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# Hepato-splenic Gamma Delta T-cell Lymphoma in Bangladesh: Case Report on a Challenging Entity

Maruf Al Hasan[1*], M Morsed Zaman Miah[1], Romena Alom[1], Tamanna Nourin[2]

*1 Department of Haematology, Rajshahi Medical College Hospital, Rajshahi*
*2 Department of Radiotherapy, Rajshahi Medical College Hospital, Rajshahi*

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**ABSTRACT:** With a unique development pattern and clinical context, Hepato-splenic Gamma Delta Lymphoma is an unusual but distinct T-cell lymphoma. Hepatosplenomegaly, anemia, thrombocytopenia, no swelling of superficial lymph nodes, and an aggressive clinical course are its defining features, which manifest at a young age. In this case report, a 48 years old male Hb-E trait patient with a history of splenectomy attended the Department of Hematology of Rajshahi Medical College and Hospital with hepatomegaly, weakness, anorexia and feverish feeling. The hematological report revealed anemia whereas total WBC and platelet count were within normal range. Bone marrow aspiration showed hypercellularity with all precursors. Bone marrow biopsy showed hyperplastic marrow with focal abnormal infiltration of medium-sized lymphoid cells. The diagnosis was confirmed by flow cytometry correlating clinical and other investigation findings. This lymphoma is difficult to diagnose due to its rarity, absence of nodal involvement, and symptoms that mirror other entities, particularly infectious etiologies. In such circumstances, whereas bone marrow is the primary diagnostic modality, the pattern of involvement can be modest. As a result, understanding the pattern of involvement and supporting research would aid in precise diagnosis, early treatment, and increased survival rates.

**Keywords:** Hepato-splenic Gamma Delta Lymphoma, Hb-E Trait, Hepatomegaly, Splenectomy, Flow Cytometry.

## INTRODUCTION

Within the subset of Non-Hodgkin lymphomas, Hepatosplenic γδT cell lymphoma (HSγδTL) accounts for less than 1% and is associated with poor prognosis.[1, 2] The extranodal involvement with a distinguished sinusoidal pattern of infiltration of the liver, red pulp of the spleen, and bone marrow with unique immunophenotypical and chromosomal aberration than other subtypes of gamma delta T cell lymphomas is the distinctive feature of this type of T cell lymphoma.[3, 4] The World Health Organization (WHO) reclassified γδT cell lymphoma in 2008, splitting it into two groups: Primary cutaneous γδT cell lymphoma (PCγδTCL) and Hepatosplenic γδT cell lymphoma (HSγδTL).[5-7] Less than one-third of individuals with a history of immune suppression are affected by this extranodal lymphoma, which typically affects young adults with a median age of 35.

It also appears to be more common in men.[8-11] Appropriate management is unknown because of its rarity and the scarcity of published information. Additionally, response rates and survival rates are low, and current treatment options are restricted.[1, 8-14]

Within the gastrointestinal system, mucosal locations, lymphoid and cutaneous tissues, and the red pulp of the spleen, γδT cells are frequently present and account for less than 5% of circulating lymphocytes in healthy adults. While they make up only 1% to 5% of circulating lymphocytes, they are most prevalent in the spleen, where they account for 30% of the T-cell population.[15, 16] However, Hepatosplenic γδT cell lymphoma (HSγδTL) is

characterized by monomorphous infiltration of medium-sized lymphocytes with a considerable amount of big pale basophilic cytoplasm, loosely condensed nuclear chromatin, and small inconspicuous nucleoli. The spleen has crimson pulp sinuses and atrophic white pulp. The liver is largely involved in the sinusoids. Bone marrow involvement has a primarily intrasinusoidal distribution.[17] The majority of HSTCL cases develop de novo, although around 20% occur in the setting of immunosuppression or immunological dysregulation, including autoimmune illnesses, inflammatory bowel disease (IBD), hematologic malignancies, and prior solid organ transplant.[18] Disease development is characterized by an interstitial pattern of bone marrow involvement, with a trend towards blastic cells. The involvement of lymph nodes is quite unusual. Patients most frequently experience hepatic and splenic enlargement, cytopenias, and constitutional symptoms; hemophagocytic syndrome is another possible complication. Most instances of HSTCL have mutations in genes related to chromatin modification or the JAK/STAT system. Isomerism 7q and trisomy 8 are the most common chromosomal abnormalities linked to the condition.[18] This case study describes a patient diagnosed with Hepato-splenic gamma delta mature T cell neoplasm which is rarely found in our country.

## CASE SUMMARY

Written informed consent was obtained from the patient to publish this case report and accompanying images. This article follows the CARE reporting checklist (available at https://www.care-statement.org/checklist). A male of 48 years old attended the Department of Hematology of Rajshahi Medical College and Hospital with hepatomegaly, weakness, anorexia and feverish feeling. He is a known case of Hb-E trait and had splenectomy recently. He didn't give any history of weight loss. The patient takes anti-diabetic medication and his BP was found 115/65 mm Hg. On general examination, the patient was found anemic. Liver is enlarged 4 cm from the right costal margin along the right mid clavicular line. He didn't have jaundice and the temperature was normal. No enlarged lymph node was found during palpation. On query he gave history splenectomy 6 months back due to huge splenomegaly. He didn't show sufficient documents about this operation. The blood test showed a decreased Hb level (10.2 g/dl) with a reduced total RBC count (3.75 million/cumm) with 30% HCT/PCV lower than the reference value. Total WBC and platelet count were within normal range. The differential count for neutrophils was 8176.5 × 10^3/uL and for lymphocytes 1449 × 10^3/ uL.

**Table 1: Hematology Report Findings**

| Parameter | Result of the patient | Reference value |
|---|---|---|
| Hemoglobin | 10.2 g/dL | 13-17 g/dL |
| Total count for WBC | 10, 350/cumm | 4,000- 11,000/cumm |
| Neutrophil | 79% | 40-80% |
| Lymphocyte | 14% | 20-40% |
| Total RBC count | 3.75 million/cumm | 4.5-5.5 million/cumm |
| HCT/PCV | 30% | 40-50% |
| RDW-CV | 20.9% | 11.6± 14% |
| Total Platelet count | 3,34,000/cumm | 1,50,000 – 4,10,000/cumm |

Bone marrow aspiration showed hypercellularity with all precursors. The bone marrow biopsy report revealed hyperplastic bone marrow with focal abnormal infiltration of medium-sized lymphoid cells. Flow cytometry demonstrated a cell cluster with low SSC and moderate CD45 expression. According to the pattern, there was dim to moderate expression of TCRgd and moderate expression of CD2, CD3, CD7 and CD56. The rest of the markers were found negative. The findings were suggestive of mature T-cell neoplasm with the possibility of Hepatosplenic γδT cell lymphoma (HSγδTL). Clinically the patient was suspected of primary myelofibrosis and low-grade lymphoma as a differential diagnosis, through correlating the findings of clinical, and other hematological parameters, the diagnosis was confirmed as HSγδTCL by flow cytometry.

**Table 2: Flow Cytometry of CLL Diagnostic Panel Comprehensive Findings**

| Markers | Intensity | Interpretation |
|---|---|---|
| **T-Cell Markers** | | |
| CD2 | Moderate | Positive |
| CD3 | Moderate | Positive |
| CD7 | Moderate | Positive |
| TCRγδ | Dim to moderate | Positive |
| **B-Cell Markers** | | |
| CD19, CD20, CD23, CD79b, CD200, FMC-7 etc. | N/A | Negative |
| **Other Markers** | | |
| CD45 | Moderate | Positive |
| CD56 | Moderate | Positive |
| CD10, CD16, CD25, CD38, CD103, CD11c, HLADR | N/A | Negative |

## DISCUSSION

This is a case study of a 45 years old male patient with a history of Hb-E trait and splenectomy with hepatomegaly diagnosed with Hepato-splenic gamma delta T-cell lymphoma (HSGDTCL). This uncommon lymphoid tumor belongs to the heterogeneous PTCLs (Peripheral T-cell lymphoma) category. However, it is more common in men at a younger age though multiple shreds of literature showed an inconsistency in age and sex distribution.[19-21, 23] Madabhavi et al., reported two cases of Hepatosplenic Gamma Delta T-cell lymphoma.[22] A 63-year-old female with a history of progressive abdominal distension, anorexia and weakness presented with moderate non-tender hepatosplenomegaly and moderate ascites. The hemogram showed moderate anemia with thrombocytopenia whereas Immunohistochemistry (IHC) showed positivity for leucocytes Common Antigen (LCA) and T cell markers like CD2. On the other hand, a 60-year-old male chronic alcoholic patient presented with a 2-month history of severe weight loss followed by jaundice and abdominal pain diagnosed with HSγδTL, though there was no palpable lymphadenopathy and hepatosplenomegaly.[22] Usually, splenomegaly is a constant finding in HSγδTL, hepatomegaly could be lacking in 10–15% of cases. Our case had a history of splenectomy due to marked enlargement with hepatomegaly as well consistent with the usual findings. Anemia is present in 75% of cases and thrombocytopenia is seen invariably in these patients differs from our case as platelet count was within normal range. In a case series of 6 patients diagnosed with HSγδTL found a similar result for Hb whereas platelet was within the normal range which is similar to the current study findings.[23]

Neoplastic cells in HSγδTL tend to spread among normal hematopoietic cells, therefore it requires a high level of suspicion and is often diagnosed through bone marrow or liver biopsy.[24] According to Belhadj *et al*. and Lu *et al*., bone marrow involvement in HSγδTL is identified in around two-thirds of patients at diagnosis as a consistent feature at presentation.[25, 26] The results of the biopsy include aberrant lymphocytes, which are usually bland and monotonous with irregular nuclei, condensed chromatin, and a trace quantity of pale cytoplasm.[27] Immunophenotyping and flow cytometry of biopsy specimens aid in the diagnosis.[10] HSγδTL has been found to exhibit the following phenotypes: CD2+, CD3+, CD4-, CD5-, CD7+, CD8-, and TCRγδ+. This observation correlates with the following study as CD2, CD3, CD7 and TCRγδ markers were positive including CD4 and CD56. According to the literature, other activation-related molecules not exclusive to T cells, including CD11b, CD11c, CD38, CD43, and Fas ligand, are also commonly expressed. TCR-αβ chain, TdT, immunoglobulins, B cell markers (CD19, CD20, CD21 and CD22), CD10, CD15, CD25, CD33, CD34, CD41, and CD68 were all variable in their expression, whereas CD5, CD7, CD8, CD16 and CD56 were consistently negative.[28] In a recent study by Tham *et al*. on 6 cases of HSγδTL ranging from 14–65 years had CD2, CD3 and CD7 in common.[30, 31] In a case report, Mutreja *et al*., (2013) found CD3, CD2, CD7, CD56, T-cell receptor (TCR) γδ found positive whereas negative for TCR αβ, CD4 and CD8 in a 13-year-old Indian boy with visceral leishmaniasis.[29] This case

report was focused on correlating leishmaniasis with the development of HSγδTL. However, Falciparum malaria, Epstein–Barr virus and Hepatitis B infections were discussed in some studies. Viral hepatitis was excluded in the current study. Although the majority of cases develop spontaneously, it has been proposed that HSγδTL is connected with immunodeficiency or immune-mediated conditions.[30] The current case has a known history of Hb-E trait condition. According to a case series and literature analysis, 89% of patients with autoimmune disorders received immunosuppressive therapy.

## CONCLUSION

The histological properties of HSγδTL are extremely consistent. HSγδTL is an uncommon, extremely aggressive T-cell lymphoma that presents difficult treatment and diagnosis decisions. A strong index of suspicion is necessary for an early and precise diagnosis of HSγδTL in the clinical context of pancytopenia with hepatosplenomegaly in the absence of lymphadenopathy because of its rapid and aggressive clinical progression. There is relatively little information available about the therapy of HSγδTL. Some therapy regimens, including bone marrow transplantation, have been tried, but no successful treatment has been found. Early recognition of this disease might prolong the duration of survival.

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***Correspondence:** Dr. Md. Maruf Al Hasan, Email: marufhasan4954@gmail.com

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