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CORRESPONDENCE

Development of mycosis fungoides with peripheral blood involvement after a single use of dupilumab

A Japanese man in his sixties with a 15-year history of generalized erythema was referred to our clinic. He underwent a histopathological examination of the skin and a peripheral lymph node at disease onset, and there were indications of cutaneous T-cell lymphoma (CTCL). The patient was treated for refractory atopic dermatitis (AD). His skin rash worsened rapidly after a single dose of dupilumab, and atypical lymphocytes were found in his peripheral blood, which had not been observed before. At the time of his initial visit to our clinic, he had erythroderma and superficial lymph node swelling (Figure 1A–C). His temperature was 38.1°C, and he complained of nocturnal sweating.

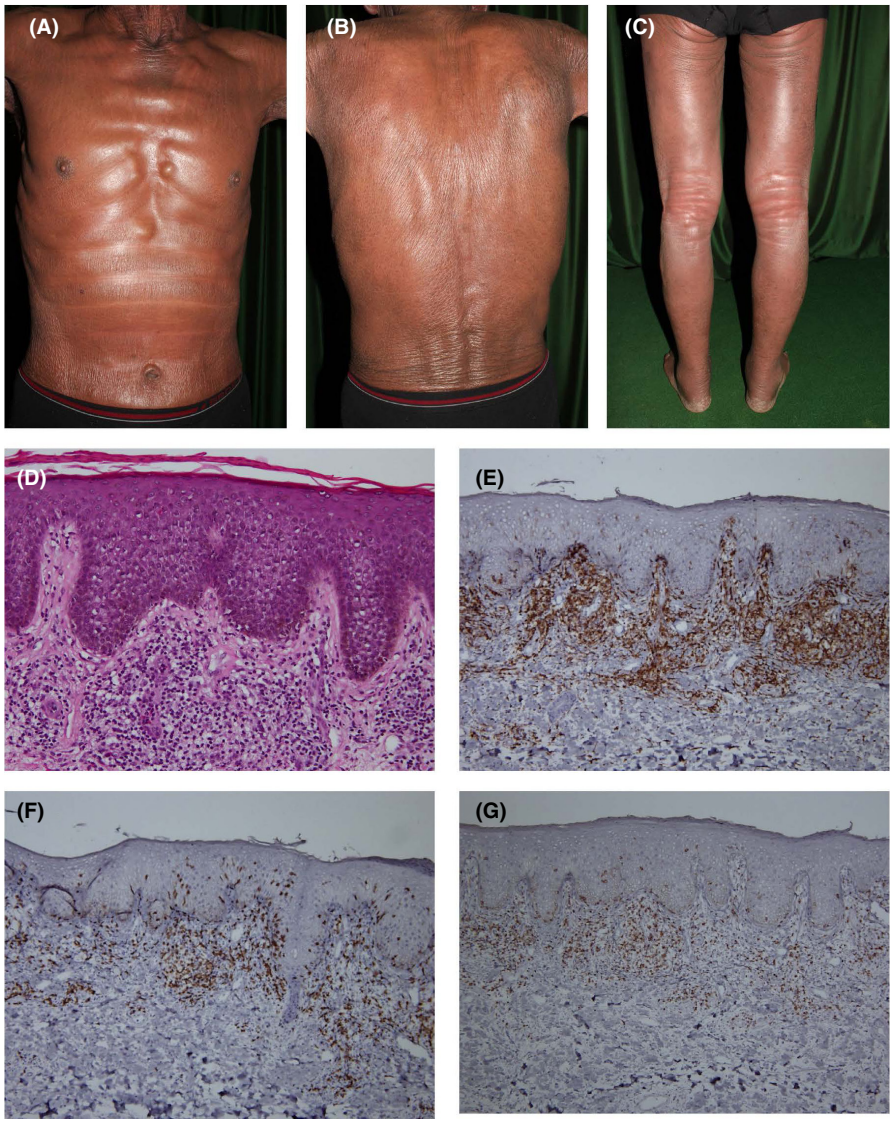

FIGURE 1 Clinical presentation of the anterior (A) and posterior aspect (B) of the trunk and posterior aspect of the legs (C) at the first visit. Histopathology of the skin biopsy sample collected from the abdomen revealed dense mononuclear cell infiltration in the superficial dermis with irregular acanthosis (D) (H&E staining, original magnification: ×200). Immunostaining for CD4 (E), CD8 (F), and CD7 (G) (original magnification: ×100)

The laboratory findings were as follows: increased white blood cell count of 15,220/μl with abnormal cells (28%, 4200/μl); elevated eosinophil count (21.5%); lymphocyte count of 4490/μl with 94.5% $CD3^+$ cells; CD4/8 ratio of 2.7; $CD4^+CD7^-$ cells at 20.4%; and $CD4^+CD26^-$ cells at 36.1%. Serum lactate dehydrogenase, soluble interleukin-2 receptor, immunoglobulin E, and thymus- and activation-regulated chemokine levels were elevated to 446 IU/L, 13,932 U/ml, 17,387 IU/ml, and > 30,000 pg/ml, respectively. The human T-lymphotropic virus-1 antibody test result was negative.

Histopathological findings revealed irregular acanthosis with superficial dense lymphoid cell infiltration (Figure 1D). No apparent Pautrier microabscesses were detected. Most of the infiltrating cells were $CD3^+$ and $CD4^+$, with a small number of $CD8^+$ cells; however, there were far fewer $CD7^+$ cells (Figure 1E–G). The pathological findings of the inguinal lymph node showed dermatopathic lymphadenopathy, but flow cytometric analysis revealed increased $CD4^+CD26^-$ cells (33.9%). In contrast, Southern blotting did not detect T-cell receptor monoclonality in the samples collected from peripheral blood mononuclear cells or lymph nodes. The patient was diagnosed with mycosis fungoides (MF) (T4N1M0B1, stage IIIB), and prednisolone was administered at 30 mg/day, followed by bexarotene.

We believed that his preceding skin symptoms may have been caused by MF, which flared up after dupilumab was administered. He had previously been treated with cyclosporine, but it had been discontinued more than 2 months prior to the exacerbation of the rash. Furthermore, the exacerbation occurred soon after dupilumab was administered. Therefore, we attributed the rash exacerbation to dupilumab.

Dupilumab is a human monoclonal antibody that targets the interleukin-4 receptor subunit α (IL-4Rα) of the IL-4 and IL-13 receptors. Since the Chiba et al. case report,[1] there have been several reported instances where CTCL became apparent after dupilumab was administered for AD. IL-13Rα2, another subunit of IL-13R, is involved in CTCL proliferation.[2] This receptor has been suggested to be involved in the exacerbation of CTCL upon dupilumab administration; however, the underlying mechanism remains unclear.[3] To date, 13 cases of CTCL after dupilumab use have been reported, all of which appeared or worsened after multiple (often three or more) doses of dupilumab.[4] The present case is unique in that the skin symptoms worsened immediately after only one dose of dupilumab.

Although dupilumab is effective for AD, the possibility of CTCL should be considered in patients with an atypical clinical presentation or atypical course after treatment.

DECLARATION SECTION

Approval of the research protocol: Not applicable.
Informed Consent: The written informed consent was obtained from the patient.
Registry and the Registration No. of the study/trial: Not applicable.
Animal Studies: Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

Kazuyasu Fujii MD, PhD
Hisao Kawahira MD
Mitsuhiro Hisadome MD, PhD
Takuro Kanekura MD, PhD

Department of Dermatology, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan

Correspondence
Kazuyasu Fujii, Department of Dermatology, Kagoshima University Graduate School of Medical and Dental Sciences, 8-35-1 Sakuragaoka, Kagoshima 890-8520, Japan.
Email: kazfujii@m2.kufm.kagoshima-u.ac.jp

ORCID

Kazuyasu Fujii https://orcid.org/0000-0002-6482-8953
Hisao Kawahira https://orcid.org/0000-0001-5288-8089
Mitsuhiro Hisadome https://orcid.org/0000-0002-4408-8855
Takuro Kanekura https://orcid.org/0000-0003-3904-5954

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