Correspondence

Phenotypic switch from atopic dermatitis to psoriasis during treatment with upadacitinib

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Dear Editor,

Previously, we reported on the case of a 44-year-old man with severe atopic dermatitis (AD) who developed histologically confirmed plaque psoriasis during treatment with dupilumab.[1] As the patient's psoriasis also recently relapsed on upadacitinib (UPA), we report an update on his clinical course, exemplifying the mutual antagonism between AD and psoriasis in predisposed individuals.

The patient was first referred to our clinic in 2016 due to early onset AD with nummular eczema as the dominant phenotype. His medical history included allergic rhinoconjunctivitis and polysensitization to food and aeroallergens. Previous treatments had included topical and systemic corticosteroids, ciclosporin and antihistamines. Full remission was never achieved. In November 2018, dupilumab, a monoclonal antibody targeting the common alpha subunit of the interleukin (IL)-4 and IL-13 receptors, was initiated. Excellent disease control was achieved almost immediately. However, in March 2019, the patient developed biopsy-proven plaque psoriasis, with diffuse, well-demarcated erythematous papulosquamous lesions. Dupilumab was interrupted and a new course of ciclosporin was undertaken. Owing to an AD relapse, dupilumab was then reintroduced without discontinuing ciclosporin, and temporary remission ensued. A new psoriasis flare in April 2020 forced permanent discontinuation of both drugs. Methotrexate (MTX) 10 mg/day and topical corticosteroids in association with calcipotriol (plus topical corticosteroids and calcineurin inhibitors on frankly eczematous lesions) were able to partially control the cutaneous picture for over a year. In July 2021, because of the incomplete control of both the AD and psoriasis, MTX was halted and UPA 30 mg/day was initiated (Fig. 1a), which quickly lead to complete skin clearance. Unfortunately, 3 weeks after MTX discontinuation, progressive reappearance of psoriatic manifestations was documented (Fig. 1b). Therefore, in September 2021, UPA was interrupted (Fig. 1c) and MTX was reintroduced at a higher dose (15 mg/day), resulting in better, almost complete disease control (Fig. 1d).

The development of psoriasis in patients with AD following treatment with dupilumab has been described previously.[2,3] IL-4 is responsible for T-helper (Th)2 polarization whereas IL-13 represents the main Th2 effector cytokine. By blocking the former, dupilumab hampers Th2

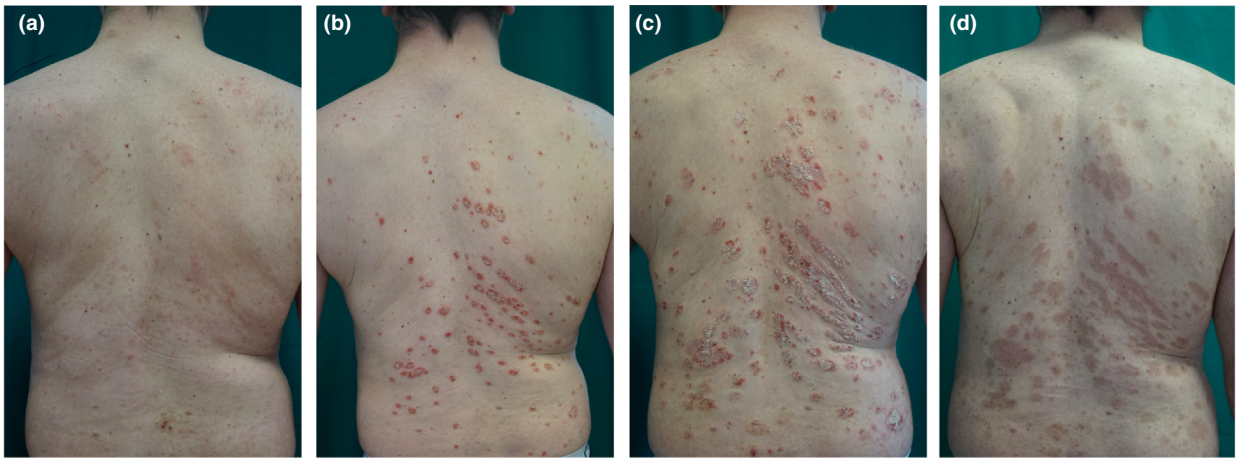

Figure 1 (a) Intensely itchy eczematous lesions on the patient's back at the time of upadacitinib initiation (July 2021); (b) appearance of a psoriasis flare approximately 3 weeks later; (c) diffuse erythematous papulosquamous lesions on the patient's back 2 months after upadacitinib initiation (September 2021); and (d) hyperpigmentation 2 months after methotrexate reintroduction.

polarization and allows disinhibition of Th1 and Th17 polarization. Indeed, it has been hypothesized that exclusive inhibition of IL-13 may prevent the phenotypic switch towards psoriasis observed with dual IL-4/IL-13 blockade.[2] UPA is a relatively selective Janus kinase (JAK)1 inhibitor. The actual degree of inhibition depends on the stimulating cytokines and cell types, being greater in the case of JAK1/3-dependent signalling pathways, but also extending to JAK2/2- and JAK2/tyrosine kinase (TYK)2-dependent pathways.[4] This broad activity (albeit with a focus on AD critical pathways), together with its efficacy on psoriatic arthritis, encouraged the compassionate use of UPA in our case. Suboptimal inhibition of TYK2-mediated cytokines (e.g. IL-12, IL-23) may be responsible for the observed clinical course. Indeed, MTX is speculated to inhibit both JAK1 and JAK2,[5] possibly providing wider inhibition of the culprit inflammatory pathways of AD and psoriasis.

Further studies are needed to better understand the pathophysiology and to predict the risk of JAK-inhibitor-induced phenotypic switch to psoriasis. Our findings also emphasize the importance of not overlooking traditional systemic agents such as MTX in the management of chronic inflammatory dermatoses.

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