Received: 15 February 2021 | Accepted: 14 April 2021

DOI: 10.1002/cia2.12178

Journal of Cutaneous Immunology and Allergy

WILEY

CORRESPONDENCE

Development of diffuse large B-cell lymphoma during dupilumab treatment in a patient with atopic dermatitis: A case report

This case report describes a 44-year-old male patient with atopic dermatitis who developed malignant lymphoma (diffuse large B-cell lymphoma) during the dupilumab treatment.

Dupilumab demonstrated high efficacy and effectiveness for atopic dermatitis (AD) in clinical trials[1] and real-world data.[2,3] Regarding safety, dupilumab increases the risk of conjunctivitis in atopic dermatitis patients[4,5]; however, malignancy has not been sufficiently discussed because of the small number of enrolled patients and a short period of observation. We herein report an AD patient who developed malignant lymphoma during dupilumab treatment and discuss its association with AD or dupilumab.

A 44-year-old man had been diagnosed with severe AD during his childhood and had applied high-potency topical corticosteroid (TCS) on eruptions over his entire body. Immediately after approval of dupilumab for the treatment of AD, he started

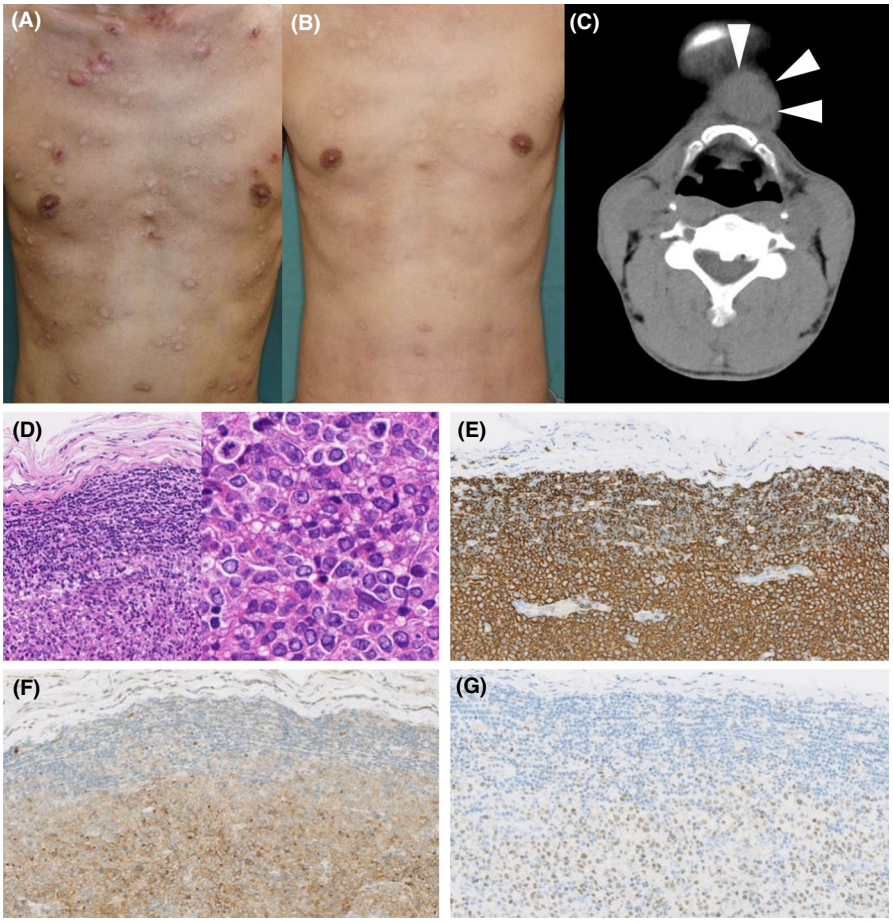

FIGURE 1 (A, B) Representative clinical manifestations on the trunk of the patient with severe AD at the time of initiation of dupilumab (A) and 12 months later (B). (C) Computed tomography scan detected an enlarged cervical lymph node with a diameter of 26 mm in the anterior neck (white arrows). (D-G) Pathological and immunohistological findings of the cervical lymph node. (D) Hematoxylin-eosin. Left panel: Magnification, ×200. Right panel: Magnification, ×400. (E) CD20. Magnification, ×200. (F) CD10. Magnification, ×200. (G) BCL-6. Magnification, ×200

to receive dupilumab. At initiating dupilumab, he presented with slight-to-moderate erythema and lichenification spreading over his whole body, and scattered refractory nodular lesions (Figure 1A). His investigator's global assessment score was 4, and total eczema area and severity index (EASI) was 43.6. Dupilumab ameliorated his eruption including nodular lesions with his total EASI decreasing to 36.4, 18.8, 17.7, and 4.9 at 1, 3, 6, and 12 months after the initiation of dupilumab, respectively (Figure 1B), which resulted in reduction in the amount and potency of TCS applied. One year after initiation of dupilumab, he noticed a nodule on the anterior region of his neck and visited an otolaryngologist. Computed tomography scan detected an enlarged cervical lymph node with a diameter of 26 mm in the anterior neck (Figure 1C). Lymph node biopsy revealed pathological findings of loss of the normal structure of lymph nodes and the proliferation of atypical cells (Figure 1D). Immunohistochemical staining demonstrated that the atypical cells were positive for CD20, CD10, and BCL-6 (Figure 1E-G), and negative for CD3, CD5, CD21, MUM-1, c-Myc, and EBER. BCL-2 staining was slightly positive. The Ki-67 labeling index was more than 90%. Therefore, he was diagnosed with diffuse large B-cell lymphoma (DLBCL), germinal center B cell-like type, and was referred to another hospital for treatment. He is receiving R-CHOP chemotherapy (rituximab, cyclophosphamide, vincristine, doxorubicin, and prednisone) for the treatment of DLBCL.

Regarding the association of AD with lymphoma, a systematic review and meta-analysis revealed that the risk of lymphoma was slightly increased in cohort studies.[6] Severity of AD is a significant risk factor for the development of lymphoma.[6] Meanwhile, reports on the association of dupilumab with lymphoma are limited. Natoli et al.[7] have demonstrated that specific blocking of interleukin (IL)-4 and IL-13-mediated STAT6 activation renders Hodgkin/Reed-Sternberg lymphoma cells more prone to apoptotic killing by chemotherapeutic drugs, suggesting that inhibition of IL-4 and IL-13 pathway by dupilumab may exert a favorable effect on lymphoma. As for DLBCL, a few studies reported the possible involvement of IL-4[8,9]; however, it remains to be clarified. Our patient had severe AD, which should have increased his risk for lymphoma, while it is unknown how much effect 1 year of dupilumab treatment imposed on the development of lymphoma. Further investigation and accumulation of cases are needed in order to elucidate the association of dupilumab treatment with a risk of lymphoma.

DECLARATION SECTION

Approval of the research protocol: Not applicable because of a case report.

Informed Consent: Not applicable. Pictures are anonymized enough.

Registry and the Registration No. of the study/trial: Not applicable.

Animal Studies: Not applicable.

CONFLICT OF INTEREST

Yayoi Tada received a research grant from Sanofi; Masahiro Kamata received lecture fees from Sanofi. The other authors declare no conflict of interest.

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