

A contact allergic reaction to budesonide mimicking immediate-type allergy

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doi:10.1111/cod.12762

Key words: budesonide; case report; contact dermatitis; corticosteroids.

Dermatitis is by far the most common clinical manifestation of contact allergy, but some patients may develop more severe symptoms (1). Here, we present a patient who developed swollen lips and a swollen face following exposure to budesonide in an inhalant spray.

Case Report

In September 2014, a 51-year-old non-atopic woman was diagnosed with mild asthma and treated with an inhalant spray containing budesonide (Pulmicort Turbuhaler®), which is produced by several different companies. It is unknown which company produced the particular inhalant spray used by the patient. After 10 days of treatment, her lips and face became swollen overnight; she reported breathing difficulties, and her voice became hoarse. She stopped using budesonide, and was treated with oral prednisolone by her general practitioner, who suspected an allergic reaction. Over the following days, she developed urticaria on most of the body, but, after a few days, all symptoms disappeared.

In September 2015, she decided to try an asthma treatment again. On this occasion, she was treated with a different brand of inhalant spray containing budesonide (Giona Easyhaler®; Orion Pharma Denmark, Copenhagen, Denmark). Twenty-four hours after the start of treatment, she developed swollen lips, although there was no urticaria or other skin symptoms. She was treated with antihistamines and oral prednisolone, after which all symptoms disappeared.

In May 2016, she was investigated in the dermatology clinic. Testing was initially performed with a specialized series containing corticosteroids, including budesonide (0.1% pet.), as a 20-min open application test to determine whether there was an immediate-type reaction. This test gave a negative result. Subsequently, prick testing was performed with three different formulations containing budesonide: (i) a nasal spray (64 µg per click), (ii) an inhalation solution (0.5 mg/ml), and (iii) a patch test substrate (0.1% pet.). These tests all gave negative results after 20 min. However, 8 h later, the test area became red and itchy (Fig. 1). To test for a delayed-type hypersensitivity reaction, patch testing was performed with the European baseline series, the extended Gentofte Hospital series, and a more specialized series containing corticosteroids, including budesonide (0.1% pet.), and fragrances. Finn Chambers® (8 mm; Smartpractice, Phoenix, AZ, USA) on Scanpor® tape (Norgesplaster, Vennesla, Norway) were applied to the upper back, and remained occluded for 48 h. Readings were performed on day (D) 2, D5, and D7, according to ESCD recommendations (2). There were positive reactions to budesonide (+2



Fig. 1. Delayed reactions appearing 8 h after prick testing.

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Conflicts of interest: All authors declare that there are no conflicts of interest.

on D2, +1 on D5, and +1 on D7) and doubtful reactions to amcinonide (?+) on D5 and D7. All other tests gave negative results.

On the basis of these findings, the patient was diagnosed with contact allergy to budesonide and amcinonide, and was advised to avoid direct contact with all products containing group B corticosteroids.

Discussion

Corticosteroids are widely used in nasal sprays and inhalant sprays for the treatment of allergic rhinitis and/or asthma. The sensitization potential of inhaled corticosteroids has only been addressed in few reports, which have identified budesonide as the most common allergen (3). Budesonide is part of the European baseline series (2), and in a recent study it was found to be one of the most common topical drugs causing contact allergy (4). In contrast, corticosteroids only rarely cause immediate-type allergic reactions (5). If contact allergy to inhaled corticosteroids is suspected, it is important to remember that patients are also exposed to common additives such as propylene glycol and benzalkonium chloride, and testing should therefore include these substances (6).

In this particular case, the patient developed swollen lips and a swollen face and had breathing difficulties after 10 days of exposure to budesonide in an inhalant spray. As

the patient also developed an urticarial rash over the following days, an immediate-type allergic reaction was initially suspected, but 20-min open application testing and prick testing with three different formulations of budesonide gave negative results. Subsequently, as symptoms developed hours after exposure, attention was instead focused on a contact allergic reaction, and, notably, patch testing showed that the patient was indeed sensitized to budesonide. Also, there was redness and itching in the prick test area 8 h after pricking with budesonide, indicating strong sensitization. The patient was probably sensitized during the first treatment period, which could explain the time difference from exposure until the development of symptoms during the two treatment periods. During testing, we did not reproduce urticaria, and we do not know whether this symptom was in any way related to exposure to budesonide.

The patient also had a doubtful reaction to amcinonide. Corticosteroids can be divided into four groups (A, B, C, and D; the last of these can be divided into D1 and D2) based on their contact-allergic properties (7). Both budesonide and amcinonide belong to group B, and it is likely that the doubtful reaction to amcinonide represents cross-reactivity between the two corticosteroids.

This case highlights the importance of taking not only patient symptoms but also timing into consideration when investigating patients with allergic reactions; otherwise, a relevant contact allergy may easily be missed.

References

- 1 Goon A, Goh C L. Noneczematous contact reactions. In: *Contact Dermatitis*, 5th edition, Johansen J D, Frosch P J, Lepoittevin J P E (eds); Berlin, Heidelberg, Springer-Verlag, 2011: pp. 415–427.
- 2 Johansen J D, Aalto-Korte K, Agner T et al. European Society of Contact Dermatitis guideline for diagnostic patch testing – recommendations on best practice. *Contact Dermatitis* 2015; **73**: 195–221.
- 3 Baeck M, Pilette C, Drieghe J, Goossens A. Allergic contact dermatitis to inhalation corticosteroids. *Eur J Dermatol* 2010; **20**: 102–108.
- 4 Gilissen L, Goossens A. Frequency and trends of contact allergy to and iatrogenic contact dermatitis caused by topical drugs over a 25-year period. *Contact Dermatitis* 2016; **75**: 290–302.
- 5 Brockow K, Garvey L H, Aberer W et al. Skin test concentrations for systemically administered drugs – an ENDA/EAACI Drug Allergy Interest Group position paper. *Allergy* 2013; **68**: 702–712.
- 6 Bennett M L, Fountain J M, McCarty M A, Sherertz E F. Contact allergy to corticosteroids in patients using inhaled or intranasal corticosteroids for allergic rhinitis or asthma. *Am J Contact Dermat* 2001; **12**: 193–196.
- 7 Baeck M, Chemelle J, Goossens A et al. Corticosteroid cross-reactivity: clinical and molecular modelling tools. *Allergy* 2011; **66**: 1367–1374.