Pathol. Oncol. Res. (2011) 17:421–423
DOI 10.1007/s12253-010-9324-0

CASE REPORT

# A Rare Cause of Fever, Hepatosplenomegaly, and Thrombocytopenia: Hepatosplenic Gamma/Delta T-Cell Lymphoma

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Received: 13 March 2010 / Accepted: 20 October 2010 / Published online: 1 January 2011


## Introduction

Hepatosplenic gamma-delta T cell lymphoma (HSTCL) is a very rarely-encountered form of lymphoma [1, 2]. It constitutes less than 1% of all non-Hodgkin's lymphomas (NHL). It occurs in males more frequently. Its mean age of occurrence is 35. It is a type of lymphoma that originates from cytotoxic T lymphocytes. This disease has an aggressive clinical course. The prognosis thereof is quite poor [3].

It is a primary extranodal lymphoma, emerging with the sinus or sinusoidal infiltration of the liver and spleen. Bone marrow is virtually always involved. Lymph node involvement is very rare [4]. Patients typically present with systemic symptoms, massive hepatosplenomegaly, anemia, leucopenia and evident thrombocytopenia. It may respond initially to chemotherapy. Recurrence, however, is unavoidable in the majority of cases. The mean survival is less than 2 years [3].

## Case Report

An 18-year old male patient presented to our clinic with complaints of night sweats, weight loss, and irregular fever during the last 3 months, as well as nosebleeds during the last 10 days. He had not any medical history in his personal and family background. Neither viral/bacterial infection, nor collagen tissue disease was diagnosed. His skin had a pale appearance under physical examination. Massive hepatosplenomegaly was present. No lymphadenopathy was determined. His complete blood count resulted in $2.5 \times 10^3$/L leucocyte and $5 \times 10^9$/L platelet. His LDH level was 310 U/L (140–280). The patient has been intermittently given platelet support. In abdominal ultrasonography, the craniocaudal dimension of the liver and the dimension of spleen were determined as 25 cm and 26 cm, respectively. The flow cytometry in bone marrow demonstrated a decrease in the CD4/CD8 ratio in favor of CD8; CD4:13%, CD8: 71%.

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The bone marrow trephine biopsy was hypercellular. In addition to the hematopoietic cells, it has been noticed that atypical lymphoid cells with narrow cytoplasm, large and hyperchromatic nucleus, and with disorganized chromatins were situated in the form of small islets or in an intrasinusoidal fashion (Fig. 1). The immunhistochemical examination revealed that the above-depicted cells gave positive reaction with CD3 (Fig. 2). No numerical or structural chromosome abnormalities were observed in the karyotype analysis of the bone marrow sample. FISH analysis requested upon early diagnosis of acute leukemia and myelodysplastic syndrome did not reveal any del5q, 7q, inv(16), 20q, t(8;21) and t(9;22) abnormalities.

The patient was subjected to splenectomy for definitive diagnosis and in consideration of the role of hypersplenism in refractory thrombocytopenia. The histopathologic examination of the spleen highlighted atypical lymphoid cells of medium sizes with monotonous appearance, diffusely infiltrating, with narrow cytoplasm, irregular and hyperchromatic nucleus, and with small nucleolus in various sites (Fig. 3). It has been further established that the tumor cells were stained with LCA, CD2, CD3, CD7, CD43, CD45RO, but showed no immune reaction with CD1a, CD4, CD5, CD8, CD20, CD34, CD56, CD117, TdT, ALK, and myeloperoxidase (Fig. 4).

The patient has been diagnosed with hepatosplenic gamma-delta T cell lymphoma, in consideration of the clinical findings, as well as the morphologic and immunhistochemical examinations. Three treatment courses with CHOP (Cyclophosphamide, Adriamycin, Vincristine, and Prednisolone) have been conducted, without resulting in any response. DHAP chemotherapy (cisplatin, cytosine arabinoside, and dexamethasone) was then initiated. Two cures of DHAP therapy has been administered, with no response either. The patient had not any tissue-group HLA-matched stem cell donor among his relatives. The patient's fever, severe thrombocytopenia, and marked hepatomegalia persisted. At this phase, it was planned to administer pentostatin to the patient. Pentostatin was requested from abroad, since it is not commercially available in our country. Meanwhile IEV chemotherapy protocol was initiated due to fast progression of lymphoma. An IEV protocol (Ifosfamide 2,500 mg/m$^2$/day (days 1–3), Epirubicin 100 mg/m$^2$/day (day 1), Etoposide 150 mg/m$^2$/day (days 1–3)) has been applied. However, the patient has died on the 7th day due to infection and hemorrhage, before receiving any pentostatin. Therefore patient's response to pentostatin could not be assessed.

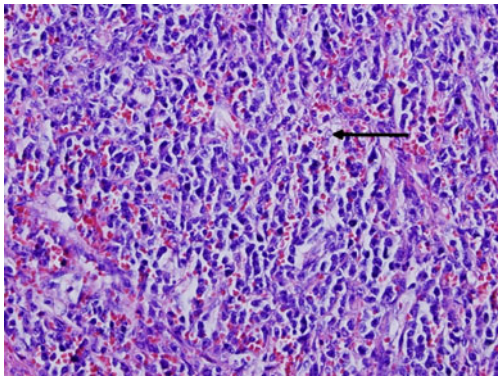

**Fig. 2** Immunhistochemical CD3 positivity in bone marrow (CD3, ×400)

## Discussion

The prognosis is poor in HSTCL, albeit the availability of anthracycline-based intense chemotherapies and stem cell transplantation [1, 5]. In line with this, our case failed to respond to CHOP and DHAP chemotherapies, as standard approaches against NHL. While, according to the scientific literature, no response is achievable with alemtuzumab only, it was reported that the combination of alemtuzumab and 2-chlorodeoxyadenosine resulted in a short-term

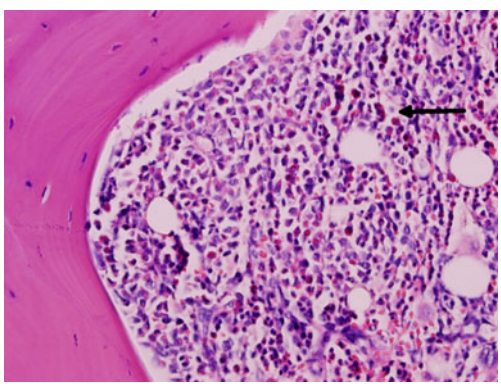

**Fig. 1** Hypercellular bone marrow infiltrated with neoplastic cells (H&E, ×400)

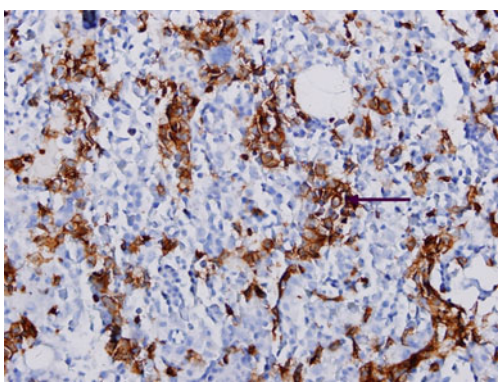

**Fig. 3** Neoplastic lymphoid cell infiltration in dilated spleen sinusoids (H&E, ×400)

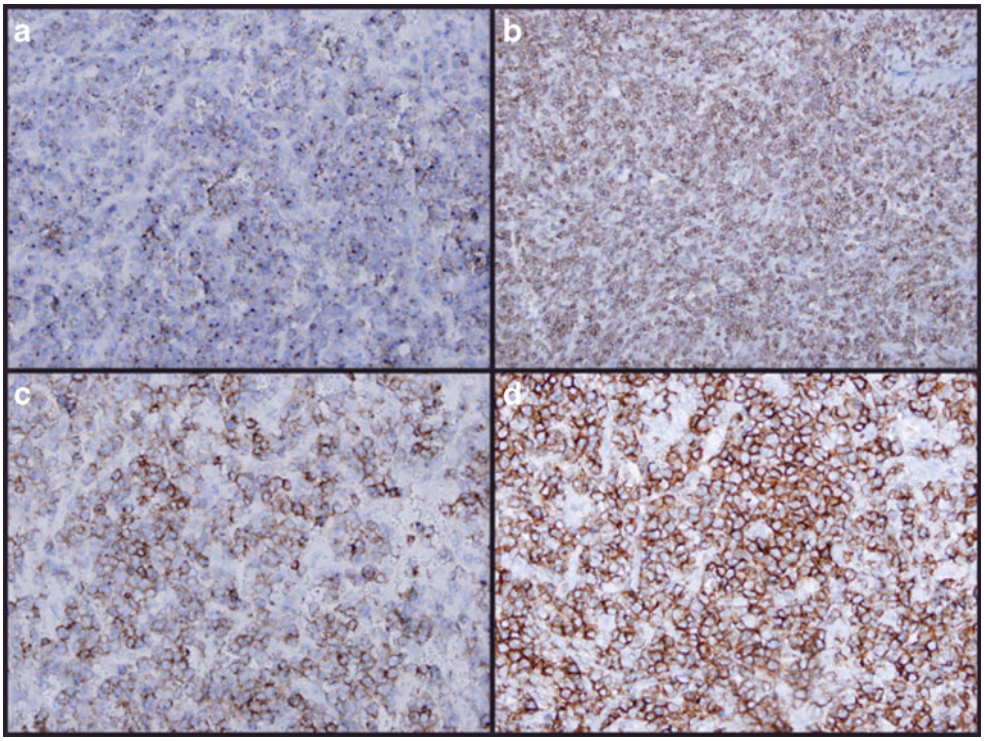


**Fig. 4** **a**: CD3 immune reaction in atypical lymphoid cells in spleen (CD3, ×200).**b**: CD2 positivity in neoplastic cells (CD2, ×400).**c**: CD7 positivity in monotonous appearing atypical cells (CD7, ×400).**d**: Immunhistochemical CD43 reaction (CD43, ×400)

response [6, 7]. To a 39 year-old case diagnosed with HSTCL in the leukemic phase, according to Gopcsa et al., was administered conventional chemotherapy and alpha-interferon, but no response could be attained. Thereafter, 2-chlorodeoxyadenosine therapy was administered, with complete remission attained for 6 months [8]. Pentostatin plays specific role in HSTCL cases, and it provides for the achievement and sustainment of clinical and histological response [9–11]. It has been further shown that complete remission could be sustained for 40 months with IEV (Ifosfamide, Epirubicin, Etoposide) chemotherapy following the end of therapy [1].

HSTCL is a rarely-encountered fatal lymphoma. Its only curative treatment is allogeneic stem cell transplantation. According to a case of Mittal et al., transient response was achieved with a combination of fludarabine and alemtuzumab until allogeneic stem cell transplantation was performed [12].

Our case has been reported in view of emphasizing that HSTCL, a rarely-seen malignancy, should be taken into etiology considerations for patients applying with fever, hepatosplenomegaly, thrombocytopenia, and that such a treatment should be planned that differs from standard lymphoma treatment approaches.

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