CD30-positive Anaplastic Large Cell Lymphoma with HTLV-I Proviral Integration: A Unique Histologic Subgroup of Adult T-cell Leukemia/Lymphoma

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In adult T-cell leukemia/lymphoma (ATL/L), 4 clinical groups can be summarized (1). Patients with acute type ATL/L usually show leukemia with flower-like cells, systemic lymphadenopathy, erythematous skin rash, hepatosplenic invasion and hypercalcemia. Patients with lymphoma type ATL/L usually show systemic lymphadenopathy without extranodal tumor; large extranodal tumor formation of ATL/L has been rarely reported except for some cases of gastric and cutaneous tumors of ATL/L (2). The above 2 groups of ATL/L mainly consist of pleomorphic medium-sized and large lymphoma cells with convoluted nuclei.

Takahara et al (3) reported that an ATL/L patient who had a primarily bone involving tumor of CD30-positive anaplastic large cell lymphoma (ALCL) showed a good response to treatment. As they pointed out, ATL/L patients with a soft tissue mass are rarely encountered even in an HTLV-I endemic area. CD30 is a member of the TNF/nerve cell growth factor receptor superfamily, and its ligand mediates proliferation of CD30-positive Hodgkin’s disease-derived cell lines and an ATL/L cell line (4). Induction of CD30 expression by HTLV-I was initially reported in the peripheral blood lymphocytes in vitro by Stein et al (5). Anagnostopoulos et al (6) also reported 6 European cases of cutaneous ALCL with fragmented and complete integration of HTLV-I proviral DNA. In an HTLV-I endemic area, 18% of the examined ATL/L patients showed CD30-positive lymphoma, and the histologic findings were pleomorphic medium-sized and large cell type and ALCL type (7). CD30-negative and CD30-positive ATL/L had similar lymphocytic surface markers and showed complete integration of HTLV-I proviral DNA, including the pX region. However, CD30-positive ATL/L of the above 2 histologic types frequently showed intrasinusoidal proliferation with a cohesive growth pattern in the lymph node and extranodal tumors. Further, these patients showed large lymph node swelling, extranodal tumors mainly of the subcutis, bone, gastrointestinal tract and soft tissue. Leukemic changes, bone marrow and hepatosplenic invasion and hypercalcemia were rarely found. Patients with CD30-positive ATL/L showed a better overall survival than those with CD30-negative ATL/L, but the difference was not significant.

On the other hand, typical ALCL is mainly distributed in a bimodal age with peaks in the third and sixth decades, and shows frequent extranodal tumor formation, expression of epithelial membrane antigen (EMA) and genotypically T or Null cell type, and patients show a good response to cytotoxic therapy and achieve complete remission (8). Chromosomal abnormality t(2;5) (p23;q35) is characteristic of younger ALCL patients, and this translocation encodes for an 80-kD anaplastic lymphoma kinase (ALK)-nucleophosmin (NPM) chimeric protein. This protein (p80) is thought to play a key role in lymphomatogenesis of ALCL. However, patients over 40 years of age with ALCL frequently do not have t(2;5) (p23;q35) and show a worse prognosis than that of younger ALCL patients. Patients with ALCL type ATL/L over 40 years old (median 67) showed frequent extranodal tumor formation (9). In the 9 examined patients with ALCL type ATL/L, t(2;5) (p23;q35) was absent, but 2 patients showed an additional aberration of 2p23 (10). Aberration of 5q35 was detected in a CD30-positive ATL/L cell line with a potential for cohesive cell growth. Loss and translocation of chromosome 17 were found in 6 patients. EMA and ALK-HPM protein (p80) were absent in ALCL type ATL/L (8, 9). These patients had a poorer prognosis than younger ALCL patients and age-matched HTLV-I-negative ALCL patients.

Patients with CD30-positive ATL/L (pleomorphic and ALCL types) had unique clinicopathologic features in the lymphoma group. Akamatsu et al (11) analyzed cell adhesion molecules (CAMs) of ALCL type ATL/L, and demonstrated that this type of ATL/L, as well as HTLV-I negative ALCL, was frequently positive for CD54 (ICAM1) and negative for LFA1α. On the other hand, CD30-negative ATL/L was mostly negative for ICAM1 and positive for LFA1α. They suspected that the positive CD54 (ICAM1) and negative LFA1α of ALCL type ATL might be related to local tumor formation and aleukemic behavior. Further genetic examination of p53 and functional study are necessary in this type of ATL/L.

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References


