

Dupilumab treatment in two patients with severe allergic contact dermatitis caused by sesquiterpene lactones

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Sesquiterpene lactones (SLs) are a group of allergenic secondary plant metabolites represented in about 10% of all flowers.^{1,2} SLs are abundant in the sunflower family, but also exist in vegetables, cosmetics, and herbal medicine.³ Airborne spread of SLs typically causes allergic contact dermatitis in exposed skin areas including face, V-line of the neck, hands, and forearms, and with a distinct seasonal variation in terms of worsening in the plant-growing season.⁴ Affected patients develop severe and widespread, often treatment-resistant eczema that can severely affect their daily lives with the need for systemic treatment.² Even though allergic contact dermatitis is predominately a T_H1-cell mediated process, certain allergens activate the T_H2-pathway.⁵ Dupilumab, a monoclonal antibody, binds to the interleukin (IL)-4 receptor alpha and inhibits IL-4 and IL-13 signaling and thus the T_H2-mediated pathway. Dupilumab has been approved for the treatment of atopic dermatitis in adolescents and adults.⁶ Furthermore, studies indicate a potential effect in allergic contact dermatitis.^{5,7} We report the treatment outcome with dupilumab in two patients with SL-induced allergic contact dermatitis.

1 | CASE REPORTS

Case 1: A 65-year-old retired woman, previous office worker, had chronic hand and foot eczema during the last 30 years. In the summer of 2017, the patient was referred due to sudden widespread eczema located on the face, arms, and hands with repeated instant flare-up after gardening, and she was diagnosed with allergic contact dermatitis to SLs with a positive patch test to SL mix 0.1% pet. The patient had no previous or concurrent diseases or history of childhood atopic dermatitis, but other patch tests, too, were positive, namely, to potassium dichromate 0.5% pet., *p*-phenylenediamine 1.0% pet., *Evernia furfuracea* (tree moss) 1.0% pet., Disperse Blue 106 1.0% pet., cobalt chloride 1.0% pet., and nickel sulfate 5.0% pet. In view of the severity

of eczema and its impact on her daily life—requiring treatment with oral prednisolone and a topical corticosteroid (mometasone furoate)—systemic treatment was indicated. Therapy with azathioprine 150 mg/day was prescribed and was effective on the eczema. However, the patient had side effects and the dose was reduced to 100 mg/day with insufficient effect. We then started therapy with dupilumab given as a 600 mg loading dose, followed by 300 mg every other week. After only 2 weeks of therapy, the eczema located on hands and arms cleared without concomitant use of topical corticosteroids (Figure 1). However, the patient experienced worsening of the eczema located to the face initially, with slight improvement within a month. Azathioprine 100 mg per day was added to the treatment, and the eczema further improved. Dupilumab treatment was paused during the winter and continued this spring.

Case 2: A 51-year-old man, working as an agricultural mechanic, had previously been diagnosed with atopic dermatitis and ultraviolet B sensitivity. He was patch-test positive to SL mix 0.1% pet., formaldehyde 1.0% aq., colophonium 20% pet., nickel sulfate 5.0% pet., cobalt chloride 1.0% pet., methylidibromo glutaronitrile 0.3% pet., iodopropynyl butylcarbamate (IBPC) 0.2% pet., Reactive Violet 5 1.0% pet., Reactive Black 5 1.0% pet., Reactive Blue 21 1.0% pet., Reactive Blue 238 1.0% pet., Reactive Orange 107 1.0% pet., and Reactive Red 228 1.0% pet. He had been followed in our clinic for more than 20 years due to severe seasonal SL-induced allergic contact dermatitis. Eczema was located on his face, neck, forearms, and hands with marked flare-up in the summer period, having a great impact on his quality of life and causing periods of sick leave. Besides use of high potency topical corticosteroids (clobetasol), the patient received various medical treatments from 2000–2019 including mycophenolate mofetil 2 g/day, methotrexate 25 mg/week, azathioprine 150 mg/day, cyclosporine 200 mg/day, and ustekinumab (45 mg s.c. every third month). However, all treatments were discontinued owing to lack of treatment response or adverse events. Accordingly, the patient



FIGURE 1 Skin manifestations of SL contact allergy on patient 1's hands and arm before dupilumab treatment (A and C) and 14 days after starting dupilumab treatment (B and D)

had received multiple courses of oral prednisolone. In June 2019, treatment with dupilumab given as a 600 mg loading dose, followed by 300 mg every other week, was prescribed. The patient was seen in our clinic after 1 month with improvement of his eczema as well as reduced itching that lasted that summer. Dupilumab treatment was paused during the winter and the future plan is to resume treatment in spring.

2 | DISCUSSION

Our two patients had severe SL-induced allergic contact dermatitis. Previous treatments failed in both, and addition of oral prednisolone was needed during their severe flare-ups. They both responded adequately to treatment with dupilumab, suggesting a possible shared immune-signaling pathway between AD and allergic contact dermatitis to SL. The explanation for the persistence of facial eczema in patient 1 is unclear, but dupilumab therapy has been associated with facial redness of unknown etiology.⁸ Previous studies with other biological treatments, such as anti-IL17 treatment, have failed to improve moderate to severe allergic contact dermatitis.⁹ Clinical studies are needed to examine the possible effect of dupilumab in allergic contact dermatitis.

CONFLICTS OF INTERESTS

I.F.R. has no conflicts of interest. L.S. has been a paid speaker for AbbVie, Eli Lilly, Novartis, and LEO Pharma, and has been a consultant or has served on Advisory Boards with AbbVie, Janssen Cilag, Novartis, Eli Lilly, LEO Pharma, UCB, Almirall, and Sanofi. She has

served as an investigator for AbbVie, Sanofi, Janssen Cilag, Boehringer Ingelheim, AstraZenica, Eli Lilly, Novartis, Regeneron, and LEO Pharma, and has received research and educational grants from Novartis, Sanofi, Janssen Cilag, and LEO Pharma. C.Z. has served as an investigator for Pfizer, AbbVie, Regeneron, and LEO Pharma and received research and educational grants from Cellgene and Leo Pharma. J.P.T. has attended advisory boards for Sanofi-Genzyme, Eli Lilly & Co, Pfizer, Abbvie, and Union Therapeutics, and received speaker honorarium from LEO Pharma, Regeneron, Abbvie, and Sanofi-Genzyme, and has been an investigator for Sanofi-Genzyme, Eli Lilly & Co, LEO Pharma, Pfizer, and Abbvie.

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