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CASE REPORT

Psoriasis in an Asian patient with atopic dermatitis treated with dupilumab

Running title: Psoriasis during dupilumab therapy

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ABSTRACT

Dupilumab is a monoclonal antibody against the alpha subunit of the interleukin (IL)-4 receptor that inhibits IL-4 and IL-13 signaling, which plays a central role in Th2 inflammation in AD.

Here, we report the first Asian case of psoriasis unexpectedly induced by dupilumab therapy for AD. Compared with European and American AD phenotype, Asian AD phenotype is characterized by changes in the psoriasiform phenotype, associating with higher Th17 activation. The blockade of IL-4/IL-13 signaling by dupilumab may induce psoriasis eruption corresponding to shift from a Th2- to Th17- mediated inflammatory response in the skin.

Keywords: Dupilumab; Atopic Dermatitis; Psoriasis; Th2; Th17

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1. Introduction

Asian patients with atopic dermatitis (AD) present a blended phenotype between that of European and American patients with AD and those with psoriasis, establishing consistent Th17/Th2 inflammation(1).

Dupilumab is a monoclonal antibody against the alpha subunit of the interleukin (IL)-4 receptor that inhibits IL-4 and IL-13 signaling, which plays a central role in Th2 inflammation in AD(2). Here, we report the first Asian case of psoriasis unexpectedly induced by dupilumab therapy for AD.

2. Case presentation

A 52-year-old Japanese man who had been diagnosed with AD in childhood was started on dupilumab therapy. He had no personal or family history of psoriasis. He was previously treated with oral prednisolone (10 mg/day) and topical steroids, but his skin symptoms were not well controlled, and he developed erythematous patches with indistinct borders on his chest, abdomen, and face (Eczema Area and Severity Index [EASI] 30) (**Figure 1(a)**). A skin biopsy of the erythema on the abdomen showed mild spongiosis and hyperkeratosis infiltrated with lymphocytes and eosinophils (**Figure 1(b)**). Serum total IgE and thymus and activation-regulated chemokine (TARC) levels were elevated to 12761.5 IU/mL and 1018 pg/mL, respectively. Shortly after dupilumab initiation, the severe itchiness dramatically reduced, and his skin lesions also improved (EASI 13.2 at 3 months). After 8 months of

treatment with dupilumab, serum total IgE levels and TARC decreased to 1405 IU/mL and 329 pg/mL, respectively, but the patient developed well-demarcated and raised plaques with coarse surfaces on the scalp, forehead, and buttocks (**Figure 1(c), (d)**). The morphology of the lesions was highly suggestive of psoriasis. Skin biopsy from the hyperkeratotic plaque on the buttock showed a para-keratotic scale, regular elongation of the rete ridges, and dilation of the vessels in the papillary dermis infiltrated with lymphocytes and eosinophils (**Figure 1(e)**). We diagnosed the patient with dupilumab-induced psoriasis, and discontinued dupilumab therapy and initiated treatment with topical steroids and vitamin D analogues. One month after the discontinuation of dupilumab, scaling on the head cleared and hyperkeratotic plaques on the buttocks gradually reduced.

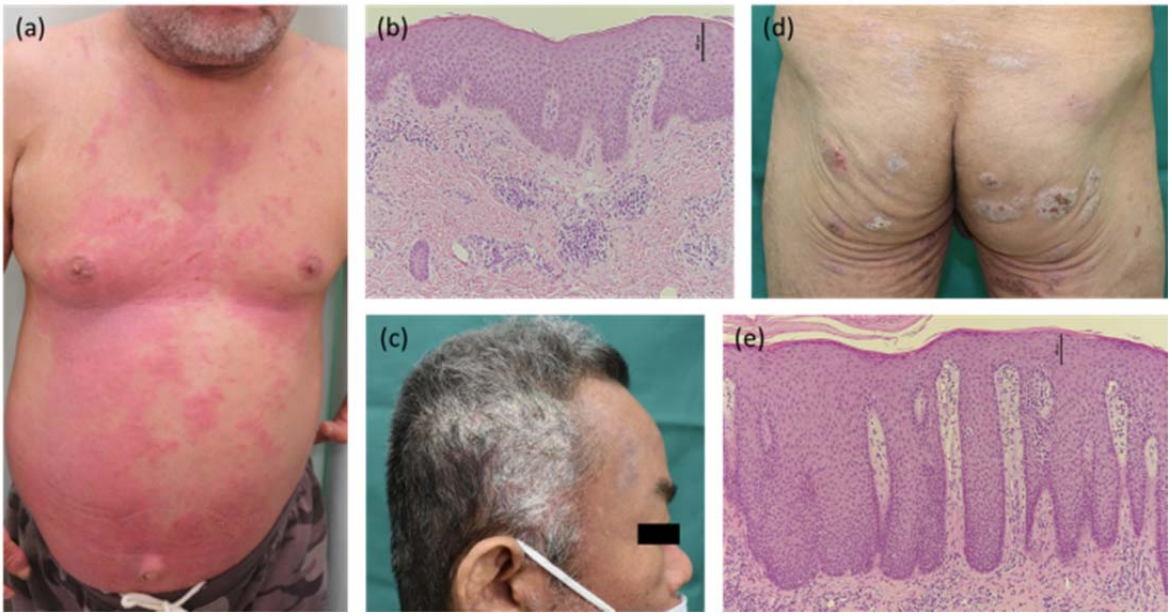

Figure 1. (a) Abdominal erythema before dupilumab treatment. **(b)** Skin biopsy from the erythema on the abdomen showed mild spongiosis and hyperkeratosis infiltrated with lymphocytes and eosinophils (Scale bar shows 100 μm). Eight months after the initiation of dupilumab treatment, psoriatic plaques have developed on **(c)** the head and **(d)** buttocks. **(e)** Skin biopsy from the hyperkeratotic plaque on the buttock showed parakeratotic scale, regular elongation of the rete ridges, dilated capillaries, and lymphocyte-dominant infiltrate in the upper dermis (Scale bar shows 100 μm).

3. Discussion

Compared with European and American AD phenotype, Asian AD phenotype is characterized by changes in the psoriasiform phenotype: increased epidermal hyperplasia, more frequent parakeratosis, and focal hypogranulosis, associating with higher Th17 activation(3). A skin biopsy before dupilumab initiation in our case also showed psoriasiform dermatitis with IgE and TARC elevation, which is typical of Asian AD phenotype.

Psoriasis and AD are suggested to be on a polar Th17-to-Th2 spectrum and show distinct phenotypes responding to different cytokines. Psoriasis is associated with the overproduction of IL-17, and AD is associated with that of IL-4 and IL-13(4). A recent study demonstrated that IL-4 abrogates Th17-mediated inflammation(5). Thus, the blockade of IL-4/IL13 signaling by dupilumab may induce Th17-dominant inflammation in the skin, resulting in psoriasis eruption.

To the best of our knowledge, this is the first report of psoriasis onset in Asian AD patient treated with dupilumab. It is possible that Asian patients show psoriasiform phenotypes more frequently after treatment with dupilumab, but further study is needed to confirm this hypothesis.

Conflict of interest disclosure

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