

Hepatosplenic T-cell lymphoma: case report & literature review

Abstract

Hepatosplenic T-cell lymphoma (HSTCL) was first described as a distinct clinicopathologic entity in 1990. HSTCL is more common among young males in their teenage years and in young adulthood. It is an aggressive tumor. Our patient presented with pancytopenia, hepatosplenomegaly but no lymphadenopathy. The key role for diagnosis was through identifying of double negative CD4, CD8 negative lymphocytes with gamma delta T-cells receptor expression. Our case is considered one of the few cases of hepatosplenic T-cell lymphoma published in Saudi Arabia according to our best of knowledge. The need for high index of suspicion and reporting such rare T-cells lymphomas need to be identified to start therapy properly and early along with understanding more regarding its pathophysiology.

Keywords: hepatosplenomegaly, lymphadenopathy, neoplastic cells, beta T-cell receptor, histiocytes, flow cytometry

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Abbreviations: HSTCL, hepatosplenic T-cell lymphoma; PTCLs, peripheral T-cell lymphomas; TCR, T cell receptor

Introduction

Hepatosplenic T-cell lymphoma (HSTCL) was first described as a distinct clinicopathologic entity in 1990.¹ HSTCL is a rare peripheral T-cell lymphoma, less than 100 cases have been described in the literature.² The term 'hepatosplenic T-cell lymphoma' was adopted for use since World Health Organization classification, 2001.³ Peripheral T-cell lymphomas (PTCLs) account for 7-10% of all non-Hodgkin lymphomas in Western countries, with HSTCL identified as a rare entity within this group.⁴ It has been estimated to contribute only 1.4% of all T-cell lymphomas.⁵ HSTCL is more common among young males in their teenage years and in young adulthood. Neoplastic cells are derived from functionally immature innate effector cells, most often of T-cell origin, characterized by pancytopenia and prominent hepatosplenomegaly without adenopathy.⁶ It is an aggressive tumor involving the liver, spleen, and bone marrow with characteristic intrasinusoidal distribution of tumor cells. Isochromosome 7q represents the primary non-random cytogenetic abnormality and plays a role in its pathogenesis. The prognosis is poor with a median survival time of 16 months.² Our patient presented with Pancytopenia, hepatosplenomegaly & bone marrow involvement a evident by flow cytometric findings of double negative (CD4, CD8) T-cell lymphoma with expression of gammadelta T-cell receptor.

Case presentation

21 years old Saudi male patient, student, was totally medically free till around one month back when presented with on and off abdominal pain and distension, fullness which increased one week before admission for which he was seen in emergency department where routine work up done and found to have pancytopenia with hepatosplenomegaly accordingly was admitted for further work up. Patient denied history of fever or night sweating or loss of appetite, but he attributed his loss of weight due to the diet he is doing in previous months. He gave history of few scattered maculopapular red spots over lower limb and back which disappeared. He gave no history of jaundice or any other gastrointestinal symptoms. No history

of blood transfusion or any surgical procedure before. No history of drug use and he is not smoker or alcoholic He is staying in Egypt for the past 3 years as medical student.

Upon physical examination he was well looking, pale but not jaundiced and not in distress. Vital signs: stable. No lymph adenopathy. Abdomen: distended, huge hepatomegaly 23cm span and huge splenomegaly 26cm BCM Other systemic review was unremarkable. CT scan abdomen shows massive hepatosplenomegaly where the liver is measuring 23.3cm and spleen is 25.6cm and is displacing the left kidney inferiorly, however no hydronephrosis. The spleen has few patching hypoperfused areas largest is seen in inferior pole measuring 7cm. No enlarged lymph nodes seen. Initial investigation shows pancytopenia with HB: 8.5g/dl (normal range 12.5-18g/dl) RBC morphology is consistent with hereditary elliptocytosis. Reticulocyte count: 1.4% (normal range 0.5-2.5%). WBC: 1100/ul (normal range is 4000-11,000/ul). Absolute neutrophil count: 0.23 (marked neutropenia) (normal range is 1.5-8.0) & mild lymphopenia (absolute count of 0.49) (normal range is 1.3-3.5). Platelet count: 35,000/ul (normal range is 150-450,000/ul) (Several giant forms are seen). No blast cells or atypical lymphocytes seen.

Coagulation studies, liver function & renal function tests, uric acid, amylase, lipase, LDH (lactic acid dehydrogenase and Calcium level are all within normal ranges. Bone marrow aspiration was hemodiluted but shows infiltration by scanty clumps of small to medium size lymphocytes with a high nucleus/Cytoplasmic ratio, irregular nuclear margins, moderately dispersed chromatin, 1-2 small nucleoli & moderate cytoplasmic basophilia (Figure 1). Myeloid: Erythroid ratio is 1:1.9. myeloid series constitutes 27% with normal sequential maturation. There is slight erythroid hyperplasia (52%, essentially micronormoblastic in maturation with presence of ragged vacuolated cytoplasm in the late precursors in addition to several mitotic figures). Lymphocytes & plasma cells constitute 19% & 1% respectively. Megakaryocytes are abundant, all stages seen & normal in morphology. There is also slight increase in histiocytes some exhibit hemophagocytic activity. Flow cytometry analysis shows that the gated population of interest is in the lymphocytes window. They are positive for CD2, CD3, CD7, CD16, CD56, & gamma/delta T-cell receptor expression & negative for CD4, CD8, and CD5.

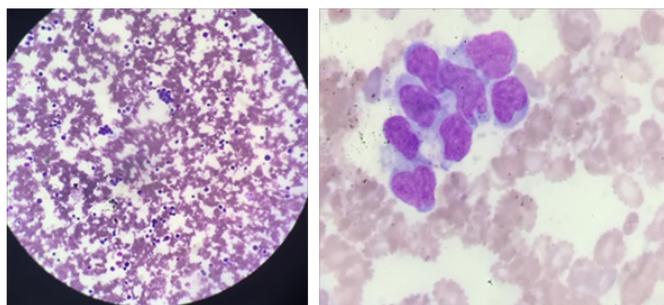


Figure 1 Bone marrow aspirate (higher magnification), clumps of cohesive atypical lymphocytes.

CD1a, CD34, TDT, CD99, CD25, CD10, CD30 & CD11C there is also benign mature T lymphocytes population with alpha/beta T-cell receptor but no aberrant loss or aberrant expression of any T- cells markers. A tiny population of polyclonal B cells is also seen. Flow cytometry of peripheral blood was done later but did not show evidence for those gammadelta double negative (CD4, CD8) T-cells. One Piece of trephine bone marrow biopsy was examined. measures 0.3×1.0cm shows crush artifact, regardless there is Adequate reportable spaces with cellularity of around 80-90% showing increase in erythroid & megakaryocytic series in addition to increase in histiocytes & small lymphocytes sinusoides appears to be dilated with minimal intrasinusoidal infiltration by the tumor cells. Reticulin Stain shows Grade III fibrosis. Karyotype shows XY, 46 with no evidence of aberrant chromosomal abnormalities, while molecular studies of T cell receptor (TCR) gene demonstrate clonal rearrangements in the gamma and delta genes. The diagnosis of hepatosplenic T-cell lymphoma was confirmed & the patient started on hyper CVAD Protocol (cyclophosphamide, vincristine, doxorubicin, dexamethasone, alternating with high-dose methotrexate and cytarabine) (Figure 2).

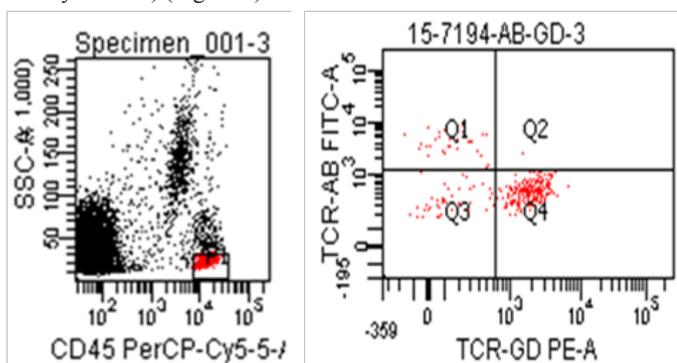


Figure 2 Flow cytometry shows that the neoplastic cells are located in the lymphocytes area (positive for CD3, CD2, CD7, CD16, CD56, dual negative for both CD4 & CD8 with aberrant loss of CD5 along with expression of gamma delta T-cell receptor).

Discussion

Peripheral T-cell lymphomas (PTCLs) account for 7-10% of all non-Hodgkin lymphomas in Western countries, with HSTCL identified as a rare entity within this group.⁴ It presents with fevers, weight loss, night sweats and hepatosplenomegaly Laboratory results are significant for neutropenia, thrombocytopenia, and anemia. The diagnosis of HSTCL requires a high index of suspicion. Bone marrow studies including immunophenotyping by flow cytometry immunohistochemical staining, and cytogenetic analysis are

mandatory. The treatment of HSTCL necessitates intensive induction chemotherapy followed by allogeneic bone marrow transplantation.⁷ HSTCL is an extremely aggressive often fatal. Even with achievement of initial remission, patients often relapse.⁷ Although HSTCL was first recognized as a distinct pathophysiological entity over 25years ago, this aggressive neoplasm still lacks any standardized treatment guideline. Moreover, survival duration for this disease varies widely from 0 to 72months and no clinical feature or biomarker has been identified to reliably predict prognosis.⁷ The diagnosis of HSTL is challenging, in our patient initially those collections of cohesive cells needed to be verified whether they are hematopoietic or not.

Flow cytometry had great role in confirming the diagnosis of our patient (presence of double negative (CD4, CD8) lymphocytes with expression of gammadelta T-Cell receptor) made the diagnosis more restricted and easier. However phenotype by itself is not enough, correlation with clinical presentation & morphology should be always made. Our case highlights the importance of a high index of suspicion for HSTCL diagnosis, besides digging in the history to look for any possible risk factors. It is important to continue reporting these rare cases, and to determine possible risk factors in our population if present. According to our best of knowledge there is only 2 published cases of hepatosplenic T-cell lymphoma in Saudi Arabia.^{8,9} One of them is 38years old Filipino who presented by jaundice and massive hepatosplenomegaly while the other is 35years lady with breast lump and diagnosed with gammadelta T-cell lymphoma. Weather its genuinely very rare in our area or there is reluctance in reporting the cases needs to be looked at.

Conclusion

Hepatosplenic T cell lymphoma is a distinct lymphoma entity & very rare T-cell lymphoma. It is not encountered frequently by the hematopathologist. This case highlights the importance of considering diagnosis of Hepatosplenic T cell lymphoma in young male patients with pancytopenia, massive hepatosplenomegaly but no lymphadenopathy. It can be distinguished from most other lymphoma types by the combination of: A typical immunophenotype, Sinusoidal involvement of the spleen and the liver& TCR- gene rearrangement, which will lead to prompt diagnosis and immediate initiation of therapy for this rare T-cell lymphoma. Knowledge of T-cell lymphomas is still lagging behind B-Cell non hodgkins lymphoma.

Consent

Written informed consent was obtained from the patient for publication of this case report & any accompanying images.

Author contribution

Mariam AlGhazal, Abdullah AlRashed was involved in the diagnosis of this patient. Alghazal defined the manuscript while AlRashed provided valuable input. All authors read and approved the final manuscript.

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Conflict of interest

The authors declare that they have no conflicts of interest.

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