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CASE REPORT

A Rare Case of Cutaneous T-Cell Lymphoma Accompanied by Acute Monoblastic Leukemia and Diffuse Large B-Cell Lymphoma

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A 70-year-old female was referred for brown-to-gray colored papules and nodules on her lower legs. She had been diagnosed with diffuse large B-cell lymphoma (DLBCL) in her stomach, and myelodysplastic syndrome (MDS) by bone marrow biopsy. Three years after complete remission of DLBCL, she experienced DLBCL recurrence in her small bowel and was hospitalized. MDS had been stationary, but during the treatment of DLBCL, her laboratory findings suggested signs of leukemia. Bone marrow biopsy was done, and acute monoblastic leukemia (AMoL) was diagnosed. After 1 cycle of chemotherapy for AMoL, skin lesions developed, and her skin biopsy showed cutaneous T-cell lymphoma (CTCL). Terminal deoxynucleotidyl transferase staining and CD123 staining were negative, and bone marrow re-biopsy conducted after the skin lesion developed still showed monoblastic proliferation. Whether the CTCL represented with an AMoL lineage switch could not be completely proved due to the absence of molecular or clonal marker evaluations, but the possibility of coexistence of three different malignancies was higher. During treatment, a neutropenic fever developed, and the patient died due to sepsis. We herein report a rare case of CTCL accompanied by AmoL and DLBCL. **(Ann Dermatol 33(2) 178～181, 2021)**

-Keywords-
Acute monoblastic leukemia, Cutaneous T-cell lymphoma, Lineage switch

INTRODUCTION

Cutaneous T-cell lymphoma (CTCL) is a term that encompasses a spectrum of lymphomas in the skin that are unified by the immunologic features of neoplastic T cells. The condition is characterized by monoclonal expansion of T lymphocytes. When it comes to patients with acute myelocytic leukemia, it is important to consider not only the possibility of coincident development of two different malignancies but also the possibility of lineage switch of leukemia from myeloid to lymphoid differentiation. Both conditions are rare, and it is worth to report when those two malignancies occur simultaneously with B-cell differentiated tumor. We herein describe a unique form of CTCL accompanied by acute monoblastic leukemia (AMoL) progressed from myelodysplastic syndrome (MDS) and diffuse large B-cell lymphoma (DLBCL), which presented as multiple papules and nodules in the lower legs.

CASE REPORT

A 70-year-old female was referred to the dermatology department with multiple skin lesions on her legs, which were noticed two days prior (Fig. 1). In 2013, she was diagnosed with DLBCL in her stomach and received chemotherapy. At that time, a bone marrow biopsy was performed, and she was diagnosed with MDS. Complete remission

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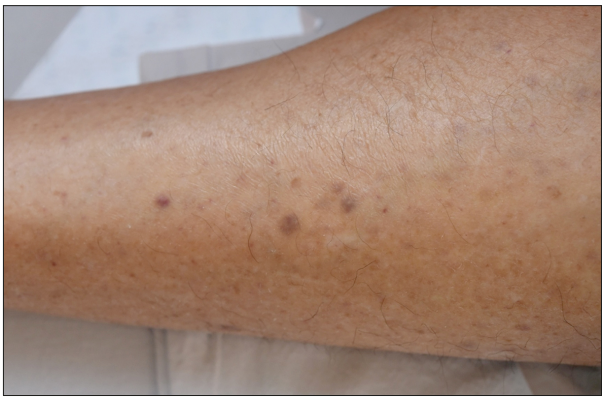

Fig. 1. Clinical manifestation of the patient; multiple brown to gray colored papules and nodules on the lower extremities.

of DLBCL was observed after four cycles of chemotherapy. During three years of the follow up period, a relapse of DLBCL was observed in her small bowel. After 4 cycles of new chemotherapy regimen, DLBCL had a partial remission but her complete blood cell counts showed abnormally increased number of white blood cells, suggesting a progression to leukemia. Bone marrow biopsy was performed again, and it showed monoblastic proliferation. She was diagnosed with a progression of MDS to AMoL. During chemotherapy that targeted leukemia, skin lesions were observed on her lower legs. Scattered brown-to-gray colored papules and nodules were observed, and a punch biopsy was performed. The histologic examination of the specimen revealed diffuse, dense, atypical lymphocytic infiltration throughout the entire dermis (Fig. 2). An immunohistochemical stains were performed, which showed pos-

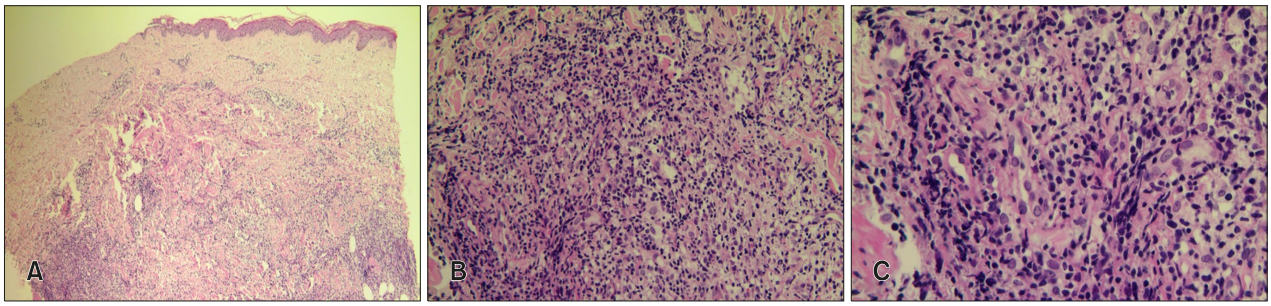

Fig. 2. Histopathologic features of skin biopsy. (A) Diffuse lymphocytic infiltration in the entire dermis (H&E, ×40). (B) Dense atypical lymphocytic infiltration in the entire dermis (H&E, ×200). (C) Atypical lymphocytes with some anaplastic cells (H&E, ×400).

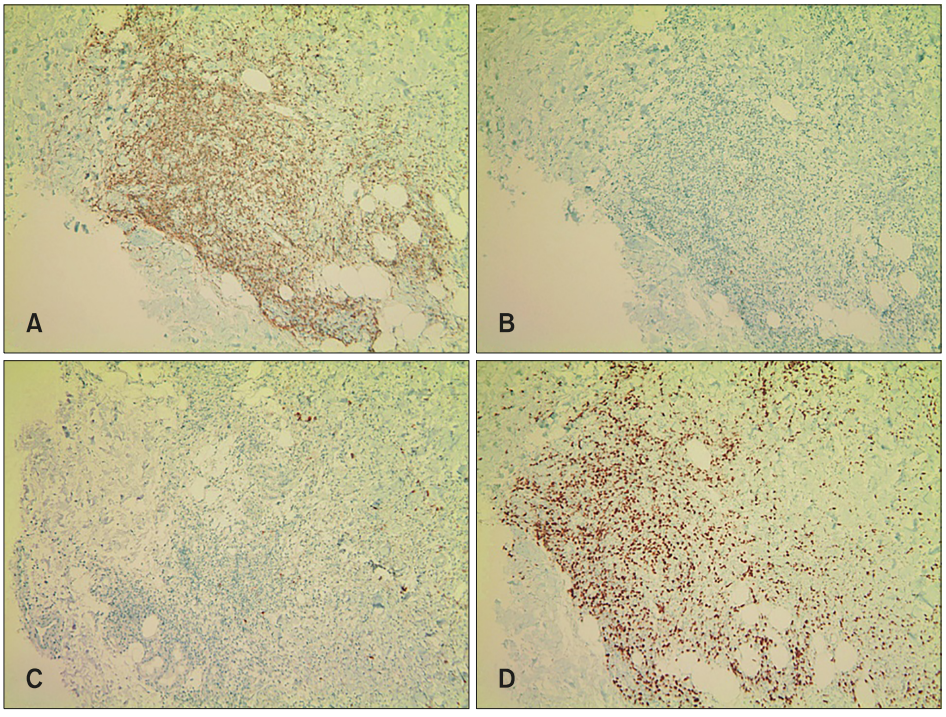

Fig. 3. Immunohistochemical staining (A) CD3 positive (×40); (B) CD20 negative (×40); (C) MPO negative (×40); (D) Ki-67 positive (×40).

itive results for CD3, CD4, CD5 and negative results for CD20, CD138, CD8, Bcl2, PAX-5, MPO, and C-kit. The Ki-67 stain showed high proliferation (Fig. 3). To confirm T-cell differentiation, a T-cell receptor beta and gamma gene arrangement test was performed, and the test showed monoclonal expansion. Terminal deoxynucleotidyl transferase (TdT) stain was performed to differentiate precursor T-cell lymphoblastic leukemia/lymphoma, and it showed negative result. CD123 stain, whose positive result means blastic plasmacytoid dendritic cell neoplasms, was also negative. Re-biopsy of her bone marrow after her skin lesion developed still showed monoblastic proliferation. According to the WHO-EORTC classification, the diagnosis was most likely to be primary cutaneous peripheral T-cell lymphoma, unspecified, considering the histopathology and immunophenotype. Therefore, the coexistence of three different types of malignancies, CTCL, AMoL, and DLBCL, was more likely to be her diagnosis rather than lineage switch from myeloid to lymphoid leukemia. During chemotherapy, neutropenic fever occurred, and she died due to sepsis. Further work-up for identifying a lineage switch could not be performed.

We received the patient's consent form about publishing all photographic materials.

DISCUSSION

The patient had DLBCL in her stomach and MDS in her bone marrow. After chemotherapy, complete remission was observed. However, DLBCL had relapsed and MDS progressed to AMoL. During chemotherapy for AMoL, a new skin lesion developed and was diagnosed as a malignancy of lymphoid cells with T-cell differentiation. There are two considerable causes of this skin malignancy.

First, there is a rare chance that the CTCL was another malignancy that emerged during chemotherapies for DLBCL and AMoL. A hypothesis for the development of another malignancy is that chemotherapy can weaken the immune system of the patient and cause another cancer. Another possible mechanism is that therapies for one malignancy can directly or indirectly damage DNA, and increase the possibility of another malignancy[1,2]. In this case, TdT staining and CD123 showed negative result, and re-biopsy of bone marrow showed monoblastic proliferation. Hence, the diagnosis was most likely to be CTCL accompanied by AMoL and DLBCL. Additional genetic analysis to verify the origin of three malignancies was not available as the patient expired.

There is also a previous report of the coexistence of three concurrent malignancies involving three different lineages; mycosis fungoides, DLBCL, and acute myeloid leukemia[3]. In the case, the patient had undergone genetic analysis due to the possibility that three malignancies might have a common origin. However, no somatic mutations in *TET2* gene were identified in the tissue of mycosis fungoides and DLBCL, with a preference for coexisting rather than a common origin.

Second, lineage switch from acute myeloid leukemia to acute lymphoblastic leukemia can be rarely occurred. Although the exact mechanism has not been explored, there are possible explanations for lineage switches. Chemotherapy can eradicate dominant leukemia clones, allowing other minor chemotherapy-resistant subclones of different phenotypes become dominant. That can change the dominant clone and the composition of the tumor[4]. Another theory suggests that gene alterations that are acquired during chemotherapy can cause deleterious effect on leukemic cell differentiation programs, which can eventually cause a lineage switch[4]. Some studies have expiscated that *MLL* gene locations in childhood leukemia are associated with lineage switches[5].

Although the patient was not able to undergo further lineage switch evaluations because of this patient's death, it is important to identify lineage switches in patients with cutaneous lymphomas, in order to select the proper chemotherapy for a specific lineage at recurrence. Sequential phenotyping and cytologic studies may facilitate the identification of the lineage switch and the selection of treatment options. The prognosis is known to be poor when lineage switches occur[5].

In conclusion, coexistence of CTCL, AMoL, and DLBCL is extremely rare. It is difficult to conclude whether a CTCL involves a lineage switch from AMoL or another primary neoplasm due to the lack of further evaluation, but it seems more likely to be CTCL accompanied by AMoL and DLBCL rather than a lineage switch. However, when a new lesion develops in patients with leukemia, it is important to consider the possibility of a lineage switch and perform further evaluations in order to select the proper treatment and improve prognosis. We herein report a rare case of a patient with coexistence of three different malignancies; CTCL, AMoL, and DLBCL.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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DATA SHARING STATEMENT

Research data are not shared.

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