

Case Study

Complete Remission in Systemic Skin Interdigitating Dendritic Cell Sarcoma after ABVD Chemotherapy

Chieko Kyogoku,¹⁾ Masanori Seki,⁵⁾ Shinichi Ogawa,¹⁾ Kana Miyamoto,¹⁾ Yufu Ito,¹⁾ Naoki Kurita,¹⁾ Yasuhisa Yokoyama,¹⁾ Mamiko Sakata-Yanagimoto,¹⁾ Naoshi Obara,¹⁾ Yuichi Hasegawa,¹⁾ Fumiyooshi Fujishima,²⁾ Ryo Ichinohasama,³⁾ Shigeo Nakamura,⁴⁾ and Shigeru Chiba¹⁾

Interdigitating dendritic cell sarcoma (IDCS) is a rare and aggressive neoplasm that is thought to arise from dendritic cells. This disease usually involves the lymph nodes and, rarely, extra-nodal sites. We report a 62-year-old man presenting skin nodules in the head, body, and extremities, as well as bone marrow involvement. Morphologic analysis of a biopsied specimen from the skin lesion was consistent with IDCS. Immunohistochemical staining demonstrated that the tumor cells were positive for IDCS-associated antigens such as CD4, CD45, CD68 (KP-1), and S-100 protein. Complete remission was achieved by treatment with 6 cycles of ABVD (adriamycin, bleomycin, vinblastine, and dacarbazine) chemotherapy. Although the optimal treatment of IDCS remains unknown, the experience in the current case supports the notion that ABVD chemotherapy may be effective for IDCS, and further extends this idea to rare patients presenting multiple skin lesions. [*J Clin Exp Hematop* 55(1) : 33-37, 2015]

Keywords: interdigitating dendritic cell sarcoma, skin, ABVD chemotherapy

INTRODUCTION

Interdigitating dendritic cell sarcoma (IDCS) is a very rare neoplasm supposed to arise from the IDCs of the lymphoid tissues.^{1,2} The tumor usually initially develops at the T-cell-rich region of the lymph node, although the involvement of extra-nodal sites such as the spleen, intestine, testis, urinary bladder, lung, kidney, and bone marrow has also been reported.³⁻⁹ Cutaneous lesions are extremely rare, and fewer than 10 cases have been reported.^{10,11}

Although various treatments such as surgery, radiation therapy, chemotherapy, and hematopoietic stem cell trans-

plantation have been attempted, there is no consensus on the preferred treatment. Numerous chemotherapeutic regimens have been chosen, including those for Hodgkin and non-Hodgkin lymphomas.^{1,2,12} Among them, ABVD (adriamycin, ADR; bleomycin, BLM; vinblastine, VBL; and dacarbazine, DTIC), a standard for Hodgkin lymphoma, has been reported to be effective in 4 case reports.¹³⁻¹⁶ Here, we add a new case of an IDCS patient successfully treated with ABVD, with a particular emphasis on the unique presentation of the disease in the skin.

CASE REPORT

A 62-year-old man visited a primary care physician with a 2-month history of skin lesions: dark-reddish subcutaneous discoid nodules (5-6 cm) on the head, limbs, and trunk (Fig. 1). They were elastic and firm, accompanied by no pain, itching, or ulcer. The patient had no particular medical and family history. Except for the skin lesions, physical and laboratory examinations did not show any abnormal findings. Histologic examination of the excisional biopsied specimen revealed diffuse infiltration of spindle cells, large pleomorphic cells, foamy histiocytes, and various inflammatory cells in the dermis through the subcutaneous tissue (Fig. 2A). Immunophenotyping by flow cytometry and immunostaining showed that the tumor cells expressed CD4, CD45 (Fig. 2B),

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¹⁾Department of Hematology, Faculty of Medicine, University of Tsukuba, Tsukuba, Ibaraki, Japan

²⁾Department of Pathology, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan

³⁾Division of Hematopathology, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan

⁴⁾Department of Pathology and Laboratory Medicine, Nagoya University Hospital, Nagoya, Aichi, Japan

⁵⁾Department of Hematology, Mito Medical Center, National Hospital Organization, Mito, Ibaraki, Japan

Corresponding author: Dr. Shigeru Chiba, Department of Hematology, University of Tsukuba, 1-1-1 Tennodai, Tsukuba-shi, Ibaraki-ken 305-8575, Japan

E-mail: schiba-t@md.tsukuba.ac.jp



Fig. 1. The patient exhibited skin lesions in the form of dark-red subcutaneous nodules (5-6 cm) on the head, limbs, and trunk. Pictures were taken before starting ABVD (adriamycin, bleomycin, vinblastine, and dacarbazine) chemotherapy.

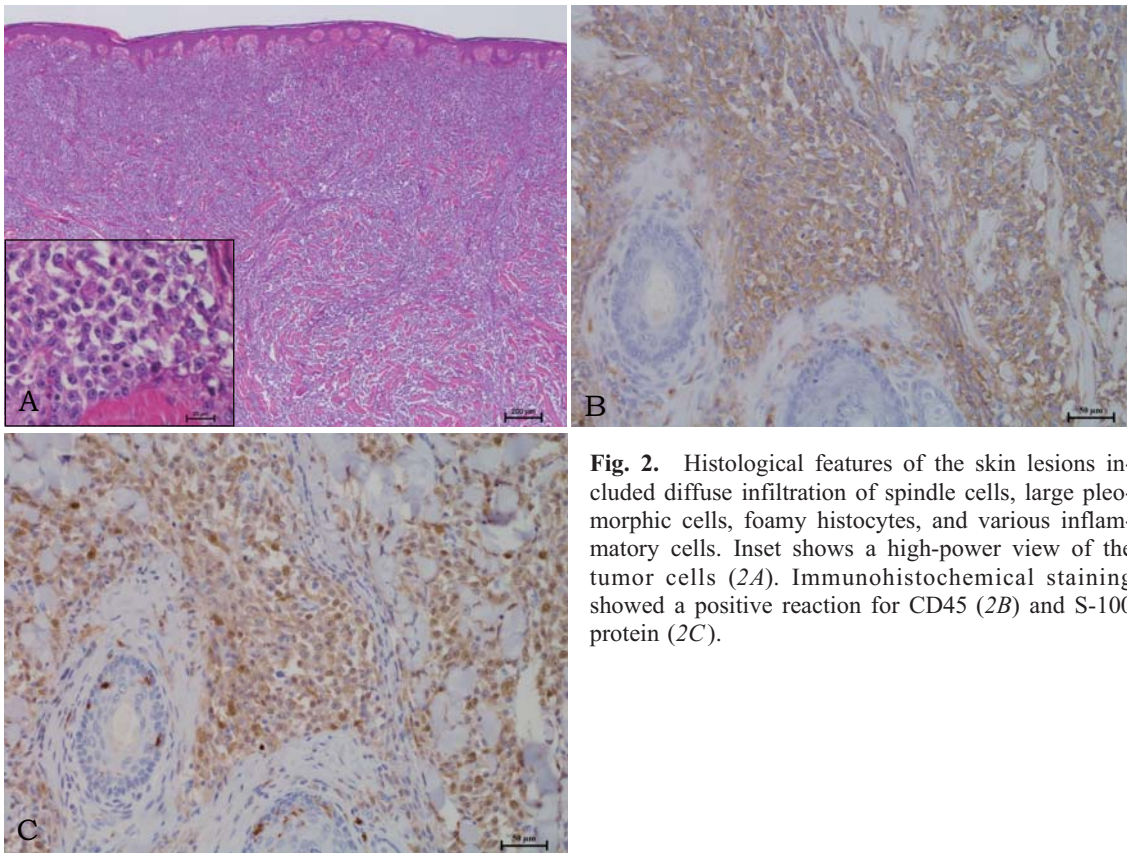


Fig. 2. Histological features of the skin lesions included diffuse infiltration of spindle cells, large pleomorphic cells, foamy histocytes, and various inflammatory cells. Inset shows a high-power view of the tumor cells (2A). Immunohistochemical staining showed a positive reaction for CD45 (2B) and S-100 protein (2C).

S-100 protein (Fig. 2C), and CD68 (KP-1), but not CD1a, CD2, CD3, CD5, CD7, CD8, CD10, CD20, CD21, CD23, CD30, CD34, CD35, CD56, CD79a, CD123, EBER, D2-40, langerin, fascin, BDCA2, TCL-1, myeloperoxidase, and granzyme B. Immunoglobulin and T-cell receptor gene rearrangements were not detected. On the basis of morphologic and immunohistochemical findings, a diagnosis of IDSC was made. He did not have any other lesions except for the



Fig. 3. Corresponding positron emission tomography/computed tomography image shows increased 18-fluoro-deoxyglucose uptake in the skin as well as the whole bone marrow (maximum standardized uptake values of 3.8 and 3.3).

multiple solitary skin nodules; however, positron emission tomography/computed tomography imaging showed increased 18-fluoro-deoxyglucose uptake in the whole bone marrow, in addition to that in the skin corresponding to the nodular lesions (Fig. 3). This suggested the infiltration of the tumor cells into the bone marrow, despite the bone marrow aspiration study not having revealed this pathologically.

Because there were multiple skin lesions and there was a possibility of bone marrow involvement, chemotherapy was selected rather than surgery or radiation therapy. About 4 months after the onset, the ABVD regimen (25 mg/m² ADR, 10 mg/m² BLM, 6 mg/m² VBL, and 250 mg/m² DTIC; days 1 and 15, every 4 weeks) was started (Fig. 4). Mild neutropenia after each course did not interfere with the continuation of the regimen, and no significant complications were documented. After 6 cycles of the ABVD regimen (Fig. 4), cutaneous lesions disappeared and the patient was judged to have achieved complete resolution.

DISCUSSION

IDCS can arise in individuals of any age, but mostly in those at or above their 60s, with a slight male predominance.¹⁷ To date, fewer than 90 cases of IDCS have been reported worldwide.⁹ Patients with IDCS present with painless lymph node enlargement and/or extra-nodal mass, in a relatively non-invasive manner. Systemic symptoms such as fever, fatigue, and weight loss are very rare.⁹

IDCS shows a germline configuration in both immunoglobulin and T-cell receptor genes. Histologically, characteristic features include diffuse infiltration of giant and spindle pleomorphic cells, foamy histiocytes, and various inflammatory cells. These histologic findings are sometimes indistinguishable from those of follicular dendritic cell (FDC) sarcoma

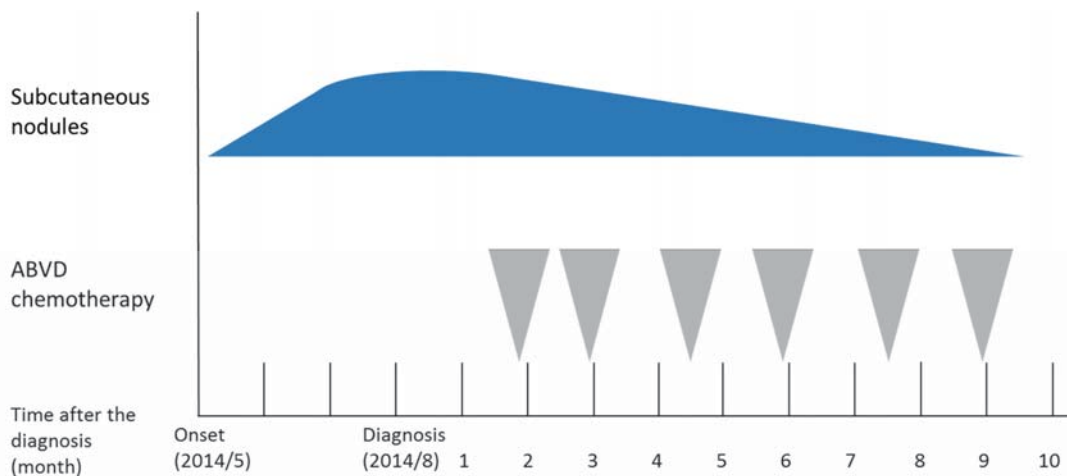


Fig. 4. ABVD (adriamycin, bleomycin, vinblastine, and dacarbazine) regimen and clinical course of the present patient.

(FDCS). By immunostaining, IDCS has been documented to be strongly positive for S-100 protein antigen, vimentin, HLA-DR, and fascin.^{18,19} Moreover, CD4, CD11c, CD14, CD45, CD68 (KP-1), lysozyme, and epithelial membrane antigen are sometimes positive. In contrast, markers for Langerhans cells (CD1a, CD56, and langerin), FDCs (CD21, CD23, and CD35), T cells (CD3, CD5, and CD8), B cells (CD20), and myeloid cells (CD34, myeloperoxidase), as well as EBER, are usually negative.^{18,19} Although S-100 protein is an important marker for the diagnosis of IDCS, it is also positive in Langerhans cell histiocytosis (LCH)/Langerhans cell sarcoma (LCS),¹⁸ so the differential diagnosis between IDCS and LCH/LCS is sometimes difficult. Furthermore, the differential diagnosis of IDCS from other cutaneous lymphomas such as blastic plasmacytoid dendritic cell neoplasm and indeterminate dendritic cell tumor is required.²⁰

In the current case, immunohistochemistry showed positive staining of CD4, CD45, and CD68 (KP-1), in addition to S-100 protein, suggesting a possible diagnosis of IDCS. Inconsistently, fascin, which was previously reported to be positive in IDCS, was not stained. However, considering the negative staining of markers for FDCS such as CD21, CD23, CD35, EBER, and D2-40; markers for LCH/LCS such as CD56 and langerin; markers for blastic plasmacytoid dendritic cell neoplasm such as BDCA2, CD123, and TCL-1; and a marker for indeterminate dendritic cell tumor, CD1a, the diagnosis of IDCS was uniquely made.

At present, there is no standard therapeutic method for IDCS. Approximately half of the cases of localized IDCS may be curable by surgery without adjuvant therapy.²¹ On the other hand, systematic radiotherapy or chemotherapy and hematopoietic stem cell transplantation are used for extensive IDCS. According to previous reports, ABVD chemotherapy has achieved complete remission in 3 cases after 5-8 cycles of ABVD and partial remission in 1 case.¹³⁻¹⁶ The optimal regimen and reliable prognostic factors as well as its mechanism of therapeutic effect remain unclear due to the absence of comprehensive studies. Meanwhile, Tanikawa *et al.* reported severe complications during ABVD chemotherapy for IDCS patients, such as pancytopenia, interstitial pneumonitis, anorexia, and muscle weakness and synesthesia of the limbs.¹⁴ In the current case, we followed the standard ABVD regimen and could prevent the major complications described above. However, without any studies comparing ABVD and other regimens, it remains to be elucidated whether ABVD is the appropriate first-line treatment for this disease. Additional case studies will be required to assess the optimal regimen and complications of chemotherapy on IDCS.

The current report supports the effectiveness of ABVD chemotherapy for IDCS patients, especially for patients presenting systemic lesions in the skin. Close follow-up is necessary to assess the recurrence and prognosis of ABVD chemotherapy.

CONFLICT OF INTEREST STATEMENT

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