Hepatosplenic T Cell Lymphoma: A Rare Case Report

Monalisa Hui · Shantveer G. Uppin ·
Tara Roshni Paul · N. Beerappa

Received: 22 August 2012 / Accepted: 26 November 2012 / Published online: 18 December 2012
© Indian Society of Haematology & Transfusion Medicine 2012

Abstract Hepatosplenic T cell lymphoma is a rare form of extra nodal and systemic neoplasm derived from cytotoxic T cells and represents less than 1 % of all non Hodgkins lymphoma. Here we present a case of hepatosplenic T cell lymphoma in a 30 year old male who presented with icterus, pancytopenia and hepatosplenomegaly, highlighting the diagnostic conundrum and pointers towards an accurate diagnosis. Histologically the sinusoids of liver and splenic red pulp were infiltration by CD 3 positive neoplastic lymphoid cells. The pattern of marrow involvement was very subtle and diagnosis was difficult to establish without the help of immunohistochemistry. This case highlights the importance of considering hepatosplenic T cell lymphoma as differential diagnosis in the clinical setting of pancytopenia with hepatosplenomegaly to allow timely diagnosis of these aggressive neoplasms.

Keywords Hepatosplenomegaly · Lymphoma · Pancytopenia · T cell

Introduction

Hepatosplenic T cell lymphoma (HSTL) was originally recognized as a distinct entity in 1990 by Farcet et al. [1].

M. Hui · S. G. Uppin (✉) · T. R. Paul
Department of Pathology, Nizam's Institute of Medical Sciences,
Punjagutta, Hyderabad 500082, Andhra Pradesh, India
e-mail: drsguppin@yahoo.co.in

N. Beerappa
Department of Surgical Gastroenterology, Nizam's Institute
of Medical Sciences, Punjagutta, Hyderabad 500082,
Andhra Pradesh, India

The typical features include an aggressive clinical course, massive splenomegaly with sinusoidal infiltration of the liver, spleen and bone marrow, no lymphadenopathy and expression or rearrangement of the $\gamma\delta$ T cell receptor [1]. Of the affected patients, 10–20 % are immunocompromised with prior history of renal transplantation, Hodgkins lymphoma, leukemia and inflammatory bowel disease [2]. These unique features have led to incorporation of HSTL as a distinct entity within the new World Health Organization classification of hematopoietic disorders [3].

Case Report

A 30 year old male presented with fever since 3 months, heaviness of abdomen for 2 months and dry cough of 10 days duration. The patient was apparently well 3 months back. He had high grade fever with chills and rigor. On examination he had mild pallor, icterus, and enlarged right axillary lymph node. There was massive splenomegaly extending up to right iliac fossa and liver was just palpable. Laboratory investigations revealed pancytopenia. Liver function tests were within normal limit except for elevated total serum bilirubin. Ultrasonography of abdomen showed mild hepatomegaly and gross splenomegaly. Bone marrow aspirate revealed reactive marrow. Biopsy of right axillary lymph node was suggestive reactive hyperplasia. The patient was treated conservatively and as the symptoms improved the patient was discharged on request. He was admitted one and half months later with the same complaints. He underwent splenectomy along with wedge biopsy of liver. On gross examination the spleen was markedly enlarged weighing 1 kg. Cut surface was beefy red in colour with tiny subcapsular infarcts. There were no discrete nodules or discernable expansion of white pulp. Microscopically the

splenic cords and sinuses of the red pulp were infiltrated by medium sized atypical lymphoid cells with moderate rim of pale cytoplasm and round nucleus with condensed nuclear chromatin (Fig. 1a). The white pulp was atrophied and focal subcapsular infarcts were noted. The liver biopsy showed atypical lymphoid cell infiltration within the dilated sinusoids with sparing of portal tracts (Fig. 2a, b). Immunohistochemistry (IHC) was done on spleen and liver biopsy. The neoplastic cells were positive for CD3 and negative for CD20 suggestive of HSTL (Figs. 1b, c and 2c, d). The trephine biopsy sections were hyper cellular and revealed tiny cluster of CD3 positive atypical lymphoid cells in the interstitium and sinusoids suggestive of marrow involvement in HSTL (Fig. 3a, b). The pattern of infiltration was subtle and difficult to detect on routine hematoxylin and eosin sections but accentuated on IHC. The post operative recovery was uneventful and the patient was discharged in stable condition with advice to consult the medical oncology services for further management.

Discussion

HSTL is an uncommon but distinct T cell lymphoma with the characteristic growth pattern and clinical setting. It occurs at a young age and is characterized by hepatosplenomegaly, anemia, thrombocytopenia, no swelling of superficial lymph nodes and an aggressive clinical course [4]. Varying degrees of pancytopenia have been reported in patients with HSTL [5]. Thrombocytopenia is usually the most striking finding which may be due to marked splenomegaly. The present case had clinical symptoms

largely attributable to hepatosplenomegaly and pancytopenia and included fatigue, fever, and abdominal pain.

The clinical diagnosis is difficult at times and is frequently misdiagnosed as hepatobiliary disease. In these cases, the neoplastic cells infiltrate the portal tract with apoptosis of periportal hepatocytes which might explain high alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels [6]. In the present case sinusoidal infiltration and high serum bilirubin with normal AST and ALT levels were indicative of intrahepatic cholestasis rather than parenchymal damage.

HSTL is remarkably uniform in its histological characteristics. The involved tissues show a striking localization of tumor cells within sinuses. Infiltration is most conspicuous in the splenic red pulp and liver [5]. According to the literature bone marrow involvement in HSTL is found in approximately in 2/3rd of patients at diagnosis. Belhadj et al. [7] have shown that it can be regarded as a constant feature at presentation and careful histological and IHC examination of a trephine biopsy specimen appears to be the adequate and easily feasible procedure enabling the recognition of lymphoma infiltration. Lu et al. [8] reviewed 17 Chinese cases of HSTL and found bone marrow involvement in 53.3 % cases. The neoplastic cells in HSTL have a tendency to percolate between normal hematopoietic cells. The different patterns of bone marrow involvement that has been reported are exclusively sinusoidal, interstitial and mixed sinusoidal and interstitial [9]. The sinusoidal localization in the bone marrow makes detection of tumor cell infiltration more difficult, especially without the aid of IHC early in course of disease [7]. The present case showed subtle changes in the bone marrow biopsy

Fig. 1 **a** Neoplastic cells infiltrates the cord and sinuses of the splenic red pulp (Hematoxylin and eosin; $\times 100$). **b** CD3 highlights the neoplastic cells ($\times 100$). **c** CD20 is negative in the neoplastic cells ($\times 100$)

Fig. 2 **a** and **b** Hepatic sinusoids are dilated and infiltrated by neoplastic cells (Hematoxylin and eosin; **a** $\times 100$, **b** $\times 400$). **c** Immunohistochemical reactivity of neoplastic cells in hepatic sinusoids by CD3 ($\times 100$). **d** Neoplastic cells are negative for CD20 ($\times 100$)

Fig. 3 Bone marrow biopsy. **a** The marrow is hypercellular (Hematoxylin and eosin; $\times 100$); **b** Clusters of CD3 positive neoplastic cells are highlighted in the interstitium (*black arrows*) ($\times 100$)

section and atypical cells were highlighted by CD3. This discrepancy is likely due to the result of peculiar sinusoidal distribution of tumor cells which at initial examination is

difficult to recognize without IHC. In a case series of 21 patients reported by Belhadj et al. [7] this lymphoid infiltration was initially not diagnosed in six patients but was

documented by histological review together with appropriate IHC. Thus in our experience and in several previous reports reviewed by Weidman it has been seen that underestimation of bone marrow involvement has led to splenectomy for diagnostic purposes [10]. Improvement in recognizing discrete marrow involvement using immunophenotypic studies can result in a change in diagnostic strategy in HSTL [11].

The course of the diseases is aggressive. Despite use of various treatment regimens including bone marrow transplantation, it has not been possible to establish an effective treatment. As the disease is rare its biology is not well understood yet. However because of the dilemma of an aggressive clinical course and unsatisfactory response to treatment, early recognition of this entity might prolong the duration of survival [11]. The present case was referred to medical oncology and lost on follow up.

A prompt and accurate diagnosis of HSTL requires a high index of suspicion in a clinical setting of pancytopenia with hepatosplenomegaly in absence of lymphadenopathy. In such cases, though bone marrow is the initial diagnostic modality, the pattern of involvement may be subtle. Hence the knowledge of pattern of involvement and ancillary studies would help in accurate recognition with earlier therapy and improved survival.

Conflict of interest None.

References

1. Farcet JP, Gaulard P, Marolleau JP, Le Couedic JP, Henni T, Gourdin MF et al (1990) Hepatosplenic T-cell lymphoma: sinusal/sinusoidal localization of malignant cells expressing the T-cell receptor gamma delta. *Blood* 75:2213–2219
2. Falchook GS, Vega F, Dang NH, Samaniego F, Rodriguez MA, Champlin RE, Hosing C, Verstovsek S, Pro B (2009) Hepatosplenic gamma-delta T-cell lymphoma: clinicopathological features and treatment. *Ann Oncol* 20:1080–1085
3. Harris NL, Jaffe ES, Stein H, Banks PM, Chan JK, Cleary ML et al (1994) A revised European American classification of lymphoid neoplasms: a proposal from the International Lymphoma Study Group. *Blood* 84:1361–1392
4. Sadahira Y, Notohara K, Manabe T (2003) Hepatosplenic T cell lymphoma with no expression of cytotoxic molecules. *J Clin Pathol* 56:631–633
5. Cooke CB, Krenacs L, Stetler-Stevenson M, Greiner TC, Raffeld M, Kingma DW et al (1996) Hepatosplenic T-cell lymphoma: a distinct clinicopathologic entity of cytotoxic gamma delta T-cell origin. *Blood* 88:4265–4274
6. Sadahira Y, Ohmoto K, Yamamoto S, Nishihara H, Wada H, Yawata Y et al (1998) Expression of cytotoxic molecule TIA-1 in malignant lymphomas mimicking fulminant hepatitis. *Pathol Int* 48:695–704
7. Belhadj K, Reyes F, Farcet JP, Tilly H, Bastard C, Angonin R et al (2003) Hepatosplenic gammadelta T-cell lymphoma is a rare clinicopathologic entity with poor outcome: report on a series of 21 patients. *Blood* 102:4261–4269
8. Lu CL, Tang Y, Yang QP, Wang M, Zhao S, Bi CF, Jiang NG, Zhang WY, Liu JP, Xu X, Liu WP (2011) Hepatosplenic T-cell lymphoma: clinicopathologic, immunophenotypic, and molecular characterization of 17 Chinese cases. *Hum Pathol* 42:1965–1978
9. Vega F, Medeiros LJ, Bueso-Ramos C, Jones D, Lai R, Luthra R et al (2001) Hepatosplenic gamma/delta T-cell lymphoma in bone marrow. A sinusoidal neoplasm with blastic cytologic features. *Am J Clin Pathol* 116:410–419
10. Weidmann E (2000) Hepatosplenic T Cell lymphoma. A review on 45 cases since the first report describing the disease as a distinct lymphoma entity in 1990. *Leukemia* 14:991–997
11. Gaulard P, Kanavaros P, Farcet JP, Rocha FD, Haioun C, Divine M et al (1991) Bone marrow histologic and immunohistochemical findings in peripheral. T-cell lymphoma: a study of 38 cases. *Hum Pathol* 22:331–338