

Unusual case of cutaneous T-cell lymphoma with a prominent reactive population of B lymphocytes

Yoshihiro Nozawa¹⁾, Kazuhiro Tasaki¹⁾, Mikio Ohtsuka²⁾, Keiji Iwatuki²⁾,
Kunihiko Tominaga³⁾ and Masafumi Abe¹⁾

¹⁾Department of Pathology

²⁾Department of Dermatology, School of Medicine, Fukushima Medical University, Fukushima, Japan.

³⁾Surgical Pathology Division, Takeda General Hospital, Aizuwakamatsu, Japan

A 58-year-old Japanese woman presented an eruption in the region of the back and the upper extremities, a subcutaneous nodule on the right breast, and a left cervical lymphadenopathy. The excision biopsy specimens, of a subcutaneous nodule and a lymph node, showed a vaguely nodular growth pattern comprising a small CD20⁺ IgD⁺ lymphocyte infiltrate around clusters of medium-sized or large CD3⁺ lymphoid cells, in which histological distinction between malignant lymphoma and reactive lymphoid hyperplasia was difficult. Southern-blot analysis revealed the presence of rearranged bands for the beta chain of the T-cell receptor, but not for the immunoglobulin heavy chain. The neoplastic cells were therefore identified to be of T-cell origin. This case represents an unusual cutaneous T-cell lymphoma with a prominent reactive population of B lymphocytes.

Key words B-cell, T-cell, cutaneous T-cell lymphoma,

INTRODUCTION

B-cell lymphomas are known to contain reactive T-cells to variable extent in neoplastic lesions¹⁻⁴. T-cell-rich B-cell lymphoma is a B-cell neoplasm with reactive T lymphocytes as prominent components⁵, and its origin is identified by a careful immunohistochemical and molecular genetic examination. However, T-cell lymphoma with a prominent reactive population of small B lymphocytes is rare⁶. We report a case of cutaneous T-cell lymphoma characterized by small clusters of neoplastic T cells and a prominent reactive population of small B lymphocytes.

CASE REPORT

A 58-year-old Japanese woman noticed an eruption in the region of the back, in June 1994. She did not have a medical history except for a liver dysfunction involving a fatty liver, which

lasted several years. In March 1995, she presented an asymptomatic subcutaneous nodule on her right chest and eruption in the back and upper extremities. The breast tumor and eruption of the back (Fig. 1) were biopsied, and a diagnosis of malignant lymphoma was pronounced based on the histological findings. In September 1995, computed tomography revealed a mediastinal lymphadenopathy. In October 1995, lymphadenopathy of the left cervical region and arthralgia declared, and she was admitted in the Department of Dermatology of Fukushima Medical University in January 1996. The left cervical lymph node was biopsied. On admission, physical examination showed no remarkable abnormalities. The abnormal laboratory data were as follows: white blood cell count 15,100/mm³ with 4% of atypical lymphocytes, serum IgG: 2709 mg/dl (normal <1910 mg/dl), IgA: 704 mg/dl (normal <359 mg/dl), and IL-6 concentration: 76 pg/dl (normal <1pg/dl). Test with antibodies against human T-cell lymphotropic virus-I was negative.

The present case was diagnosed as a cutaneous T-cell lymphoma and the patient

Received: December 15, 2000

Revised: January 29, 2001

Accepted: January 30, 2001



Fig. 1. Eruption at the back and the upper extremities

received chemotherapy with VEPA, since the patient presented skin lesions for six months without lymphadenopathy. The eruption at the back and extremities disappeared, while lymphadenopathy and serum IL-6 concentration also reduced to normal level. The patient became victim of several recurrences and died of pulmonary fungal infection without lymphomatous lesion 4 years after the first chemotherapy.

PATHOLOGICAL FINDINGS

Hematoxylin and eosin-stained paraffin sections of a subcutaneous nodule and lymph node showed irregularly shaped and vague nodules consisting of many small lymphocytes around small clusters of medium-sized and large lymphoid cells (Fig. 2). The architecture of the lymph node disappeared, and no residual follicles were found. At a higher magnification, the small lymphocytes had round nuclei and scanty cytoplasm, whereas medium-sized or large lymphoid cells from the vague nodules had slightly irregular nuclei and varying amounts of cytoplasm (Fig. 3). Distinguishing malignant lymphoma from reactive lymphoid hyperplasia was made



Fig. 2. Histology of lymph node showing a large number of small lymphocytes around vague nodules (x32)

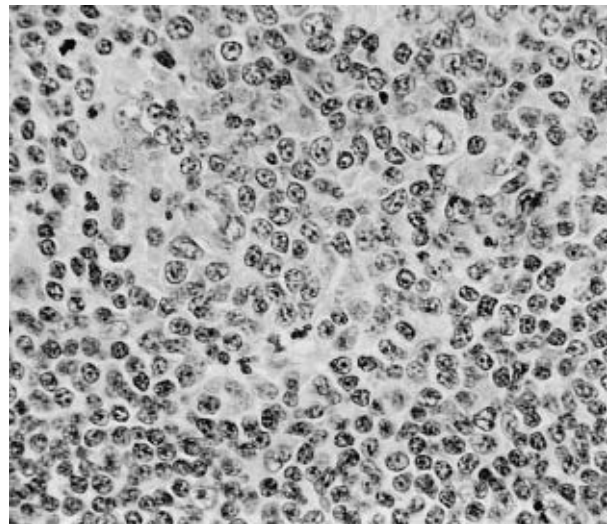


Fig. 3. Small lymphocytes surrounding the clustered medium-sized and large cells (x420).

difficult by their histological appearance. The skin biopsy revealed a diffuse small lymphocyte infiltrate admixed with scattered or small clusters of medium-sized lymphoid cells in the dermis.

In the immunohistochemical study (Figs. 4-6), the medium-sized and large lymphoid cells from the small clusters were positive for CD3 and CD4, but not for CD8, CD57 (Becton Dickinson), LMP-1 and EBNA2 (DAKO, Japan). Most of the cells were positive for MIB1 (DAKO). On the other hand, the small lymphocytes surrounding the clusters were positive for CD20 (DAKO), IgM

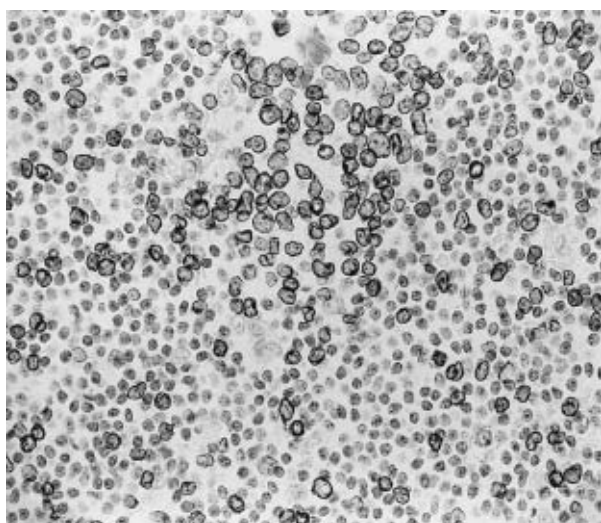


Fig. 4. Medium-sized and large cells are positive for CD3 (x315)

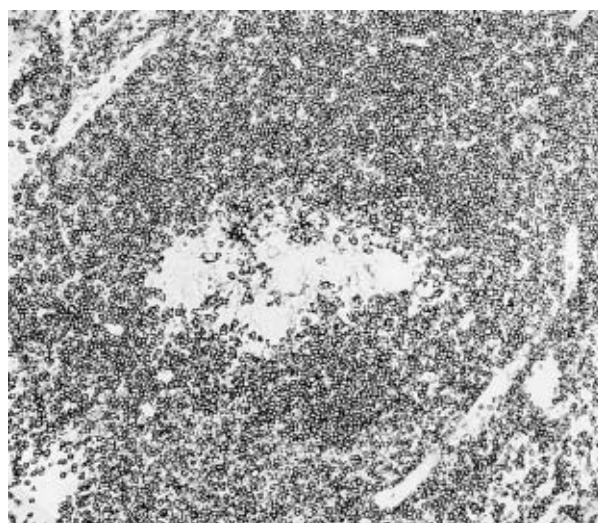


Fig. 5. Positive reactivity of small lymphocytes for CD20 (x93)

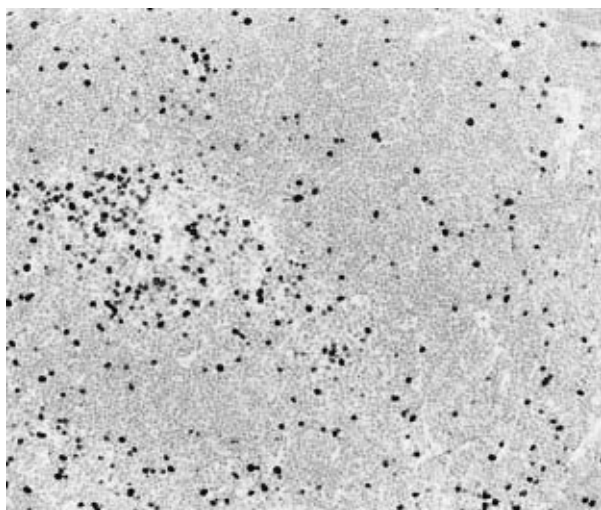


Fig. 6. Positive reactivity of medium-sized and large cells for MIB1 (x93)

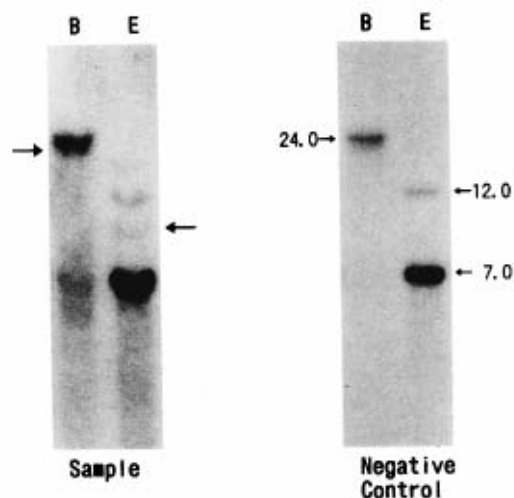


Fig. 7. Southern-blot analysis of T-cell receptor (TCR) $C\beta 1$ chain (B: BamH I, E: EcoRV)

and IgD (DAKO). CD21 (DAKO) positive networks were not found in the vague nodules.

Flow cytometric analysis of cervical lymph node cells using a dual-color counter plot for CD3 and CD19 (DAKO) showed that CD19-positive cells and CD3-positive cells accounted for approximately 44% and 28%, respectively. Among the CD3-positive cells, CD4- and CD8-(DAKO) positive cells were 33% and 7%, respectively.

In the Southern-blotting analyses, DNA extracts from the lymph node biopsy specimen were used. Rearrangement bands for the T-cell receptor beta chain were weakly detected in the

sample digested with both EcoR V and BamH I (Fig. 7). With the JH probe, only germ line bands were found.

DISCUSSION

In the present case, histological findings in the lymph node and subcutaneous nodule made the distinction between the malignant lymphoma and the reactive lymphoid hyperplasia difficult. Immunohistochemically, a small number of medium-sized or large lymphoid cells expressed CD3, and many small lymphoid cells expressed CD20, IgM and IgD. Enumeration by flow

cytometric analysis also showed that CD20-positive cells outnumbered CD3-positive cells. The findings favored a diagnosis of reactive lymphoid hyperplasia or B-cell lymphoma (B-CLL/SLL) rather than T-cell lymphoma. However, the present case was interpreted as cutaneous T-cell lymphoma with a predominant population of non-neoplastic B cells, since many MIB-1 positive cells were medium-sized and large lymphoid cells, and TCR beta gene rearrangements were detected. The neoplastic T cells were not derived from CD57-positive cells from the germinal center, because follicular dendritic cell networks and CD57 expression were not found in the clusters of T cells.

B-cell lymphomas are known to contain many reactive T cells¹⁻⁴, and T-cell-rich B-cell lymphoma (TCRBL) first reported by Ramsay et al.⁵ is a neoplastic proliferation of large B cells with a prominent reactive population of T cells. TCRBL has been erroneously identified as T-cell lymphomas until retrospective analysis of paraffin-embedded material was performed using immunohistochemical methods. On the other hand, there is only one report on T-cell lymphoma with a prominent reactive population of B lymphocytes in the literature. Yagi et al.⁶ reported a case of cutaneous T-cell lymphoma that had atypical large CD3-positive lymphoid cells dispersed in a background of many CD20-positive small lymphocytes. Furthermore, Southern-blot analysis of TCR genes demonstrated that this case was a T-cell lymphoma. Although the present case is histologically different to some extent from the case mentioned above, both show unusual histological appearance of T-cell lymphoma and are important for a proper differential diagnosis of malignant lymphoma. Such cases may be classified as unspecified peripheral T-cell lymphoma, since they do not belong to any of the better defined entities.

Some cytokines contribute to the histopathological features of T-cell-rich B-cell lymphoma (IL-4), anaplastic large cell lymphoma (IL-9), and Hodgkin's disease^{7,8}. In angioimmunoblastic T-cell lymphoma, the differences in the capacity

of tumor cells to produce IL-6 may contribute to the variability of the reaction of plasma cells and to hypergammaglobulinemia⁹. In the present case elevations of serum IL-6, IgG and IgA were observed. IL-6 may be produced by neoplastic cells but IL-6 was not detected immunohistologically in the neoplastic cells. The increase of IL-6 may play an important role for the elevation of serum IgG and IgA.

REFERENCES

- 1 Stein H, Bonk A, Tolksdorf G, Lennert K, Rodt H, Gerdes J: Immunohistochemical analysis of the organization of normal lymphoid tissue and non-Hodgkin's lymphomas. *J Histochem Cytochem* 28: 746-760, 1980
- 2 Stein H, Gerdes J, Mason DY: The normal and malignant germinal centre. *Clin Haematol* 531: 11, 1982
- 3 Mirchandani I, Palutke M, Tabaczka P, Goldfarb S, Eisenberg L, Pak MSY: B-cell lymphomas morphologically resembling T-cell lymphomas. *Cancer* 56: 1578-1583, 1986
- 4 Isaacson PG, MacLennan KA, Subfuswamy SG: Multiple lymphomatous polyposis of the gastrointestinal tract. *Histopathology* 8: 641-656, 1994
- 5 Ramsay AD, Smith WJ, Isaacson PG: T cell-rich B-cell lymphoma: *Am J Surg Pathol* 12: 433-443, 1988
- 6 Yagi H, Ogai M, Izumi T, Ebihara T, Sugiura M, Tokura Y, Takigawa M: Cutaneous T-cell lymphoma with massive co-infiltration of polyclonal B cells. *Br J Dermatol* 130: 226-230, 1994
- 7 Macon WR, Cousar JB, Waldron JA Jr., Hsu SM: Interleukin-4 may contribute to the abundant T-cell reaction and paucity of neoplastic B cells in T-cell rich B cell lymphomas. *Am J Pathol* 141: 1031-1036, 1992
- 8 Hsu SM, Waldron JA Jr., Hsu PL, Hough AJ Jr.: Cytokines in malignant lymphomas: Review and prospective evaluation: *Hum Pathol* 24: 1040-1056, 1993
- 9 Waldron JA Jr., Fink L, King C: Significance of interleukin-6 in angioimmunoblastic lymphadenopathy (AILD)-type T cell lymphoma. *Lab Invest* 66: 89A, 1992 (abst)