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Short Communication

CD20-Positive and CD4/CD8-Double-Negative Peripheral T-Cell Lymphoma of Spleen Complicated with Severe Disseminated Intravascular Coagulation and Enteropathy

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A 71-year-old woman presented with massive splenomegaly. Open splenectomy was performed, and the diagnosis of peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS), was made, with a characteristic immunophenotype of $CD3^+$, $CD4^-$, $CD8^-$, T-cell receptor (TCR)$\alpha\beta^+$, and TCR$\gamma\delta^-$. After splenectomy, she suffered abrupt exacerbation of the lymphoma with disseminated intravascular coagulation and enteropathy. Although chemotherapy was started, her medical condition did not improve and she died a week later. Postmortem reevaluation of the pathological specimen confirmed her diagnosis as $CD20^+$ PTCL-NOS. Although it is a rare disease entity, $CD20^+$ T-cell lymphoma can demonstrate aggressive clinical behavior. 〔*J Clin Exp Hematopathol 52(2) : 133-136, 2012*〕

Keywords: CD20-positive T-cell lymphoma, CD4/CD8-double-negative PTCL, disseminated intravascular coagulation

INTRODUCTION

Expression of CD20, a surface marker of mature B-cells, in T-cell lymphoma (TCL) cells is a rare phenomenon, and the clinicopathological features of $CD20^+$ TCL remain poorly understood. Here, we describe a case of $CD20^+$ peripheral T-cell lymphoma of spleen with a quite characteristic immunophenotype : $CD2^+$, $CD3^+$, $CD5^+$, $CD7^-$, and CD4/CD8-double-negative. The clinical course was also very peculiar : severe and rapid disease progression with disseminated intravascular coagulation (DIC) and enteropathy after splenectomy. Chemotherapy could not control the disease. Consistent with a previous review of $CD20^+$ TCL,[1] our case also demonstrated aggressive clinical behavior.

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CASE REPORT

A 71-year-old woman with pancytopenia and abdominal distention was referred to our department in May 2010. Laboratory data at presentation were as follows : white blood cell count 1,920/μL (neutrophils 62%, lymphocytes 27%, monocytes 7%, eosinophils 3%, and basophils 1%), hemoglobin 11.0 g/dL, platelet count 67,000/μL, lactate dehydrogenase (LDH) 202 IU/L, and soluble interleukin-2 receptor (sIL-2R) 1,360 U/mL. Computed tomography scan revealed massive splenomegaly and enlarged parasplenic lymph nodes. No other lymphadenopathy was detected. Although no apparent infiltration of abnormal cells was detected in her bone marrow by microscopic examination, flow cytometry (FCM) revealed a definite population (approximately 20% of total bone marrow cells, shown in Fig. 1a) of abnormal T-lymphocytes, which were $CD3^+$, $CD4^-$, $CD5^+$, $CD7^-$, and $CD8^-$. There was no evidence of infection with human T-cell leukemia virus-1 or human immunodeficiency virus. These findings were highly suggestive of splenic malignant lymphoma of T-cell origin with bone marrow infiltration and hypersplenism. For diagnostic purposes, open splenectomy was performed with no perioperative problems, and the patient's blood cell count showed marked improvement. FCM of parasplenic lymph nodes revealed a population of abnormal T-lymphocytes, which were $CD2^+$, $CD3^+$, $CD4^-$, $CD5^+$, $CD7^-$, $CD8^-$, $CD10^-$, $CD19^-$, and $CD56^-$ (Fig. 1b). They were also

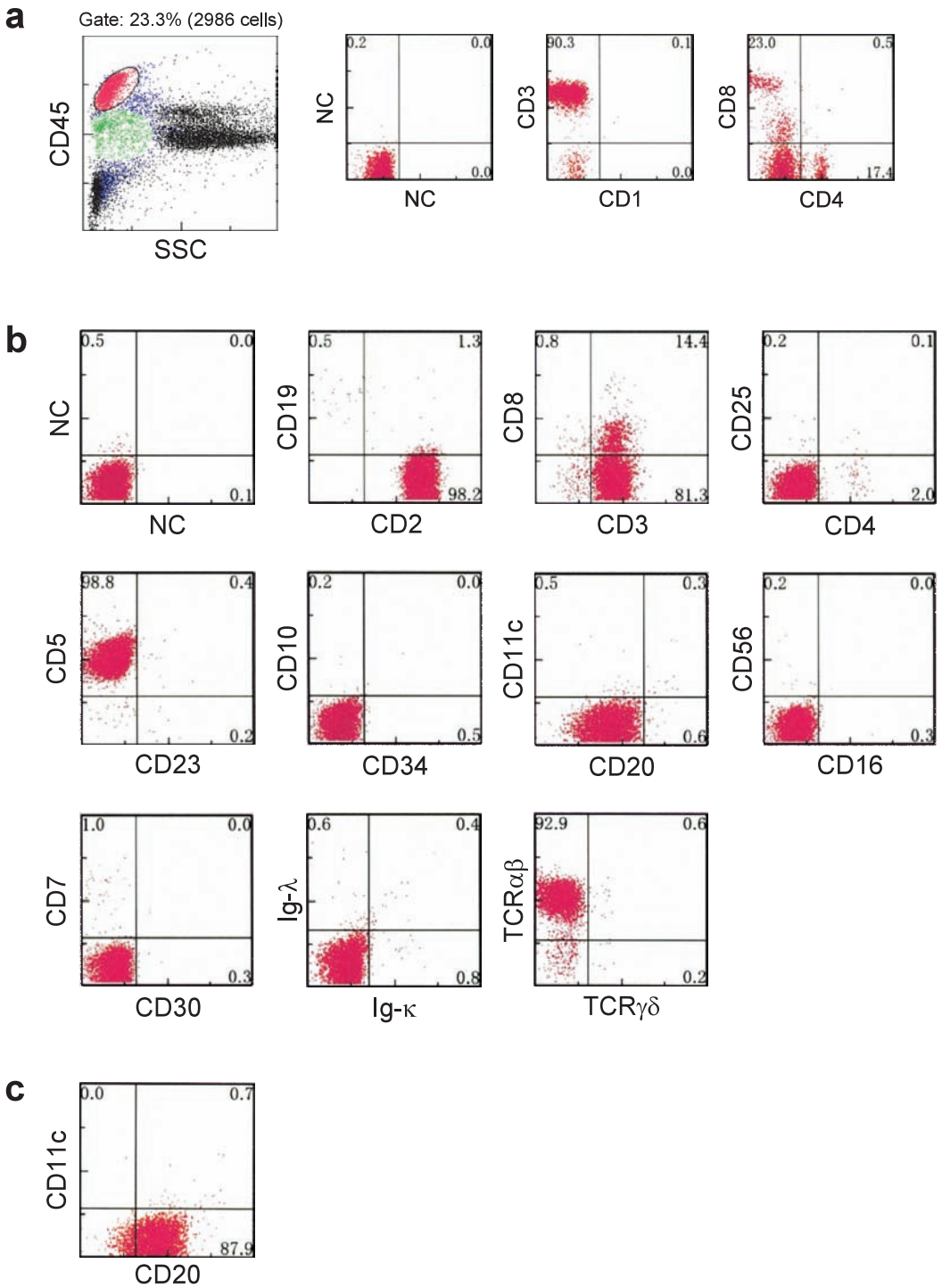

Fig. 1. Flow cytometry (FCM) analysis. (***1a***) FCM histogram of bone marrow cells gated on CD45. Area enclosed by an ellipse, strongly positive for CD45, represents the lymphoma cell population, which accounts for 23% of the total bone marrow cells. (***1b & 1c***) Two-color FCM scattergrams of the lymphoma cells of parasplenic lymph nodes gated on CD45. CD20 was initially considered as negative by a commercial testing service (*1b*), but finally judged as weakly positive after reconsideration of the cut-off value of CD20 expression by comparison with a negative control (*1c*). Immunophenotype of the nodal lymphoma cells was identical to that of atypical cell population detected by FCM of bone marrow cells.

positive for $\alpha\beta$ T-cell receptor (TCR), and negative for $\gamma\delta$ TCR and terminal deoxynucleotidyl transferase. CD20 was initially considered as negative by a commercial testing service. Southern blot analysis showed rearrangement of the *TCR Cβ1* gene, but no rearrangement of the *immunoglobulin heavy chain* gene. Pathologically, the lymph node showed effacement of the ordinal architecture by sheets of small lymphoid cells in a diffuse or pseudonodular pattern (Fig. 2b). Analysis of 2 metaphase cells revealed an abnormal karyotype : 46, X, −X, +5, t(6;16) (p23;p13.3). On the basis of the above findings, we made a diagnosis of peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS).

One week after splenectomy, the patient suffered high fever and diarrhea with high C-reactive protein (CRP) level, which was initially considered to be due to infectious colitis. Despite antibiotic therapy, her high fever was sustained and her general status declined rapidly. Two weeks after the operation, severe coagulatory disturbance and high levels of serum LDH (884 IU/L), ferritin (5,141 ng/mL), and sIL-2R (9,120 U/mL) were detected, which were considered indicative of acute exacerbation of malignant lymphoma with secondary hypercytokinemia, and subsequent DIC. Hemophagocytosis was not detected by bone marrow aspiration. We began administration of high-dose corticosteroids, recombinant thrombomodulin, and chemotherapeutic agents (cyclophosphamide, doxorubicin hydrochloride, and vincristine). Although high fever and diarrhea were improved and serum LDH and CRP were decreased transiently, coagulatory disturbance was not improved. Three days after chemotherapy, the patient's respiratory condition showed sudden exacerbation, which was speculated to be due to pulmonary hemorrhage caused by DIC, and she died 4 days later. Autopsy was not performed as her family refused to grant permission. Reevaluation of the pathological specimens (Fig. 2a-2d) of spleen and parasplenic lymph nodes revealed weak CD20 positivity, and her pathological diagnosis was confirmed as CD20$^+$ PTCL-NOS. Reevaluation of FCM histograms also revealed weak CD20 positivity (Fig. 1c).

DISCUSSION

CD20 expression by TCL is a rare phenomenon. CD20$^+$ TCL has recently been documented in several reports,[1–6] but the clinical and pathological characteristics of CD20$^+$ TCL are unclear. Some clinicopathological characteristics have been documented on the basis of analysis of 35 cases of CD20$^+$

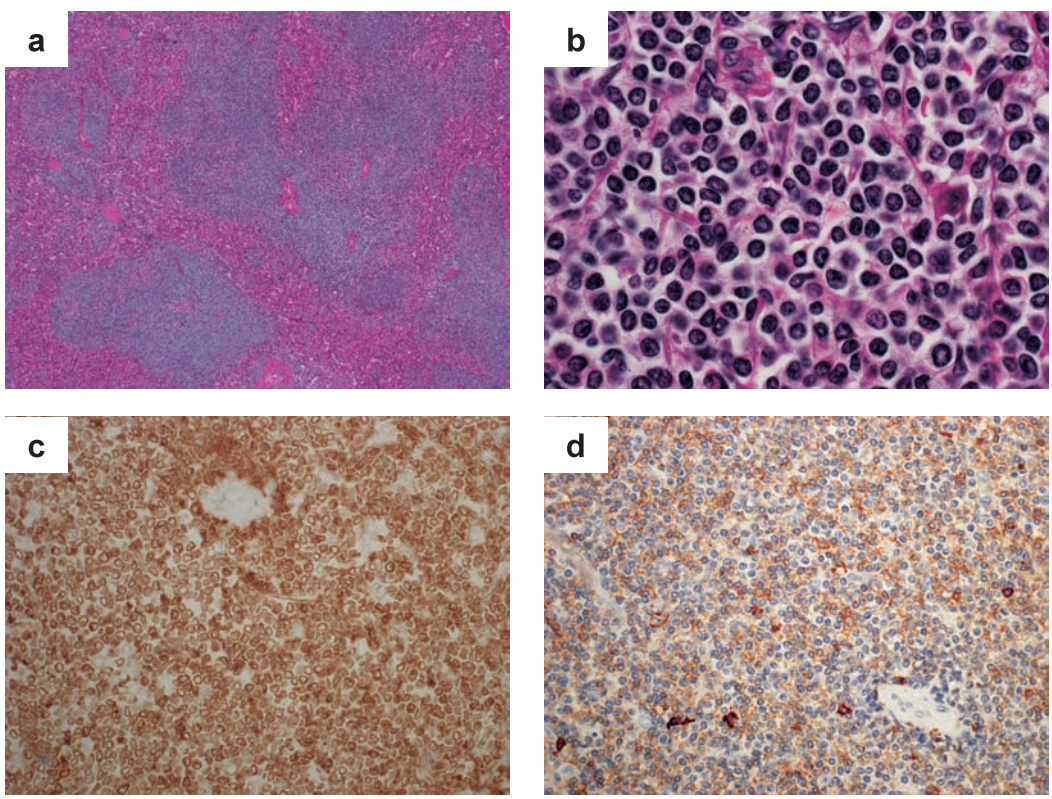

Fig. 2. Histological findings of the spleen. Hematoxylin-eosin staining (*2a*, × 4; *2b*, × 100) demonstrated the enlarged white pulp of the spleen occupied by small lymphoid cells in a diffuse or pseudonodular pattern. Immunological staining showed strong CD3 positivity (*2c*) and weak CD20 positivity (*2d*).

TCL (9 cases from direct experience and 26 cases referred from the literature).[1] Although they could be basically heterogeneous, most cases are histologically diagnosed as PTCL-NOS and show an aggressive clinical course. These features were in agreement with the present case.

Immunophenotypic features of $CD20^+$ TCL are also reported to be heterogeneous.[1,7] The lymphoma cells of the present case had a peculiar immunophenotype : $CD2^+$, $CD3^+$, $CD5^+$, $CD7^-$, $CD20^+$, and CD4/CD8-double-negative. The karyotype was also characteristic ; the chromosomal abnormality, t(6;16) (p23;p13.3), detected in this case has never been reported before in TCL. As far as we know, only one case of $CD20^+$ PTCL-NOS with a similar immunophenotype, presented with bilateral parotid enlargement, has ever been reported.[1] However, it is reported to have been resolved by corticosteroids alone, so the clinical characteristics are thought to be considerably different from those of the present case.

It is unclear whether the anti-CD20 antibody rituximab is effective for $CD20^+$ TCL as in B-cell lymphoma. Rituximab administration for $CD20^+$ PTCL-NOS has been documented in two case reports[2,4] ; however, it is difficult to judge whether rituximab was clinically effective in these cases. In the present case, we could not use rituximab because CD20 positivity was revealed postmortem. Considering the low CD20 signal intensity by immunostaining, rituximab may have been ineffective for the lymphoma in this case.

In the case described here, high fever, enteropathy, and coagulatory disturbance developed after splenectomy. Serum ferritin and sIL-2R levels were also markedly elevated, which was not suggestive of infectious colitis. Kaizu *et al.* reported a case of aggressive natural killer cell leukemia/lymphoma with giant splenomegaly in which splenectomy resulted in hypercytokinemia and hemophagocytosis.[8] In our patient, splenectomy could have caused hypercytokinemia leading to enteropathy and DIC, or lymphoma itself could have been exacerbated rapidly after splenectomy. It seems unlikely, although it cannot be refuted, that enteropathy is caused by direct lymphoma cell infiltration to the intestine because the enteropathy described above appeared exclusively after splenectomy.

In summary, we report a case of $CD4^-CD8^-CD20^+$ PTCL with aggressive clinical course. Further accumulation of clinical experiences is needed to recognize clearly the clinical and pathological features of $CD20^+$ TCL.

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