

using sunscreen, have more pronounced mild–moderate acne in summer because of the increased sebum secretion and the use of cosmetics. In an online survey of 1036 Korean acne patients, 27.6 per cent of subjects responded that they do not use sunscreen ‘due to trouble’.⁵ It is also well known that some sunscreens in the market contain comedogenic ingredients that can induce acne. Although our study is limited by its retrospective design, its relatively large sample size makes it reliable. To better identify seasonal flare patterns of acne, prospective studies considering variable factors should be conducted in the future.

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DOI: 10.1111/jdv.15806

Acquired hypersensitivity to dupilumab: first case report

Dear Editor

Dupilumab is the first targeted biologic therapy for the systemic treatment of atopic dermatitis.¹ It is a fully human monoclonal

antibody (mAb) directed against the shared alpha subunit of the interleukin (IL)-4-receptor component of the type I and type II receptors, thereby inhibiting IL-4 and IL-13 signalling.^{2,3} Injection site reactions are among the most common adverse effects reported.^{4,5} We herein report the first case of acquired hypersensitivity to Dupixent[®] confirmed by cutaneous allergy testing necessitating treatment cessation.

A 39-year-old Caucasian female presented with a history of atopic dermatitis since infancy. Physical examination at presentation while on cyclosporin A (CsA) demonstrated multiple eczematous patches affecting the neck, chest, the flexures of the elbows and knees. The atopic dermatitis score (SCORAD) was 21. Due to past intestinal side effects, CsA was stopped and the patient was started on dupilumab 600 mg subcutaneously on day 0, followed by 300 mg subcutaneously (s.c.) every 2 weeks. Dupilumab injections were initially well tolerated. However, at week 18, the patient presented with an erythematous, indurated, tender, swollen plaque on the right lower abdomen (Fig. 1), 1 day after subcutaneous self-injection of 300 mg dupilumab s.c. into this area. She reported that the swelling had become apparent 1–2 h after the injection and disappeared within 4 days. Dupilumab treatment was stopped. Furthermore, she reported having noticed a wheal at the injection site immediately after every dupilumab administration from week 10 on and prolonged local swelling with increasing intensity since week 14. The patient denied any systemic symptoms.

Skin tests were performed 2 months after the last hypersensitivity reaction. Both patch test with readings after 48 and 72 h and skin prick test (SPT) with Dupixent as is gave negative results. Intradermal testing (IDT) revealed a positive result (10 mm wheal after 20 min) lasting for 4 h with appropriate



Figure 1 Injection site reaction showing a 10 × 10 cm erythematous, indurated, tender, swollen plaque on the right lower abdomen 1 day after subcutaneous Dupixent[®] administration.

positive (histamine, 10 mm) and negative (saline, 0 mm) control reactions (Fig. 2). In addition, patch tests with standard, cosmetic and disinfectant series as recommended by the German Contact Dermatitis Research Group gave negative results.

To further elucidate the positive IDT to dupilumab, we also performed skin tests with Polysorbate 80, an excipient of Dupixent[®] with a likely allergenic potential⁶. However, SPT with Polysorbate 80 (0.1 mg/mL) and IDT in 1 : 1000, 1 : 100 and 1 : 10 dilutions and undiluted were all negative. Thus, the reaction observed in the intradermal testing with dupilumab points to an immediate-type allergy to the antibody itself.

The appearance of wheals directly after dupilumab administration reported by the patient and the positive IDT to dupilumab suggested a type β immunoglobulin E (IgE)-mediated reaction.⁷ Type β refers to IgE, IgG or T-cell mediated hypersensitivity reactions to mAbs as previously proposed in a classification of adverse reactions to mAbs into five types depending on the pathogenic mechanism.⁷ IgE type β reactions can cause a

local wheal and flare reaction at the injection site if applied s.c., but may also cause generalized urticaria and anaphylaxis.⁷ Furthermore, considering the negative test results to Polysorbate 80, we suggest a hypersensitivity to dupilumab itself in this case. However, no enzyme-linked immunosorbent assay (ELISA) was yet performed to confirm presence of antibodies to dupilumab. The prolonged ISR irrespective of the immediate hypersensitivity mechanism might be explained by the retention of s.c. injected drugs at the injection site, and thus extended release.⁸ Prolonged ISR with positive IDT has been reported for etanercept and adalimumab.⁹

To the best of our knowledge, this is the first report of acquired hypersensitivity to Dupixent[®], which might be consistent with a type β IgE-mediated reaction to dupilumab. However, the clinical reaction after the injection observed at the injection sites showed both immediate-type and prolonged reactions that cannot completely be explained by a potential IgE-mediated mechanism. Notably, although the patient did not yet experience systemic reactions, the drug should not be applied again.

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Figure 2 Positive intradermal test to Dupixent[®] as is after 20 min (10 mm wheal).

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DOI: 10.1111/jdv.15807