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# Hepatosplenic T-Cell Lymphoma in visceral leishmaniasis young girl

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## Abstract

Hepatosplenic T-cell lymphoma (HSTCL) is a rare, aggressive T- cell lymphoma that is characterized by hepatosplenic and bone marrow sinusoidal infiltration of cytotoxic T cells, usually of gamma-delta (γδ) T-cell receptor type. The diagnosis was challenging as he required an extensive investigation that ultimately showed the characteristic clinical, histopathologic, and cytogenetic features of hepatosplenic T-cell lymphoma. We report a case of 12-year-old girl patient with HSTCL and visceral leishmaniasis, presented with progressive jaundice, massive hepatosplenomegaly, and weight loss. The diagnosis was required an extensive investigation that ultimately revealed the characteristically clinical, histopathological and cytogenetic features of hepatosplenic T-Cell Lymphoma. The clinical course was aggressive and multi-agent chemotherapy are used. The importance of considering it in a differential diagnosis of hepatosplenomegaly in young girl who present with constitutional symptoms and visceral leishmaniasis without lymphadenopathy.

**Keywords**: HSTCL; Visceral leishmaniasis; Chemotherapy; Lymphadenopathy

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## Introduction

Hepatosplenic T-cell lymphoma (HSTCL) is a rare, aggressive T-cell lymphoma that accounts for less than 1% of non-Hodgkin lymphomas [1]. It is characte-rized by hepatosplenic and bone marrow sinusoidal infiltration of cytotoxic T cells, usually of gamma-delta (γδ) T-cell receptor type [2].

The majority of patients have liver, spleen, and bone marrow involvement at presentation [3]. As a result, they tend to be anemic, jaundiced, have prominent hepatosplenomegaly, with no or minimal lymphadenopathy, and constitutional or 'B' symptoms. The predominant laboratory findings include pancytopenia and abnormal liver chemistry with elevated liver enzymes and alkaline phosphatase. Visceral leishmaniasis is relatively common parasitic infection among children in Greece [4, 5, 6].

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## Case presentation

12-year-old girl, presented to the Emergency Department with 8-week history of fever, fatigue, anorexia and loss of weight. She recent traveled abroad without history of drugs or alcohol consumption. On physical examination she was febrile 39.8ºC and tachycardia, with palpable tender liver and spleen (4.1 cm and 3.9 cm respectively) below the costal margin, in the absence of peripheral lymphadenopathy.

## Investigations

Initial laboratory work revealed pancytopenia (haemoglobin 10.4 g/dL, white cell count 2.1 x $10^9$/L, platelet count 71 x$10^9$/L) and elevated ESR at 64 mm/h. Both prothrombin time and partial thromboplastin time were prolonged (68% and 21.5 seconds, respectively). Lactic dehydrogenase was elevated 301U/L, Serology tests for hepatitis A, B and C, cytomegalovirus, and parvovirus B19 were all negative. Examination of a stained bone marrow specimen showing macrophage cells containing multiple Leishmania amastigotes **Fig. 1, 2**. After admission in hospital her fever subsided, blood counts rose and discharged from the hospital after 14-days with normal blood tests. 3- weeks later, the patient developed recurrent fever, malaise and peripheral edema. She was readmitted to the hospital and her laboratory studies showed pancytopenia, hypoalbuminemia of 2.1 g/dL and elevated liver function tests at four times the normal values. New CT scan of the chest, abdomen and pelvis was performed, revealing homogeneously enlarged liver (long axis, 25 cm) and massive splenomegaly (23 cm), with no evidence of lymphadenopathy. Furthermore, the positron emission tomography (PET) scan of the patient with HSTCL demonstrates high metabolic activity in the liver, spleen and the bone marrow **Fig. 3, 5**. A new bone marrow sample was harvested that showed extensive infiltration by small mature T-lymphocytes mostly in a nodular pattern.

Flow cytometry revealed tumor cells that expressed CD2, CD3 positivity, but lacked expression of CD5, CD4, and CD8. In addition, malignant cells expressed the natural killer (NK) cell marker CD56, but were negative for B-cell-associated markers (CD19, CD20, CD22 and CD23) **Fig. 6**.

As the patient's symptoms continued to progress, a transjugular liver biopsy was performed, revealing portal and sinusoidal infiltration by small to medium size lymphocytes with hyperchromatic nuclei, some of which showed atypical mitoses. Few small non-caseating granulomas were seen within the hepatic lobules. Immunohistochemiacal stains showed positive staining for CD3, CD7, CD56, TIA1 and Granzyme B, similar to that seen within the bone marrow **Fig. 7, 8**.

## Treatment

Patient initiated chemotherapy with CHOP regimen (cyclophosphamide, hydroxy doxorubicin, vincristine, prednisone) in association with methotrexate, with a transitory response. Autologous stem cell transplant was considered. Sitamaquin used at a dose of 1 mg/kg for 28 days, for treatment

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leishmaniasis. Positron emission tomography scan executed after the fourth cycle of chemotherapy showed lymphoproliferative disease with high metabolic activity in the liver, spleen, bone marrow. Despite the aggressive treatment with four cycles of multiagent chemotherapy, remission was not achieved and the patient died 6 months after the diagnosis.

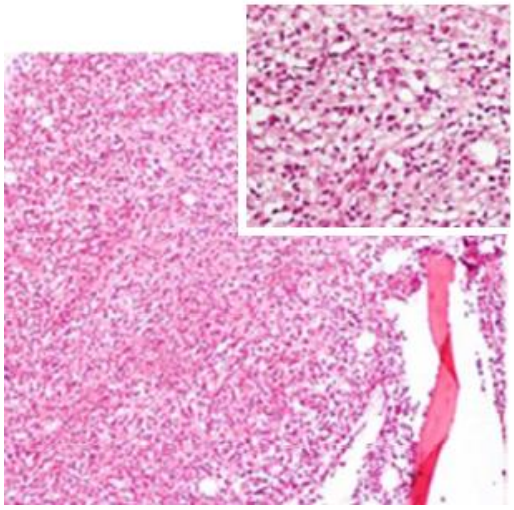

**Figure 1.**

Bone marrow biopsy revealing extensive infiltration by small mature T-lymphocytes (hematoxylin and eosin staining at x100 and x200 magnification) 49x18mm (300 x 300 DPI).

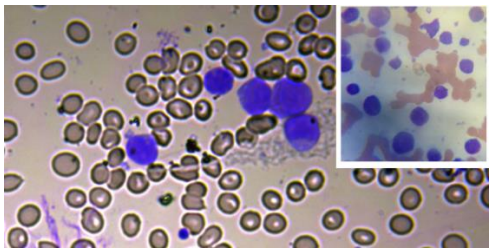

**Figure 2.**

Bone marrow biopsy revealing (hematoxylin and eosin Giemsa stain at x100 and x200 magnification) 49x18mm (300 x 300 DPI).

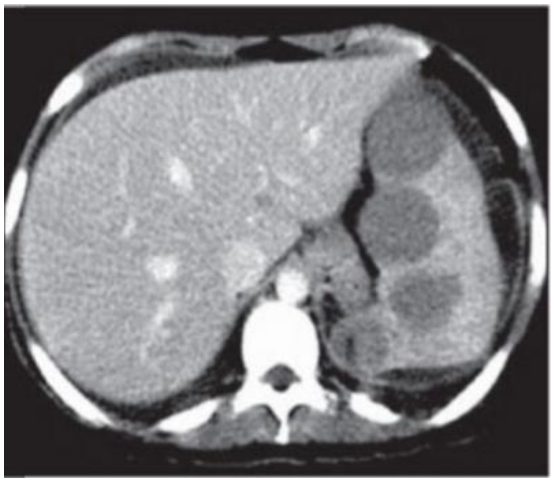

**Figure 3.**

Abdominal CT demonstrates hepatosplenomegaly in a patient with hepatosplenic T-cell lymphoma and visceral leishmaniasis.

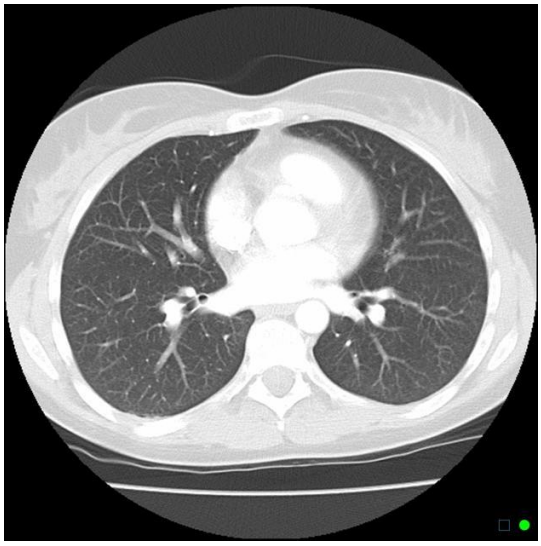

**Figure 4.**

Normal chest CT (lung window) in a patient with hepatosplenic T-cell lymphoma and visceral leishmaniasis.

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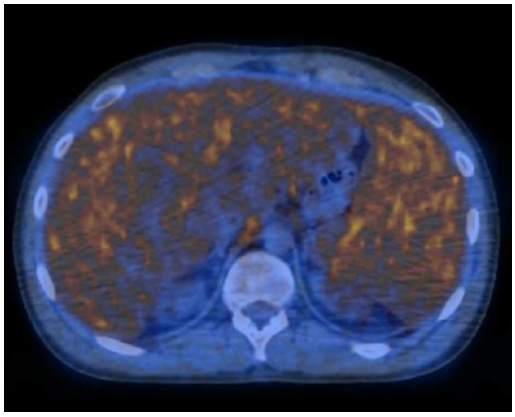

**Figure 5.**

A positron emission tomography (PET) scan of the patient with HSTCL demonstrates high metabolic activity in the liver, spleen and the bone marrow 59x43mm (300 x 300 DPI).

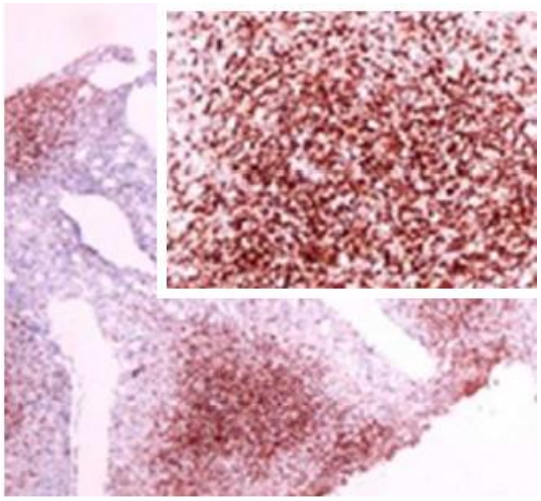

**Figure 6.**

Immunohystochemical staining on the bone marrow biopsy specimen showing tumor cellsinfiltrates, mostly in a nodular pattern (magnification x40 and x100).

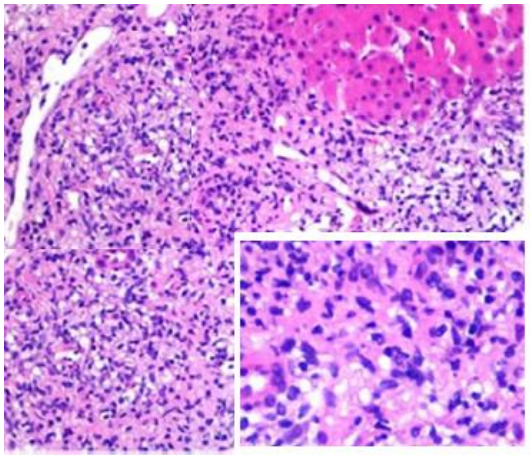

**Figure 7.**

Histology and immunohistochemistry of a transjugular liver biopsy showing portal and sinusoidal infiltration by atypical small to medium sized lymphocytes with hyperchromatic nuclei and low mitotic activity, similar to that seen within the sinusoids of the bone marrow. (Hematoxylin and eosin staining at x200 and x400 magnification) 59x22mm (300 x 300 DPI).

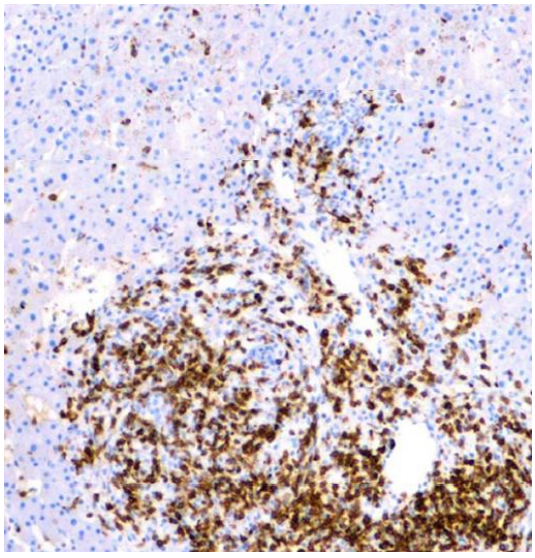

**Figure 8.**

Immunohystochemical staining on a liver biopsy specimen at x100 magnification 59x44mm (300 x 300 DPI).

## Discussion

Hepatosplenic T-cell lymphoma is a rare subset of the peripheral T-cell lymphomas, accounting for less than 1% of non-Hodgkin lymphomas and about 3% of all T-cell lymphomas/leukaemias [7-9]. It was first described as a distinct clinicpathologic entity in the 1990 REAL (Revised European American Lymphoma) Classification and it is characterrizeed by extranodal infiltration and proliferation of malignant T-cells within the sinusoids of the liver, sinuses and red pulp of the spleen, and the sinuses of the bone marrow [10, 11].

Although the pathogenesis of HSTCL is poorly understood, it has been postulated that chronic antigen stimulation in the setting of immune deficiency or dysregulation might be important [13]. Ten to twenty percent of patients have a history of chronic immune suppression, such as that associated with treatment for a lymphoproliferative disorder, prior solid organ transplantation or inflammatory bowel disease [14]. Regarding the latter, there has been an association between the development of HSTCL with the use of tumor necrosis factor (TNF) blockers, thiopurine, and the anti-TNF monoclonal [15].

## Competing interests

Authors declare that we have no competing interests.

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