De novo case of lichenoid eruption following dupilumab treatment

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INTRODUCTION

Lichenoid drug eruption is an uncommon adverse effect of several drugs, including antihypertensives, diuretics, and antimalarials. The pathogenesis has not been completely identified. As in lichen planus, activation of $CD8^+$ autocytotoxic T lymphocytes promoted by helper T (Th) cell type 1 immune response seems to be the crucial pathophysiologic factor.[1]

Dupilumab, which blocks both interleukin 4 and interleukin 13 signaling, has been used to treat moderate-to-severe atopic dermatitis (AD).[2] This results in the downregulation of Th2-mediated inflammation. Consequently, Th2 pathway inhibition shifts the Th cell profile to a Th1/Th17 predominant pattern.[3] Here, we present an unreported association between dupilumab and de novo lichenoid eruption.

CASE REPORT

A 44-year-old man with no underlying disease other than severe AD visited the dermatology clinic for treatment. He had been treated with cyclosporine, antihistamines, topical steroids, and tacrolimus for 18 years, after which he started dupilumab treatment at the first dose of 600 mg and subsequent doses of 300 mg. After 3 months of treatment, the eczema area and severity index score decreased significantly from 43.2 to 12.5. However, at week 16 of treatment, despite the clinical remission of AD, localized flat-topped erythematous to violaceous papules and plaques appeared on the dorsum of both hands (Fig 1, *A*). The lichenoid lesions did not involve other areas, including the mucous membrane. Histopathologic examination of a biopsy specimen obtained from dorsum of his right hand revealed liquefaction degeneration of the basal cell layer and a band-like lymphocytic infiltrate in the upper dermis (Fig 2). These findings were consistent with lichen planus or lichenoid drug eruption. The patient requested to stop dupilumab treatment because of cost issues, and the dupilumab treatment was interrupted. Instead, the patient was administered cyclosporine at a low dose (1.25 mg/kg/d) to treat AD. Three months after the termination of dupilumab treatment, the lichenoid lesions showed clinical improvement (Fig 1, *B*).

Abbreviations used:

AD: atopic dermatitis
Th: helper T

DISCUSSION

It has been reported that inhibited Th2 immunity by dupilumab may enhance Th1/Th17 dominated response in patients with AD. Stout et al[4] reported psoriasis-like dermatitis that developed in a patient with AD who was treated with dupilumab. Histopathologic examination showed typical characteristics of psoriasiform dermatitis, such as epidermal hyperplasia and an increased number of ectatic capillaries. Hence, the authors speculated that Th1 hyperresponse caused by the suppression of Th2 immunity triggered psoriasis.

Considering that recent reports indicate that Th2 blockade by dupilumab may activate Th1-mediated dermatosis, we hypothesize that de novo lichenoid eruption in the patient in our case is a dupilumab-induced skin reaction. In this patient, the temporal relationship between the

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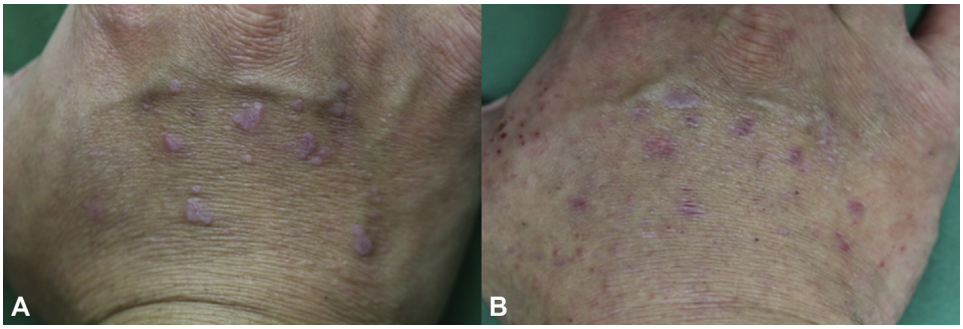

Fig 1. Lichenoid eruption. **A,** At week 16 of treatment, localized flat-topped erythematous papules and plaques appeared on the dorsum of hands. **B,** After 3 months of discontinuation of dupilumab treatment, lichenoid lesions showed partial clinical improvement.

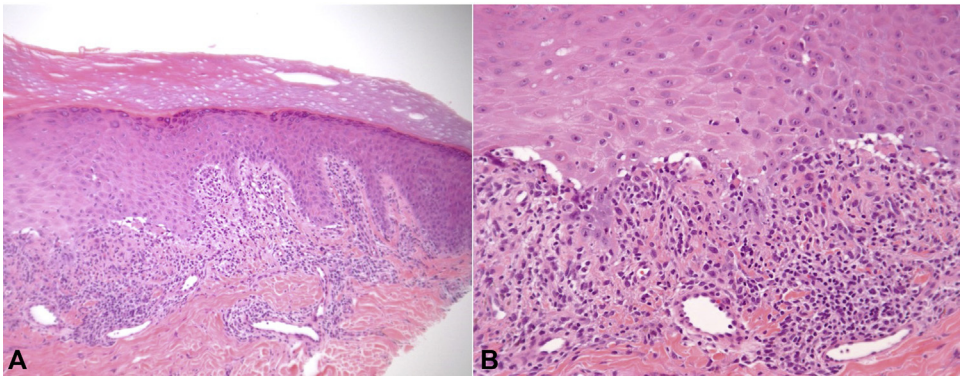

Fig 2. Histologic image. **A,** The specimen shows typical features of lichenoid dermatitis: compact orthokeratotic hyperkeratosis, vacuolar alteration of the basal layer, and band-like dermal lymphocytic infiltrate in the papillary dermis. **B,** Detail of vacuolar alteration of the basal layer and band-like dermal lymphocytic infiltrate in the papillary dermis. (**A** and **B,** Hematoxylin-eosin stain; original magnifications: **A,** ×100; **B,** ×200.)

initiation of dupilumab treatment and the onset of the lichenoid eruption, coupled with the improvement in lichenoid eruption after discontinuing dupilumab treatment, indicated a causative association between dupilumab and lichenoid eruption. Although the patient was administered cyclosporine at a very low dose (1.25 mg/kg/d) for approximately 2 months for AD, it is difficult to completely exclude cyclosporine as a contributor to the improvement in the lesions. This case provides another clinical evidence that dupilumab causes an imbalance in the Th cell signaling pathway. Nevertheless, further investigation is needed to understand the definitive pathogenesis.

Conflicts of interest

None disclosed.

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