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Case report

Four hepatosplenic T-cell lymphoma cases of Japanese patients

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ABSTRACT

Hepatosplenic T-cell lymphoma (HSTCL), a rare type of γδ T-cell lymphoma, is characterized by hepatosplenomegaly and cytopenias. It is associated with immunodeficiency and its age of onset is reportedly between the 20s and 30s. We herein report 4 Japanese HSTCL cases. Three of them, including an elderly case that was 74 years of age, were not at adolescence. No cases had a history of immunodeficiency. All other disease phenotypes were similar to the typical HSTCL cases. These findings suggest that there are a certain proportion of HSTCL patients who presented after middle age.

1. Introduction

Hepatosplenic T-cell lymphoma (HSTCL) is a rare subtype of peripheral T-cell lymphoma, which is derived from cytotoxic T-cells typically expressing γδ T-cell receptor (TCR). It usually occurs in young men and is characterized by B symptoms such as a fever, weight loss and night sweats, hepatosplenomegaly, thrombocytopenia, and anemia. The patient's prognosis is typically poor [1].

Approximately 20% of all HSTCL cases are associated with immunodeficiency which include chronic immunosuppressive therapies after solid-organ transplantation and collagen diseases such as SLE, HIV, malaria infection, AML, Hodgkin's lymphoma, and inflammatory bowel diseases [2], suggesting that the immunodeficient status may contribute to the development of HSTCL.

Histologically, the lymphoma cells have medium-sized nuclei and a rim of pale cytoplasm, and homogeneous medium-sized CD3-positive lymphoma cells infiltrate the cords and sinuses in the red pulp of the spleen, sinusoids of the liver and the bone marrow [1]. Immunohistochemistry analyses generally show CD3(+), CD4(−), CD5(−), CD8(−/+), CD56(+/−), TCRδ1(+), TIA-1(+), and granzyme B(−).

HSTCL accounts for only 3% of all T-cell lymphomas in the United States and 2.3% in Europe. Notably, it occurs less frequently in Eastern and South-eastern Asian countries (0.2%) [3]. Because HSTCL is especially rare in Asia, its actual characteristics in Asia have not been well-documented [4]. We experienced 4 cases of HSTCL out of 292 cases (1.3%) of T cell lymphoma according to the clinical and pathological records between 1998 and 2014 in our institution. Surprisingly, 3 out of the 4 cases were middle-aged to elderly patients (cases 1–3), and only one case was an adolescent male [5].

We herein report these 4 HSTCL cases of Japanese patients.

2. Case presentation

The clinical and laboratory features of these 4 cases are summarized in Table 1 (cases 1–4). None of the patients had previous illness that was related to immunodeficiency, immunosuppression or an abnormal immunological status. All of the patients had B symptoms, hepatosplenomegaly and cytopenias at diagnosis, resulting in a high or high-intermediate International Prognostic Index (IPI).

Case 1 was a 74-year-old female. A liver biopsy demonstrated the infiltration of small to medium-sized lymphoma cells in the sinusoids and portal area, and these cells were CD3(+), CD4(−), CD5(−), CD8(−), CD56(+), TIA-1(+), granzyme B(−) and Epstein–Barr virus-encoded RNA (EBER) *in situ* hybridization(−) (Fig. 1). The patient had a CR by treatment with 6 cycles of CHOP, and has remained alive for more than 12 months after achieving a CR.

Case 2 was a 64-year-old male. A liver biopsy demonstrated the infiltration of small to medium-sized lymphoma cells in the sinusoids

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Table 1
Summary of the 4 cases of HSTCL.

Case no.	Age (y)/Sex	Country	Immuno-deficiency	Clinical stage (cs)	B symptoms	Hepato-megaly	Spleno-megaly	IPI
1	74/F	Japan	−	IVB	+	+	+	High
2	64/M	Japan	−	IVB	+	+	+	High
3	59/M	Japan	−	IVB	+	+	+	High
4	23/M	Japan	−	IVB	+	+	+	High-int

Peripheral blood					Histological detection of tumor cells
WBC (10^9/L)	Hgb (g/dL)	Platelet (10^9/L)	Elevated LD (U/L)	anti-HTLV1	
5.9	7.2	109	449	−	Liver, BM
1.8	12.2	54	390	−	Liver, BM
0.3	5.2	25	577	−	BM
7.1	9.1	95	522	−	BM

Immunohistochemical staining of tumor cells											Outcome/follow-up (months)
CD2	CD3	CD4	CD5	CD7	CD8	CD56	TIA-1	Granzyme B	EBER	TCR	
+	+	−	−	+	−	+	+	−	−	γδ	Alive/12M
+	+	−	−	+	+	+	+	+	−	γδ	Dead/37M
NS	+	−	−	NS	−	NS	NS	NS	−	NS	Dead/11M
+	+	−	−	+	−	−	+	−	−	γδ	Dead/19M

PS, performance status; IPI, International Prognostic Index; WBC, leukocyte count; Hgb, hemoglobin level; LD, lactate dehydrogenase level; BM, bone marrow; EBER, EB virus-encoded small RNAs; TCR, T-cell receptor; PSL, Prednisolone; NS, not specified

and portal area, and these cells were CD3(+), CD4(−), CD5(−), CD8(+), CD56(+), TIA-1(+), granzyme B(+) and EBER(−). He was treated with 6 cycles of THP-COP (pirarubicin, cyclophosphamide, vincristine and prednisolone) to achieve a PR for 10 months. Combination chemotherapy with 2 cycles of CHASE (cyclophosphamide, cytarabine, etoposide and dexamethasone) was administered after the disease progression, however, the tumor cells infiltrated the central nervous system. He ultimately died 37 months after the diagnosis.

Case 3 was a 59-year-old male. A bone marrow clot demonstrated hypercellular bone marrow with medium- to large-sized lymphoma cells that were CD3(+), CD4(−), CD5(−), CD8(−) and EBER(−). He was initially treated with 2 cycles of CHOP followed by 2 cycles of ESHAP (etoposide, methylprednisolone and cytarabine), resulting in a PR. An autologous stem cell transplantation preceded by a preparative regimen MCEC (ranimustine, carboplatin, etoposide and cytarabine) provided a CR. He relapsed 3 months post-transplant and died 11 months after the diagnosis.

Case 4 was a 23-year-old male. A bone marrow biopsy demonstrated hypercellular bone marrow with medium- to large-sized lymphoma cells that were CD3(+), CD4(−), CD5(−), CD8(−), CD56(−), TIA-1(+), granzyme B(−) and EBER(−), as previously reported [5]. He was treated with 1 cycle of CHOP followed by 3 cycles of IVAC (ifosfamide, etoposide and cytarabine), resulting in a PR. Allogeneic bone marrow transplantation from an unrelated donor preceded by a preparative regimen composed of etoposide, cyclophosphamide and total body irradiation provided

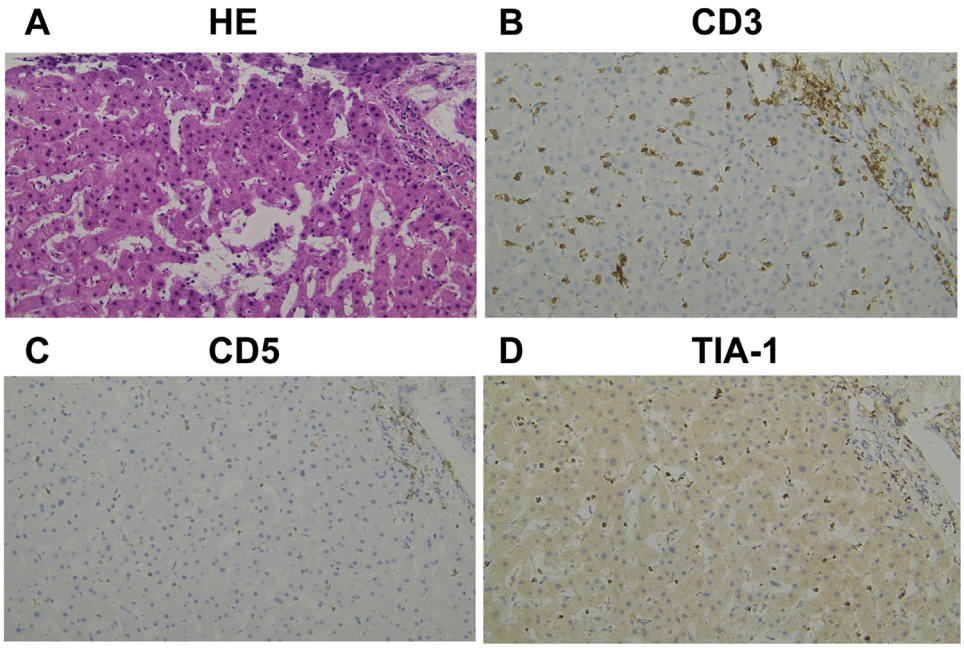

Fig. 1. Histologic appearance of the liver in Case 1. (A) Lymphoma cells infiltrated the sinusoids of the liver (hematoxylin and eosin stain, 200×). (B), (C), (D) An immunohistochemical analysis showed that the malignant cells were positive for CD3 and TIA-1, and negative for CD5.