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Marked Skin Prick Test Reactivity During Selective IL-23p19 Inhibition: A Case Report

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Abstract

Skin prick testing (SPT) is widely used to identify immunoglobulin E (IgE) -mediated sensitization, although wheal size alone does not independently establish clinical allergy. We report a 27-year-old man with longstanding food allergy and Crohn's disease who experienced clinically significant worsening of pre-existing allergic rhinoconjunctivitis during maintenance therapy with guselkumab, a selective IL-23p19 inhibitor, and exhibited markedly pronounced SPT responses to multiple unrelated aeroallergens and foods, with wheal diameters reaching 45 mm. Despite marked cutaneous reactivity, clinical correlation varied substantially among food allergens: some sensitizations corresponded to established clinical allergy, whereas others occurred despite regular asymptomatic consumption. Notably, worsening allergic rhinoconjunctivitis requiring allergen immunotherapy and pronounced immediate cutaneous reactivity were observed during ongoing IL-23 inhibition. This observation is of interest in light of the proposed role of IL-23 in Th2-associated allergic inflammation and emerging reports of worsening allergic disease during IL-23-directed therapy. Although causality cannot be inferred from a single case, this report documents pronounced IgE-mediated cutaneous reactivity during IL-23 inhibition and supports further investigation into the effects of this therapy on established allergic disease.

Categories: Allergy/Immunology
Keywords: allergic conjunctivitis, allergic rhinitis, guselkumab, hypersensitivity, interleukin-23 inhibition, skin prick test

Introduction

Skin prick testing (SPT) remains a standard method for detecting IgE-mediated sensitization. A wheal diameter of ⩾3 mm is generally considered positive when interpreted according to the applicable testing protocol, although quantitative responses vary according to the allergen, testing technique, population, and individual cutaneous reactivity [1]. Larger wheals may increase the probability of clinical relevance for certain allergens; however, SPT positivity indicates sensitization rather than, by itself, establishing clinical allergy, and results should therefore be interpreted in conjunction with the clinical history and, when appropriate, oral food challenge [2,3].

The magnitude of SPT responses varies considerably among individuals and allergens, and published studies do not consistently report the full distribution of exceptionally large wheal diameters. Moreover, the distinction between wheal and surrounding erythematous flare measurements is important when interpreting skin test results. Herein, we describe pronounced immediate cutaneous reactivity, including two SPT wheals measuring 45 mm in diameter at their largest diameter, excluding the surrounding flare, alongside clinically significant worsening of pre-existing allergic rhinoconjunctivitis in a patient receiving maintenance therapy with guselkumab, a selective IL-23p19 inhibitor.

Case Presentation

A 27-year-old man presented to our Allergy Clinic with allergic rhinitis and conjunctivitis and a longstanding history of food allergies to seafood and various nuts. He also reported a history of suspected allergic reactions to ibuprofen and cephalosporins, although the nature of these reactions and confirmatory investigations were not available. His rhinoconjunctivitis had worsened and become clinically significant over the preceding four months. A 12-hour reflective Total Nasal Symptom Score (rTNSS) of 9/12 was recorded based on the patient's reported symptom severity over the preceding 12 hours, whereas the corresponding reflective Total Ocular Symptom Score (rTOSS) was 5/9. Both scores were used as established measures of nasal and ocular symptom burden, consistent with symptom assessment approaches employed in allergic rhinoconjunctivitis research and described in international consensus recommendations [4]. He also reported an occasional pruritic rash localized to the chest and upper limbs but no episode of anaphylaxis, urticaria, or angioedema.

His medical history was significant for Crohn's disease, for which he was receiving guselkumab (Tremfya®; Johnson & Johnson, USA) 200 mg subcutaneously every four weeks. Treatment had been initiated one year earlier and continued as maintenance therapy; the most recent dose had been administered three weeks

before presentation. His Crohn's disease had shown substantial endoscopic improvement after treatment, with the Simple Endoscopic Score for Crohn's Disease (SES-CD) decreasing from 11 before guselkumab initiation to 3 on colonoscopy performed three months before presentation.

SPT was performed on the patient's back using standardized commercial allergen extracts (Inmunotek S.L., Spain) and a Multi-Test® II Applicator (Lincoln Diagnostics, USA), following a standardized skin-prick technique. Reactions were assessed after 15 minutes, and the largest wheal diameter was measured in millimeters using a calibrated SPT ruler, excluding the surrounding erythematous flare. In accordance with European SPT standards [1], a wheal diameter ⩾3 mm was considered positive, without subtracting the diameter of the negative control. Accordingly, allergen-induced wheals measuring 2 mm were considered non-positive, whereas those measuring ⩾3 mm met the recommended positivity threshold. Exceptionally large wheal responses were observed to multiple unrelated allergens, as shown in Figure *1*. The largest responses were to *Dermatophagoides farinae*, 45 mm; white fish mix, 45 mm; *Dermatophagoides pteronyssinus*, 35 mm; sesame, 32 mm; tuna, 26 mm; cat dander, 25 mm; king prawn, 22 mm; almond, 20 mm; *Blattella germanica*, 20 mm; chicken, 15 mm; egg white, 11 mm; and pistachio, 10 mm.



FIGURE 1: Skin prick testing (SPT) demonstrating marked polysensitization with exceptionally large wheal responses to multiple aeroallergens and food allergens

Test sites were arranged into six panels (right: A–C; left: D–F). (A) 1, Histamine dihydrochloride 0.1% (positive control, 13); 2, *Dermatophagoides pteronyssinus* (35); 3, *Dermatophagoides farinae* (45); 4, Cat dander (25); 5, Horse dander (3); 6, *Candida albicans* (3); 7, *Penicillium notatum* (5); 8, sodium chloride 0.9% (negative control, 2). (B) 1, Russian thistle (*Salsola kali*) (3); 2, Bahia grass (*Paspalum notatum*) (3); 3, Rye grass (*Lolium perenne*) (3); 4, Date palm (*Phoenix dactylifera*) (5); 5, Timothy grass (*Phleum pratense*) (2); 6, mugwort (*Artemisia vulgaris*) (2); 7, common reed (*Phragmites australis*) (2); 8, Grass mixture (2). (C) 1, German cockroach (*Blattella germanica*) (20); 2, Bermuda grass (*Cynodon dactylon*) (3); 3, fire ant (*Solenopsis invicta*) (5). (D) 1, Histamine dihydrochloride 0.1% (positive control, 9); 2, peach (2); 3, cocoa (2); 4, apple (2); 5, orange (2); 6, pineapple (2); 7, lamb meat (2); 8, sodium chloride 0.9% (negative control, 2). (E) 1, Fresh cow's milk (5); 2, egg white (11); 3, peanut (4); 4, pine nut (4); 5, almond (20); 6, sesame seed (32); 7, tuna (26); 8, white fish mix (45). (F) 1, soy flour (2); 2, chickpea (2); 3, watermelon (2); 4, Turkey meat (5); 5, king prawn (22); 6, chicken meat (15); 7, pistachio (10).

* The scale bars in the figure were estimated using the SPT ruler visible in the bottom-right corner of the source photograph, in which each blue segment corresponds to 10 mm.

SPT reactivity did not uniformly correspond to clinical food allergy. Although his allergic history included clinically documented reactions to white fish, tuna, king prawn, and almond, he regularly consumed egg, chicken, and pistachio without symptoms. Because sesame was not regularly consumed, its clinical relevance remained uncertain despite a 32-mm wheal.

Total serum IgE was elevated at 1,817 IU/mL (reference range, <100 IU/mL). However, previous total IgE

levels for longitudinal comparison, quantitative allergen-specific IgE, and component-resolved diagnostics (CRDs) were not available. The patient was counselled regarding avoidance of allergens associated with his clinically relevant allergies, and symptomatic treatment was prescribed for rhinoconjunctivitis. Given his clinically significant house dust mite-associated respiratory allergy, allergen-specific sublingual immunotherapy was initiated (Oraltek® House Dust Mite Perlingual Solution Spray 30,000 TU/mL; Inmunotek S.L., Spain).

Discussion

This case demonstrated an unusually high degree of immediate cutaneous reactivity, with multiple SPT wheals exceeding 20 mm and two wheal diameters reaching 45 mm. Responses of this size appear to be uncommon in published SPT series. The case also illustrates the important distinction between the magnitude of SPT reactivity and clinically relevant allergy.

Although increasing wheal size may increase the probability of clinical allergy for particular allergens and populations, diagnostic thresholds are allergen- and population-dependent and cannot, in isolation, substitute for clinical history or, when indicated, oral food challenge [1-3]. In this patient, substantial SPT responses to egg, chicken, and pistachio occurred despite regular asymptomatic consumption, whereas large responses to white fish, tuna, king prawn, and almond correlated with established clinical allergy. Sesame represented a third category, with marked sensitization but uncertain clinical significance.

The absence of previous SPT, total IgE levels, quantitative allergen-specific IgE, and CRDs represents a limitation. Nevertheless, the combination of objective SPT measurements, photographic documentation, detailed clinical correlation, and evidence of both clinically relevant and asymptomatic sensitization provides a useful illustration of the limitations of interpreting SPT magnitude in isolation.

An additional immunological feature of this case is that the pronounced cutaneous phenotype was observed during maintenance therapy with guselkumab, a monoclonal antibody selectively targeting the p19 subunit of IL-23 [5]. Experimental evidence from murine models suggests that IL-23 may contribute to the development and amplification of allergic sensitization and Th2-associated inflammation, with IL-23 blockade attenuating allergic responses in these models [6,7]. However, whether IL-23 inhibition modulates established IgE-mediated immediate hypersensitivity in humans remains unclear. Although the overall safety profile of IL-23-directed therapies in autoimmune diseases is reassuring, several publications have described worsening of concomitant allergic disease during treatment with IL-23 inhibitors. Schmiedeberg et al. reported recurrence of severe allergic asthma after a 24-year asymptomatic period in a patient with psoriatic arthritis receiving guselkumab, ultimately leading to treatment discontinuation [8]. In a randomized, double-blind, placebo-controlled trial of risankizumab, another IL-23p19 inhibitor, Brightling et al. reported unfavorable asthma-related outcomes compared with placebo in patients with severe asthma [9]. In a retrospective single-center study, Sugiura et al. reported a significantly higher incidence of elevated total serum IgE among patients with psoriasis receiving Risankizumab compared with those receiving non-biologic treatment [10]. However, this finding does not establish increased allergen-specific sensitization or enhanced immediate cutaneous reactivity. Beyond IgE-mediated disease, guselkumab has also been associated with reports of delayed T-cell-mediated hypersensitivity. Kishibe et al., for example, described allergic contact dermatitis to *Chrysanthemum* that developed during guselkumab therapy in a patient with previously reported tolerance [11].

In the present case, longstanding allergic sensitization preceded guselkumab therapy, precluding attribution of the underlying allergic disease to IL-23 inhibition and limiting any inference that the marked SPT responses were caused by treatment. Nevertheless, the subsequent worsening of rhinoconjunctivitis and the presence of exceptionally pronounced immediate cutaneous reactivity during ongoing guselkumab treatment are noteworthy. Together with the limited emerging clinical observations described above, this case raises the possibility that IL-23 inhibition may influence the clinical expression of pre-existing allergic disease in selected patients.

Conclusions

Although a causal relationship between IL-23 inhibition and the observed allergic manifestations cannot be established from a single case, the clinically significant worsening of pre-existing allergic rhinoconjunctivitis during guselkumab therapy, together with pronounced immediate cutaneous reactivity, warrants further investigation. Importantly, the absence of pre-treatment SPT measurements prevents determining whether the unusually large wheal responses were already present before treatment or emerged during IL-23 inhibition. Clinical and mechanistic studies are needed to determine whether IL-23-directed therapies can modify the clinical expression of established IgE-mediated disease and to identify patients who may be susceptible to worsening allergic responses during treatment. Clinical monitoring for changes in allergic symptoms may be appropriate in patients with pre-existing allergic disease receiving IL-23 inhibitors.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Abu Dhabi Stem Cells Center (ADSCC)/Yas Clinic Khalifa City (YCKC) issued approval MF-5527-2026-16. The ADSCC–YCKC Institutional Review Board (IRB) has granted an exemption of ethics review as this report involves the retrospective collection of existing data, and no patient identification is disclosed. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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