

Furthermore, omalizumab has been safely used in children 6 to 11 years of age with severe asthma.¹⁰ In our review, no adverse events related to omalizumab were reported, suggesting that omalizumab can be a safe therapeutic option for patients with CU in this age group.

Our systematic review has a number of limitations. First, the number of patients included in our analysis was small, likely because omalizumab is not approved by the US Food and Drug Administration for CU treatment in children younger than 12 years. Second, the studies included in our review were case reports or small case series, which translates into weak evidence. Third, given the heterogeneity of reports, we relied on descriptive outcomes rather than validated efficacy end points, such as changes in UAS-7. Nonetheless, our study provides preliminary data that support the use of omalizumab for treating CU in children younger than 12 years and highlights the need for randomized controlled trials to better investigate the safety and efficacy of omalizumab in this age group.

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Supplementary Data

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The first pathological specimen from a rare local reaction after subcutaneous allergen immunotherapy



Local cutaneous reactions typically described as injection site tenderness, pain, induration, and erythema are frequently experienced by patients undergoing subcutaneous immunotherapy (SCIT), occurring with a frequency of 0.7% to 7.3% of injections.^{1–3} We describe a curious and rare case of bullous vesicles forming in a delayed local reaction to SCIT. We also provide and discuss the pathological results of shave and punch biopsies obtained from this reaction to consider a possible mechanism of action.

A 57-year-old man with a history of allergic rhinitis and nasal polyposis presented approximately 24 hours after SCIT injection in his left arm because of the formation of blistering lesions of his skin at the injection site. The initial formation of these blisters occurred several hours after his subcutaneous injection. The patient denied any local pruritus, pain, burning, or systemic symptoms such as malaise, fever, headache, or vomiting. He had a history of a single World Health Organization grade 2 systemic reaction to immunotherapy approximately 5 months prior, and he had no history of prior abnormal local cutaneous reactions. His SCIT extract contained grasses, weeds, dog hair, and cat dander, and treatment was initiated approximately 7 months prior. His goal maintenance dosing was 0.5 mL of a 1:1 v/v concentration every 4 weeks, which he had reached 1 month before this reaction. Of note, on initiation of his maintenance dose, the frequency of injections was extended to every 4 weeks from his buildup dose frequency of once- to

twice-weekly injections. All extracts were administered in a single injection at each visit. Despite recommended avoidance, the patient owned 3 dogs at home, and this reaction occurred late in the local grass season and during the peak of the local weed season. Other medical therapies for his chronic rhinitis included daily cetirizine, montelukast, and intranasal fluticasone. He had no personal or family history of autoimmunity or bullous skin disease.

On physical examination, two erosions from ruptured bulla, each approximately 2 cm in diameter, as well as 2 tense bulla containing clear, serous fluid, each approximately 1 cm in diameter, were observed on the left posterior arm of the patient at the injection site. All were grouped into a close proximity, and they had surrounding erythema extending out approximately 1 cm from the lesions. Shave and punch biopsies were performed on the day of presentation. Pathology reported a nonspecific, subepidermal vesicular dermatitis containing neutrophils and abundant eosinophils with underlying superficial perivascular lymphohistiocytic inflammation with neutrophils and eosinophils (Fig 1). Direct immunofluorescence staining was performed using immunoglobulin (Ig) A, IgG, IgM, C3, and fibrinogen, which failed to reveal a known diagnostic pattern of antibody deposition, such as in bullous pemphigoid or other autoimmune blistering diseases. Fluid stains and cultures obtained from the vesicular fluid failed to identify bacterial or fungal organisms.

The patient's lesions were treated symptomatically with sterile wound dressings, which he changed at home as needed until his lesions healed. Of note, he was not prescribed antibiotics, steroids,

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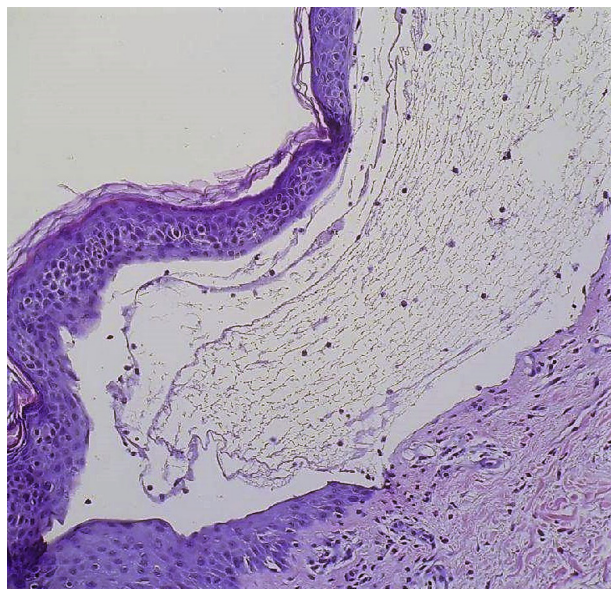


Figure 1. Low-power view of biopsy specimen with hematoxylin and eosin staining showing subepidermal vesicle formation containing neutrophils and abundant eosinophils.

or any anti-inflammatory medications. Examination 10 days after his initial reaction demonstrated resolution of any bullous lesions. Despite this reaction, the patient wished to continue allergen immunotherapy, and SCIT was resumed 4 weeks after his previous injection at a decreased dose of 0.25 mL of a 1:1 v/v concentration. He subsequently built back up to maintenance dosing and remains on immunotherapy with a self-reported 95% improvement of his allergic rhinitis symptoms. He has had no further local or systemic reactions.

Local reactions are typically defined as reactions occurring in the immediate vicinity of the injection site, and they are usually less than or equal to the size of the patient's palm. Most frequently these are associated with erythema, pain, tenderness, and induration. To our knowledge there has only been 1 other case report of a local reaction resulting in bulla formation from SCIT; this also occurred in a delayed fashion 1 hour after the injection.⁴ Regarding that case, the patient was treated with cephalexin and prednisone; however, cultures demonstrated no growth, and no skin biopsy was obtained. Our case suggests that such reactions are self-limited and

may not warrant treatment with antibiotics or steroids, similar to more typical local reactions. We also provide biopsy results to suggest that these rare, local bullous reactions after administration of SCIT are not typical of other better understood antibody-dependent autoimmune bullous processes. However, biopsies of more classic large local cutaneous reactions to venom immunotherapy have demonstrated findings with similar inflammatory infiltrates, which involved many eosinophils.⁵ The perivascular lymphohistiocytic inflammatory infiltration seen in this case, although a nonspecific histologic finding, can also be found in drug reactions.⁶

Consistent with both documented instances of cutaneous bullous reactions to SCIT, consideration can be given to continue immunotherapy in patients in whom such reactions occur, because no evidence has been found of correlation with future adverse reactions. However, more data on these reactions need to be collected when possible to suggest more definitive treatment recommendations when confronted with these rare occurrences.

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Beer allergy

When malt is the culprit

Beer is the most widely consumed alcoholic beverage in the world, and beer allergy is rare.^{1–3} The fundamental ingredients of beer, according to the Bavarian Purity Law, include barley malt, hops, yeast, and water, but each individual beer may differ in malt content and brewing procedures.⁴ Malt is obtained by roasting germinated cereal and is essential to beer flavoring.³ In

beer-allergic subjects, the most frequent allergenic sources involved are cereals, particularly barley malt² and wheat.³ Pan-allergens, namely lipid transfer proteins, also have been involved.⁵

The diagnostic workup for allergen identification in a patient suspected to have recurrent anaphylaxis to beer is presented.

A 71-year-old man was referred to our department after 3 episodes of anaphylaxis. His medical history included chronic obstructive pulmonary disease, hypertension, dyslipidemia, and osteoarticular disease. He was medicated daily with carvedilol,

