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CORRESPONDENCE

Development of tinea corporis in a Japanese patient with atopic dermatitis under treatment with upadacitinib in a real-world clinical setting: Possible contribution of the suppression of Th17

Various biologics and small-molecule compounds are continuously emerging for the novel treatment of atopic dermatitis (AD). Upadacitinib, an oral, selective Janus kinase (JAK) 1 inhibitor, was approved in August 2021 for moderate-to-severe AD in Japan. The efficacy and safety of upadacitinib have been demonstrated in clinical trials in Japan.[1] However, no reports of fungal infections were noted in patients with AD treated with upadacitinib. Herein, we report a rare case of a patient with AD who developed tinea corporis during upadacitinib treatment in a real-world clinical setting.

A 68-year-old Japanese man presented to our department with a 2-year history of whole-body rash. He had been treated with topical application of very strong steroid ointment and 5-15 mg of oral prednisolone for approximately half a year. Oral prednisolone had been discontinued for 3 months before visiting our hospital. Physical examination revealed erythema with scratch marks on his trunk and extremities including on his left lumber without annular plaque (Figure 1A-C). Investigator's Global Assessment and Eczema Area and Severity Index scores were 3 and 18, respectively. He was diagnosed with moderate AD and received 30 mg upadacitinib daily along with a very strong topical steroid. The eczema lesions and itching immediately improved after a few days, but the patient developed erythema with annular scaling on the left lumbar region 2 weeks later (Figure 1D-F). A potassium hydroxide test revealed fungal filaments and septate hyphae. He was diagnosed with tinea corporis and treated with topical application of terbinafine hydrochloride cream, and upadacitinib was continued. Then, tinea lesion was improved.

Recent studies demonstrated the heterogeneity of AD, and elevated Th22 and Th17 immunity are reported more in Asians than European and American patients.[2] Previous studies have shown that the interleukin (IL)-23/Th17 pathway is less expressed in AD than in psoriasis, but it is upregulated when compared to healthy controls.[3] The IL-23 heterodimer binds to the signaling receptors IL-12Rβ1 and IL-23R and activates downstream signaling via phosphorylation of JAK2/tyrosine kinase 2 (TYK2). Upadacitib is a selective JAK1 inhibitor, but its inhibitory effect on JAK2/2- or JAK/TYK2-dependent cytokines has also been reported.[4] Han et al.[5] reported that *Aspergillus fumigatus*–stimulated dendritic cells promoted a Th17 response in $CD4^+$ T cells via the JAK/STAT signaling pathway. Moreover, there is a care report, which demonstrated disseminated tinea corporis under baricitinib therapy for AD.[6] These findings suggest that the suppressive effect of Th17 immunity by upadacitinib possibly has contributed to the development of fungal infection, and that suppression of Th17 may be one of the mechanisms by which upadacitinib strongly improves AD symptoms. However, there is a possibility of accidental development of tinea corporis under upadacitinib treatment. Therefore, a large cohort study is necessary to clarify whether upadacitinib increases the risk of tinea corporis in AD or not.

In conclusion, it may be important to be aware of the development of fungal infections in AD treated with JAK inhibitors. However, further studies are required to clarify the precise immunological mechanisms of upadacitinib in AD.

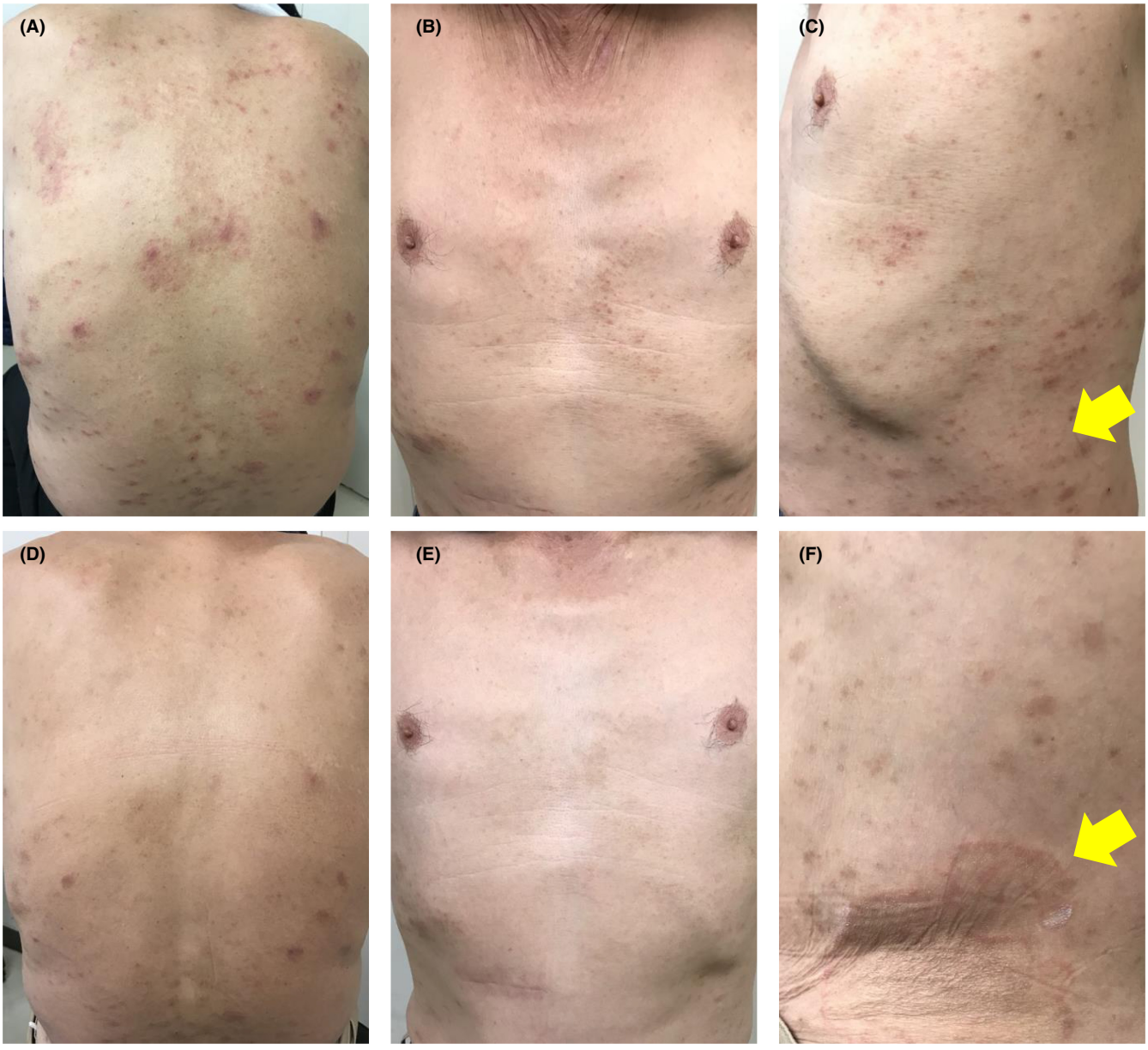

FIGURE 1 (A-F) Representative images of physical examination at weeks 0 (A-C) and 2 (D-F) after upadacitinib treatment. (C) Small-sized erythema without annular plaque on his left lumbar (yellow arrow). (F) Annular plaque on his left lumbar region, characteristic of tinea corporis (yellow arrow)

DECLARATION SECTION

Approval of the research protocol: N/A.

Informed Consent: Informed consent was given to the patient, and approval was received.

Registry and the Registration No. of the study/trial: N/A.

Animal Studies: N/A.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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