Ki-1 (CD30)-positive Anaplastic Large Cell Lymphoma, Sarcomatoid Variant Accompanied by Spontaneously Regressing Lymphadenopathy

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Although it has been reported that primary Ki-1 (CD30)-positive anaplastic large cell lymphoma (ALCL) of the skin may undergo spontaneous regression, it is rare for ALCL without cutaneous involvement to have spontaneously regressing lymphadenopathy. We report a case of sarcomatoid variant of ALCL accompanied by spontaneously regressing lymphadenopathy. The patient had gastric and pulmonary involvement of ALCL in addition to systemic lymphadenopathy, but with no cutaneous involvement. The lymphadenopathy spontaneously improved gradually during a period of one month without any treatment. At the same time, multiple small nodules in both lung fields decreased on chest computed tomography and multiple elevated gastric tumors with dimples were endoscopically recognized to have improved. He has since been treated with combination chemotherapy because of recurrence of the lymphadenopathy.
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Key words: Ki-1 (CD30) antigen, storiform growth pattern, pulmonary and gastric involvement, soluble interleukin-2 receptor level

Introduction

Anaplastic large cell lymphoma (ALCL) was identified as a distinct morphological entity by Stein et al (1) in 1985. This is a high-grade malignant lymphoma with morphologic features of large cells, including a Reed-Sternberg-like cell appearance, and the expression of the Ki-1 (CD30) antigen or epithelial membrane antigen (EMA) (1, 2). Although it has been reported that primary ALCL of the skin may undergo spontaneous regression (3–5), there is only one report in which ALCL without cutaneous involvement showed spontaneous regression of lymphadenopathy (6). The present report describes a 44-year-old man with a Ki-1 (CD30)-positive ALCL accompanied by spontaneously regressing lymphadenopathy.

Case Report

A 44-year-old smoking man was admitted for evaluation of multiple small nodular shadows in both lung fields in September 1997. He had been in good health until three weeks previ-

ously when he had a fever of unknown cause and a mass (40×30 mm) in the left inguinal region. On admission, his temperature was 37.8°C, heart rate 100 beat/min, respiratory rate 16/min, and blood pressure 138/90 mmHg. Fine crackles were audible over both lung fields. Arterial blood gas analysis revealed slight hypoxemia (pH 7.48, partial pressure of oxygen (PaO₂) 65.3 Torr, partial pressure of carbon dioxide (PaCO₂) 36.9 Torr, HCO₃ 26.7 mmol/l). The results of blood counts and blood chemistry tests were normal, except for increased levels of white blood cells (15,000/mm³), alkaline phosphatase (393 U/l) and C-reactive protein (6.19 mg/dl). Antinuclear, anti-DNA antibody, rheumatoid factor, and anti-varicella zoster virus, cytomegalovirus immunoglobulin M (IgM) and Epstein-Barr virus (EBV) antibody were negative. The soluble interleukin-2 receptor (IL-2R) level was 5,720 U/ml.

A computed tomography (CT) of the chest revealed hilar and mediastinal lymphadenopathy, and multiple small nodular shadows in both lung fields (Fig. 1A). A CT of the abdomen revealed paraaortic lymphadenopathy (Fig. 1B). A ⁶⁷Ga scintigram showed an abnormal accumulation in the stomach, and

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in the left supraclavicular and inguinal regions.

Histologically, sections from the inguinal mass showed a proliferation of large oval tumor cells which were pleomorphic and had abundant cytoplasm, and the presence of an abundant extracellular myxoid matrix (Fig. 2A). Some of the neoplastic cells were spindle-shaped with a storiform growth pattern (Fig. 2B). Immunohistochemical studies showed staining of tumor cells by Ki-1/Ber-H2 (CD30), UCHL-1 (CD45RO) and EMA and negative stain with leukocyte common antigen (LCA: CD45RB), cytokeratin and L26 (CD20). The stain of Ki-1/Ber-H2 was localized to the cell membrane, Golgi zone, or both in tumor cells (Fig. 2C). EBV-encoded small RNA (EBER-1) *in situ* hybridization was not detected. Analysis of T cell receptor β -chain and immunoglobulin heavy chain JH rearrangements

A

B

Figure 1. A computed tomography (CT) of the chest reveals multiple small nodular shadows and ground-glass opacities in both lower lung fields (A). A CT of the abdomen reveals paraaortic lymphadenopathy (B).

A

B

C

Figure 2. Pathological finding of the inguinal mass shows a proliferation of large oval pleomorphic tumor cells with abundant cytoplasm, and the presence of an abundant extracellular myxoid matrix (A: HE stain, $\times 400$). Some neoplastic cells were spindle-shaped with a storiform growth pattern (B: HE stain, $\times 200$). The stain of Ki-1/Ber-H2 (CD30) was localized to the cell membrane (arrowhead), Golgi zone (arrow), or both in the tumor cells (C, $\times 400$).

A

B

C

were not done. The features and immunohistochemical studies were considered to be the Ki-1 (CD30)-positive ALCL of the T-cell type, a sarcomatoid variant.

Transbronchial lung biopsy failed to obtain diagnostic material. However gastric endoscopy showed multiple elevated tumors with dimples (Fig. 3A). Pathological findings of the specimens obtained from the gastric tumors revealed the same results as those of the inguinal mass (Fig. 3B). Immunohistochemical studies showed the staining by Ki-1/Ber-H2 was localized to only the cell membrane of tumor cells (Fig. 3C).

A

B

Figure 4. Chest (A) and abdominal CT (B) after one month shows that the multiple small nodules of the lung have decreased and the lymphadenopathy has improved.

Figure 3. Gastric endoscopy shows multiple elevated tumors (arrowheads) with dimples (A). Pathological finding of the gastric tumors revealed the same result as in the inguinal mass (B: HE stain, ×400). Immunohistochemical studies showed the staining by Ki-1/Ber-H2 was localized to only the cell membrane (arrowheads) of the tumor cells (C, ×400).

Low-grade fever persisted for about two weeks. Subsequently the fever declined and the inguinal and supraclavicular lymphadenopathy improved gradually during a period of one month without any treatment. At the same time, chest and abdominal CT showed that the lymphadenopathy and multiple small nodules in the lung also decreased in size (Fig. 4A, B). The soluble IL-2R level was restored to the normal range. The patient was discharged with no enlargement of the lymph nodes and no recurrence of the multiple small nodules of the lung. However, he was readmitted two months after his discharge because of recurrence of ALCL including the lymphadenopathy and has been treated with combination chemotherapy (CHOP regimen).

Discussion

The Ki-1 (CD30) antigen is expressed by not only activated cells in non-neoplastic lymphoid tissues but tumor cells of Hodgkin's disease and various non-Hodgkin's lymphoma (7). ALCL is characterized by an increased number of the Ki-1 antigen positive cells and was incorporated into the updated Kiel classification (8). In ALCL, it has been reported that staining of Ki-1/Ber-H2, which are also antibodies to designate CD30, is localized to the cell membrane, Golgi zone, or both (9). ALCL histopathologically is characterized by preferential paracortical involvement of lymph nodes, foci of necrosis and intrasinusoidal dissemination of large atypical cells with pleomorphic nuclei, abundant cytoplasm and one or more nucleoli (10). In addition, the sarcomatoid variant (11) has been reported as one of the several morphologic variants of ALCL and corresponds to the histopathological findings of the present case. Chan et al (11) reported that the presence of a storiform or myxoid pattern does not disqualify the diagnosis of malignant lymphoma. With regard to immunophenotypic studies, the tumor cells express EMA, CD25, HLA-DR and CD45 (2, 11). It has been reported that expression of EMA and CD45, and the lack of CD15 facilitate the distinction of ALCL from Hodgkin's disease and that the expression of CD30 and a lack of cytokeratin could distinguish ALCL from most carcinomas (10, 12).

ALCL has been reported to show frequent extramedullary involvement of the skin, liver, stomach, kidney, bone and lung (13–15). Although ALCL generally has an aggressive clinical behavior, as in the case of other high-grade malignant lymphomas, this disease limited to the skin (primary cutaneous ALCL) tends to have a slower and protracted course (14). The present case had lymphadenopathy, gastric involvement and multiple small nodular shadows in both lung fields. Although transbronchial lung biopsy was of no diagnostic value due to the smallness of the lung nodules, we suspected that the pulmonary lesions indicated involvement of ALCL because they also improved with spontaneous improvement of the lymphadenopathy. It has been reported that primary ALCL of the skin may undergo spontaneous regression (3–5), however there has only been one report (6) in which ALCL without cutaneous involvement showed spontaneous regression of lymphadenopathy. The patient was a 71-year-old female who presented with

recurring cervical lymphadenopathy over a 5-year period. Dermierre et al (16) reported that the spontaneous regression occurred in lymphomas, including cutaneous ALCL, especially in cases which were borderline between benign and malignant disease. In addition, Motley et al (17) suggested that regressing atypical histiocytosis is the regressing phase of ALCL of the skin. However, it is unknown why ALCL patients without cutaneous involvement, which is classified as high-grade malignant lymphoma, have spontaneously regressing lymphadenopathy.

An optimal strategy for the treatment of ALCL has not yet been established. The responses to treatment of ALCL limited to the skin are different from those of patients with nodal or other extranodal involvements (5, 14). Primary ALCL of the skin can often be controlled by local measures, and intensive treatment does not seem justified (14, 18). On the other hand, aggressive chemotherapy should be selected for ALCL with nodal or extranodal involvement, even if the patient has spontaneously regressing lymphadenopathy.

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