CD7, and CD56; negative for CD20, TdT, MPO, CD4 and CD8. Although the liver biopsy showed the classical findings for hepatosplenic T-cell lymphoma, the hypercellular bone marrow (Fig. 4-5) showed marked erythroid hyperplasia with a predominance of pronormoblasts (M:E ratio of 0.5) and the presence of a minor population (16%) of atypical lymphocytes which shared similar immunophenotype (CD3, CD7, and CD56 positive; CD5, CD4 and CD8 negative) as the liver infiltrate. No peripheral blood involvement was identified by flow cytometry studies. Cytogenetic studies of the bone marrow showed the following karyotype: 46, XY, inv(9)(p12q13).

Table 1
Clinical Features of Gamma Delta T-Cell Neoplasms[*]

Case no.	Age/Sex	Survival	Initial Site	Hepatosplenomegaly	Bone Marrow	Blood	Lymphadenopathy	Skin
Hepatosplenic gamma delta T-cell lymphoma								
1	32/male	DOD 8 months	Spleen/Liver	+/+	+ M	+ F	—	—
2	15/male	DOD 25 months	Spleen/Liver	+/+	+ F	+ F	—	—
3	20/male	DOD 8 months	Spleen/Liver	+/+	− M	+ F	—	—
4	65/male	AWD, LTF, 3 months	Spleen/Liver	+/+	+ F	− M	—	—
5	24/male	DWD 10 months	Spleen/Liver	+/+	+ F	+ F	—	—

[*]AWD, alive with disease; DOD, dead of disease; DWD, dead with disease; F, flow cytometric immunophenotyping; LTF, lost to follow up; M, morphology.

Figures:

1. Liver biopsy (H&E 10x): sinusoidal infiltrate
2. Liver biopsy (H&E 50x): erythroid precursor (arrow head), mitosis (arrow)
3. Liver biopsy: CD3 immunohistochemistry
4. Bone marrow biopsy (H&E 10x): hypercellular, lymphocytic infiltrate
5. Bone marrow aspirate (Wright 50x): normoblasts and lymphoma cells

Discussion:

This presentation of Coombs-negative hemolytic anemia with jaundice and lack of peripheral blood involvement (present in approximately half of cases) makes this aggressive lymphoma a difficult diagnosis to make, as liver or splenic biopsy is usually not included in the initial workup for hemolytic anemia. Although anemia is frequently attributed to splenomegaly, hemolytic anemia has been explained by elevated cytokines produced by the neoplastic T-lymphocytes as reflected in the observed hemophagocytosis in a number of reported cases. Furthermore, four rare cases of immune-mediated anemia with positive Coombs have been reported to date. B-cell lymphomas are often associated with immune-mediated anemia and peripheral lymphadenopathy, but hepatosplenic T-cell lymphomas typically lack these findings. Therefore, in the setting of Coombs-negative hemolytic anemia, rare T-cell •• • • •• • • • • • • • • • • • • • • • -cell lymphoma, should be considered in the differential diagnosis to allow the timely diagnosis of these aggressive systemic neoplasms.

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