CASE REPORT

Childhood Hepatosplenic T-cell Lymphoma with Skin Involvement

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Background: Hepatosplenic T-cell lymphoma is a rare malignancy in childhood. **Case characteristics:** A 12-year-old boy who presented a pyrexia of unknown origin, multiple skin and lesions and marked hepatosplenomegaly. **Observation**: Bone marrow aspirate cytology showed no blast cells. Splenectomy was done, and spleen showed infiltration with atypical lymphoid cells positive for CD3, CD8 and T-cell-restricted intracellular antigen. **Outcome**: The skin rash of patient subsided with chemotherapy. **Message**: Skin involvement may be an unusual clinical manifestation of hepatosplenic T-cell lymphoma.

Keywords: *Diagnosis, Non-Hodgkin lymphoma, Splenectomy*.

Peripheral T-cell lymphomas are a heterogeneous group of post-thymic, mature lymphoid malignancies, accounting for approximately 10% to 15% of all non-Hodgkin lymphomas [1]. In 1990, hepatosplenic T-cell lymphoma (HSTCL) was first recognized as a distinct entity among peripheral T-cell lymphomas on the basis of clinical presentation, pattern of histological involvement resulting from the sinusoidal tropism of neoplastic cells, and expression of the γδ T-cell receptor by tumor cells [2,3]. It is an even rarer clinical entity in children; only few cases are reported. We report an unusual case of childhood HSTCL with prominent skin lesions.

CASE REPORT

A 12-year-old boy presented to a local hospital with pyrexia of unknown origin, multiple skin lesions, hematuria and weight loss for past 4 months. He had no history of prior use of immunosuppressants. He showed hemorrhagic papules on abdomen and extremities, mild lymphadenopathy, and marked hepatosplenomegaly. Initial biopsies of lymph nodes and skin indicated reactive hyperplasia. He was referred to our hospital for further evaluation, almost 24 months after initial onset of symptoms. Physical examination revealed hemorrhagic papules on abdomen and extremities (***Fig.* 1**), hepatomegaly (7 cm below the costal margin) and marked splenomegaly (13 cm below the costal margin).

Complete peripheral blood count showed hemoglobin 10.4 g/L, white blood cell 40.8×10^9/L with lymphocyte 85%, and platelet count of 361×10^9/L. No blast cells were seen in the peripheral blood smear. His liver function was normal but renal function was deranged (blood urea nitrogen 6.58 mmol/L and creatinine 98 μmol/L). Abdominal ultrasonography confirmed marked hepatosplenomegaly and slightly enlarged celiac lymph nodes. Bone marrow aspiration cytology was mildly hypercellular with eosinophilia, without infiltration of atypical lymphoid cells or blasts. Splenectomy and liver biopsy were performed for pathological examination. The spleen was markedly enlarged, weighing 730 g. Microscopically, small atypical lymphoid cells infiltrated both cords and sinuses of red pulp of spleen. Immunohistochemically, the infiltrating atypical lymphoid cells in liver and spleen were positive for CD3, CD8 and T-cell-restricted intracellular antigen (TIA-1) and negative for CD4, CD20, CD56, terminal deoxynucleotidyl transferase (TdT) and myeloperoxidase (MPO), which strongly indicated cellular origin of cytotoxic T-cell. There was no EBV-encoded RNA (EBER) 1/2 expression in liver and spleen by *in situ* hybridization. The Ki-67 cell proliferation index was about 10% and the TCR γ chain

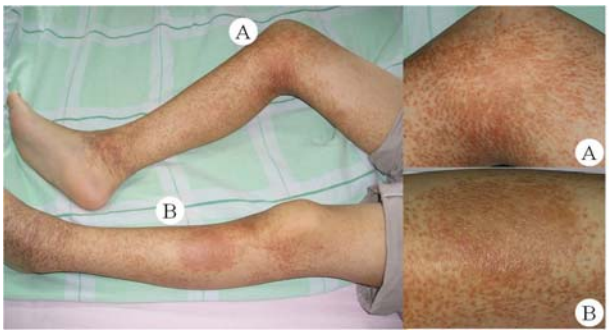

FIG. 1 *Hemorrhagic papules on both lower extremities (magnified in inset). (See color image at website)*

gene rearrangement was determined by polymerase chain reaction (PCR) analysis (***Web Fig.* 1**). All the results from pathology, immunochemistry and molecular biology supported the diagnosis of hepatosplenic γδ T-cell lymphoma. Pathological sections of skin biopsy in our patient were retrospectively reviewed by immunohistochemistry staining, and neoplastic cells were seen to infiltrate the upper dermis surrounding the appendages. Morphology and immunophenotype of these cells were similar to tumor cells infiltrating both liver and the spleen. The results supported the diagnosis of skin involvement by HSTCL. After receiving chemotherapy [cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP), along with L-asparaginase], the skin rash subsided and renal function improved.

DISCUSSION

HSTCL is a rare peripheral T-cell lymphoma, accounting for 5% of peripheral T-cell lymphoma and less than 1% of all NHL, with only 7% overall 5-year survival rate [4]. Up to 20% of HSTCL arise in the background of long term suppression of immunity, most commonly for solid organ transplantation or prolonged antigenic stimulation. HSTCL occurs predominantly in young men, with a median onset age of 34 years. Patients with HSTCL generally show aggressive clinical course with marked hepatosplenomegaly; superficial lymph node involvement is rare [3,5]. One or more than one lineage of peripheral blood cells is affected and bone marrow is commonly involved. The diagnosis of HSTCL is usually made on splenectomy. Tumor cells are usually positive for CD2, CD3, CD7 and TIA-1, while negative for CD4, and usually negative for CD5, CD8, granzyme B, perforin and EBER. Natural Killer (NK) cell related antigens CD16 and CD56 are frequently expressed. Isochromosome abnormality on the chromosome 7q is the most important cytogenetic finding [5,6].

HSTCL is even rarer in children; less than 50 cases have been reported so far. In addition to long-term fever and marked hepatosplenomegaly, this case differed from other HSTCL cases described in literature. First, skin nodules are unusual in HSTCL patients. Skin infiltration may be difficult to observe in H&E-stained sections, but it can be distinguished by immunohistochemistry staining [7]. No bone marrow involvement was found during the two-year course of disease in our patient, while about 70 percent of newly diagnosed childhood HSTCL patients have bone marrow involvement at the time of initial diagnosis. As HSTCL in children is rare, the early diagnosis of this disease is very difficult. Although malignant lymphoma was strongly suspected in our patient, the final diagnosis of HSTCL could only be made by liver and spleen biopsies.

The chemotherapeutic CHOP or CHOP-like regimes are often used in HSTCL patients, but the prognosis is poor and clinical course is usually aggressive. Recently, non-CHOP induction regimen (high dose cytarabine plus platinum-containing chemotherapy) consolidated with stem cell transplantation has been recommended [8,9]. In this case, the skin rash subsided and renal function improved shortly after CHOP plus L-Asparaginase chemotherapy, but long term prognosis remains unknown, and requires further follow-up.

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