Hepatosplenic T Cell Lymphoma

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Abstract A 26 year old lady came with intermittent fever since eight months. She also complained of abdominal pain and decreased appetite for six months. She had swelling of feet and distension of abdomen due to ascites since one month. There was history of jaundice one month back. On radiological examination, hepatomegaly with dilated portal vein, massive splenomegaly and ascites without any lymphadenopathy was noted. Chest X-ray was normal. Blood examination and bone marrow studies were inconclusive. We received her liver biopsy, which showed normal architecture and sinusoidal infiltration by a monomorphic population of small to intermediate sized lymphoid cells. Portal tracts were free of such infiltrate. These lymphoid cells were LCA, CD3, CD43 positive and negative for CD20, CD34, CD4, CD8 and c-kit. Based on all these features, a diagnosis of Hepatosplenic T cell lymphoma was made. She was treated symptomatically, however she died within two months of diagnosis.

Keywords Hepatosplenic · T cell · Lymphoma

Introduction

Hepatosplenic T cell lymphoma [HSTCL] is an aggressive subtype of extra nodal lymphoma. It accounts for less than

2 % of peripheral T cell lymphomas. In 1990, it was separated from mixed T cell lymphoma due to specific histological pattern of sinusoidal tropism of neoplastic cells in liver, spleen and bone marrow. Majority of the cases are of gamma-delta cell origin but alpha-beta origin can also be seen in a smaller subset of cases. The neoplasm is seen mostly in adolescents and young adults with a strong predilection for males. It also occurs in children who are on long-term immunosuppressive therapy for Crohn's disease. We present this rare case of Hepatosplenic T cell lymphoma.

Case History

A 26 year old lady presented with complaints of gradually progressive abdominal distension since 6 months with left upper abdominal pain and decreased appetite since six months. She had ascites and swelling of feet since one month. Eight months ago she had delivered a healthy male baby. Since then she was having fever off and on which subsided on its own after 4 months. There was history of anaemic symptoms in the form of easy fatigability, dyspnoea on exertion since 2–3 months. She had history of jaundice one month back. There was no history of malena, haematemesis, and altered sensorium. There was no history of alcohol abuse, high risk sexual behavior, drug intake. There was no past history of diabetes, hypertension, tuberculosis. Physical examination revealed pallor, bilateral pitting pedal edema. There was massive splenomegaly 15 cm below costal margin with moderate ascites. No evidence of icterus, and KF ring. No evidence of localized or generalized lymphadenopathy. Abdominal ultrasonography showed hepatomegaly (16 cm span) with dilated portal vein, massive

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splenomegaly and ascites without any lymphadenopathy. CT scan showed hepatomegaly along with marked splenomegaly extending up to the iliac crest. No mass, focal lesion or lymphadenopathy was seen. Chest X-ray was normal. Blood test revealed haemoglobin 9 gm %, total WBC count of 3,370/cumm with 65 % polymorphs, 35 % lymphocytes. Platelet count was 95,000/cumm. Peripheral blood smear showed normocytic normochromic RBCs. Bone marrow aspirate revealed hypercellular marrow with erythroid hyperplasia, no parasites. Bone marrow biopsy showed normocellular marrow showing trilineage haematopoiesis with erythroid hyperplasia, no atypical cells or no evidence of myelofibrosis on reticulin staining. Bone marrow cytogenetic study was normal. JAK2 mutation and RTPCR for BCR-ABL were also negative. Liver function tests showed albumin (2 g/dl), globulin (5 g/dl), alkaline phosphatase (484 IU/dl). Viral

markers (HIV, HbsAg, AntiHCV) were non-reactive. Ascitic fluid analysis showed total leukocyte count of 28/cumm with 5 % polymorphs and 95 % lymphocytes and albumin level of 343 mg/dl. Other investigations included a normal serum ceruloplasmin level, negative ANA and Anti-dsDNA.

We received her liver biopsy, which showed normal architecture. There was diffuse permeation of hepatic sinusoids by monomorphic population of small to intermediate sized lymphoid cells with hyperchromatic nuclei. The portal tracts were free of any infiltrate (Fig. 1). Based on these features, a diagnosis of Hepatosplenic T cell lymphoma was made and was confirmed as these infiltrating lymphoid cells were positive for LCA, CD3, CD43 and negative for CD20, CD34, CD4, CD8, c-kit. She was treated symptomatically, however she died within 2 months of diagnosis.

Fig. 1 a, b Microphotograph of liver biopsy showing diffuse permeation of sinusoids by small to intermediate sized lymphoid cells (a HE $\times$ 100; b HE $\times$ 400); c Portal tracts are spared (HE $\times$ 100); d CD3 positivity of the sinusoidal infiltrate, indicating that they are T lymphocytes

Discussion

The HSTCL is seen mostly in adolescents and young adults with a strong predilection for males (86 %), though our case is a female [1]. The gamma-delta HSTCL is a distinct entity occurring in young adult males with hepatosplenomegaly, in the absence of lymphadenopathy, peripheral blood cytopenia or B symptoms [1]. There is lymphomatous infiltrate in splenic, hepatic and bone marrow sinusoids. The pathogenesis of HSTCL is believed to be related to chronic antigenic stimulation due to immunosuppression, mostly associated with solid organ transplant and less commonly with Crohn's disease. It can also occur during and after pregnancy. Our patient also had delivered healthy baby 8 months prior to this illness of hers. It has been established that during pregnancy the placenta contains more NK cells, $\alpha\beta$ T cells and $\gamma\delta$ T cells, which express more cytotoxic molecules than T cell intracellular antigen 1, granzyme B and especially perforin. It is assumed that during pregnancy the high progesterone concentration might affect the perforin expression and that maternal immunity and hormonal changes during pregnancy and presumably delivery might eventually provide a chance for decidual lymphocytes to transform and develop HSTCL [2]. The disease is disseminated through marked sinusoidal infiltration of liver, spleen and bone marrow despite absence of lymph node involvement. The tumor cells are intermediate sized with dispersed chromatin, inconspicuous nuclei and moderate amount of cytoplasm. Abnormally permeating cells in bone marrow sinusoids may require immunostains for identification due to relatively bland appearance of cells on routine Hematoxylin eosin staining. The lymphoma cells are CD2 + , CD3 + , CD4 – , CD5 – , CD7 + , CD8 – , CD42 + , CD52 + , CD76 + , CD82 + with either gamma-delta or alpha-beta T-cell phenotypic receptor

expression [3]. Peripheral blood involvement, when present, is seen late in the course of the disease. Though overt leukemic involvement is unusual, careful examination of peripheral smear may reveal a few atypical lymphoid cells. The alpha-beta type shows female preponderance with occurrence in young (<5 years) and old age (50 years). HSTCL has an extremely poor outcome. Patients usually die within 8 months to 2 years. Splenectomy can play beneficial role in some patients at least in reducing the cytopenias so that chemotherapy can be safely given [4]. Patients respond to CHOP-like chemotherapy regimens only to relapse. Long-term survival has improved to some extent with bone marrow transplantation and the use of some newer agents like pentostatin, cladribine and alemtuzumab [5]. We were contemplating splenectomy for our patient however unfortunately before we could build her up for the surgery, she died.

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