Dear Editor,

Ustekinumab is a biological agent that is currently approved for the treatment of moderate to severe plaque psoriasis. It is a monoclonal antibody that binds the p40 subunit of IL-12 and IL-23 to limit the progression of the Th1 and Th17 inflammatory immune responses. Recently, it has been suggested that ustekinumab could represent a potential treatment for atopic dermatitis (AD). However, inadequate response to ustekinumab in AD patients has also been reported. We present a case of paradoxically exacerbated AD during the ustekinumab treatment for psoriasis.

A 21-year-old man with a 7 year history of severe psoriasis refractory to conventional systemic treatments and childhood history of atopy (atopic dermatitis-AD, asthma, seasonal rhinitis) was treated with ustekinumab. The patient was without major symptoms from respiratory system and AD lesions within a period of 5 years before the date of starting the treatment. He was taking montelukast, antihistamines, inhaled corticosteroids and formoterol for asthma. Psoriatic lesions and no clinical signs of AD were found on baseline examination (Fig. 1). Ustekinumab 45 mg (1 injection at week 0 and week 4, then every 12 weeks) was introduced (according to body weight: 76 kg). After 18 months and following excellent results, the patient decided to discontinue therapy. But 8 months later recurrence of psoriasis was observed and ustekinumab was restarted. The baseline PASI fell from 11.4 to 3.0 after 4 weeks of treatment with ustekinumab, complete remission of psoriasis was achieved after 8 weeks of therapy. However, intense generalized itching occurred since the first dose was administered. Severe AD appeared on the neck and lower limbs about 6 weeks after the reintroduction of ustekinumab (Fig. 2). Eczematous drug eruption and AD exacerbation due to stress, infection, or other external factors (i.e. topical treatments of psoriasis) was excluded in the differential diagnosis. Apart from dermatologic findings, physical examination revealed no abnormalities. Laboratory tests showed peripheral blood eosinophilia (1.48 × 10^9/L, compared to the baseline of 0.46 × 10^9/L, to the 16 weeks of 0.58 × 10^9/L, to the 28 weeks of ustekinumab therapy of 0.67 × 10^9/L, and to the recurrence of psoriasis of 0.66 × 10^9/L), as well as abnormal increase in serum allergen-specific immunoglobulin E (sIgE) level including dog-, cat-, hamster-, and grass pollen-specific IgE. Total IgE level was 12576 IU/ml (0–100.0 IU/l reference range). Other laboratory data (erythrocyte sedimentation rate, C-reactive protein level, complete blood count, biochemical parameters of liver and kidney, urinalysis) were normal at several time points. Spirometry revealed normal pulmonary function, fractional exhaled nitric oxide (FeNo) level was low (24 ppb) pointing to the well-controlled asthma (FeNo values range from 22 to 44 ppb). Ustekinumab was stopped again, improvement of AD was achieved after the administration of the short course of systemic prednisone at 40 mg daily for 6 days followed by 20 mg for 4 days and 10 mg for 4 days. Topical corticosteroid therapy was needed to control the disease. While psoriasis was stable no complete remission of AD and no reduction of peripheral eosinophilia (1.63 × 10^9/L) was observed during 12-months follow up. The biologic had no impact for the asthma course.

Our case is particularly interesting because it describes a patient with remission of psoriasis and flare of AD due to ustekinumab therapy. To our knowledge, ustekinumab has not been reported to exacerbate AD. The patient previous has been treated for 18 month without any flare suggesting the eczematous drug eruption was brought on by the biologic. The concurrent exacerbation of AD during treatment with ustekinumab may be a reflection of the Th17-mediated immune response in AD patients.

Fig. 1. Psoriatic lesions on the head before the initiating ustekinumab therapy.

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rather than AD. Drug eruptions are more likely to occur when therapy is interrupted followed by a second exposure. Some authors have described patients with an eczematous eruption that appeared after the administration of ustekinumab.\(^5,6\) However, the eczema has lasted during 12-months follow up after the final dose of ustekinumab, supporting the diagnosis of AD in our patient.

Why ustekinumab has exacerbated AD but not psoriasis paradoxically is hard to explain. It is uncommon for AD to coexist with psoriasis.\(^7\) Both diseases have distinct genetic mechanisms with opposing effects in shared pathways influencing epidermal differentiation and immune response.\(^8\) Psoriasis is believed to be mediated by Th1/Th17 cells and AD by Th2/Th22 cells.\(^9\) The Th17 axis is also activated in patients with acute AD and plays some role in the pathogenesis of the disease.\(^9\) Therefore, ustekinumab could represent a potential treatment for AD. However, this biologic blocking Th1 inflammatory pathways (IL-12) partially acts as TNF-\(\alpha\) inhibitor and possibly this may result in downregulation of Th1 cytokines and manifestation of Th2-associated disease.\(^10\) Increased Th2 activity in the presented patient might has resulted in the peripheral blood eosinophilia after initiating ustekinumab. Subsequently, AD-like skin lesions were induced by the therapy reintroduction. Therefore, we would like to highlight the possible connection between the treatment with ustekinumab and the flare of AD, while psoriasis go into remission.

**Conflict of interest**

The authors have no conflict of interest to declare.

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