Hepatosplenic $\alpha\beta$ T-Cell Lymphoma with Myelodysplastic Syndrome

Tomoiku Takaku, Keisuke Miyazawa, Goro Sashida, Nahoko Shoji, Takashi Shimamoto, Noritake Yamaguchi, Yoshikazu Ito, Shigeo Nakamura, Kiyoshi Mukai, Kazuma Ohyashiki

$^a$First Department of Internal Medicine and $^b$Department of Clinical Pathology, Tokyo Medical University, Tokyo; $^c$Department of Clinical Pathology, Aichi Cancer Center, Aichi Prefecture, Japan

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Abstract

We describe a patient with hepatosplenic $\alpha\beta$ T-cell lymphoma who showed pancytopenia and myelodysplasia. A 35-year-old man was admitted with fever, pancytopenia, and hepatosplenomegaly but with no lymphadenopathy. We also found trilineage myelodysplasia in the bone marrow on his first admission. The patient had high fever and anemia but no evidence of infection and was tentatively treated with prednisolone. This treatment resulted in a transient improvement of the cytopenia and a reduction of spleen size. However, 10 months after the first manifestation, progression of the splenomegaly and fever became apparent, and a splenectomy was performed. The pathologic findings for the spleen showed diffuse and disseminated infiltration of medium- to large-sized T-lymphocytes in the splenic red pulp. These cells were immunohistochemically positive for CD3, CD5, CD7, CD8, CD56, T-cell receptor $\alpha\beta$ (TCR$\alpha\beta$), T-cell intracellular antigen 1, and granzyme B but were negative for CD4, CD30, CD57, and TCR$\gamma\delta$. These data suggested a diagnosis of hepatosplenic $\alpha\beta$ T-cell lymphoma. A Southern blot analysis revealed gene rearrangement of the TCR $\beta$-chain gene but not the immunoglobulin heavy chain gene in the spleen cells. An in situ hybridization analysis for the Epstein-Barr virus revealed negative results. The patient received 8 courses of combination chemotherapy and achieved a partial remission; however, the dysplastic features of the marrow cells persisted after the partial remission was obtained. Additional treatment with allogeneic bone marrow transplantation resulted in a transient complete remission; however, the patient relapsed 11 months later. Because he had experienced no lymphadenopathy and showed dysplastic features in the bone marrow, the diagnosis was highly dependent on the pathologic findings for the resected spleen.

Key words: Non-Hodgkin’s lymphoma; Hepatosplenic lymphoma; Myelodysplastic syndrome; T-cell lymphoma

1. Introduction

Malignant lymphomas arising in the spleen are very rare and constitute only 1% to 3% of all non-Hodgkin’s lymphomas [1]. Most of these splenic lymphomas originate from B-cells; however, several reports have described a distinct type of hepatosplenic T-cell lymphoma (HSTCL) that arises from the population of T-cells that express $\gamma\delta$ chains of the T-cell receptor (TCR) and that preferentially resides in the sinus of the splenic red pulp [2-4]. Hepatosplenic $\gamma\delta$ T-cell lymphomas (HS$\gamma\delta$TCLs) have fairly typical clinicopathologic features. Most patients are young men who have B symptoms, massive hepatosplenomegaly, no lymphadenopathy, moderate anemia, and marked thrombocytopenia. The disease shows an aggressive clinical course [3,4]. These unique features led to the incorporation of hepatosplenic lymphoma as a distinct entity within the new World Health Organization classification of hematopoietic disorders [5,6].

Recently, some cases of HSTCL in which the cells expressed the $\alpha\beta$ TCR rather than the $\gamma\delta$ TCR have been reported [7-10]. Macon et al analyzed 14 cases in which these HS$\alpha$TCLs shared clinicopathologic features with the more common $\gamma\delta$ form of the disease and suggested that they be considered a variant form of HSTCL [9]. We report a case of HS$\alpha$TCL that showed dysplastic features in the bone marrow. In the present case, the diagnosis was difficult because the patient had no lymphadenopathy and showed pancytopenia with myelodysplasia.
Figure 1. Myelodysplastic features of the bone marrow. Bone marrow findings show erythroid hypercellularity (A) with binuclear erythroblasts (B), pseudo-Pelger anomaly in neutrophilic leukocytes (C), micromegakaryocytes (D), giant platelets (E), and a Howell-Jolly body in an erythrocyte (E, dashed arrow). Atypical lymphoid blast cells, later revealed to be lymphoma cells, were also detected in the bone marrow (F) (May-Grünwald-Giemsa, original magnification x1000).

2. Case Report

2.1. Presplenectomy Clinical Course

A 35-year-old man was referred to our hospital in September 2001 because of pancytopenia. Hepatosplenomegaly, B symptoms, but no superficial lymphadenopathy were found at the first admission. At the time of first manifestation, a physical examination revealed high fever, hepatomegaly (1 cm below the costal margin), and splenomegaly (6 cm below the costal margin). The laboratory data showed pancytopenia (a white blood cell count of 2.3 × 10^9/L, a hemoglobin level of 81 g/L, and a platelet count of 101 × 10^9/L), an elevated C-reactive protein level of 4.7 mg/dL, and an erythrocyte sedimentation rate was 19 mm/h. Treatment with intravenous methylprednisolone at 1000 mg/day for 3 days followed by oral prednisolone showed no effect on the hepatosplenomegaly or the fever. Therefore, the patient underwent splenectomy on August 30.

2.2. Pathologic Findings and Characterization of Spleen Cells

The weight of the spleen was 1700 g. A histopathologic study revealed an enlargement of the red pulp and a prominent withering of the white pulp. There was no enlargement of lymphoid follicles. The disseminated infiltration of medium- to large-sized cells without any gross lesions was observed in the red pulp. These cells had cleaved nuclei and scanty cytoplasm. The white pulp was atrophic (Figure 2A). Not shown is the presence of some erythroblastic islands, suggesting extramedullary hematopoiesis. These findings are not typically suggestive of neoplastic proliferation. However, immunohistochemical staining results showed these medium- to large-sized cells to be positive for CD3 and to comprise approximately 30% of all the cells in the red pulp (Figure 2B). Immunohistochemistry and flow cytometry analyses showed that these cells were also positive for CD7,