

Allergology Service, Hospital General Universitario Gregorio Marañón, C/Dr Esquerdo, 46, 28007 Madrid, Spain

Key words: budesonide; contact allergy; corticosteroids; cross-reaction; patch test.

Inhaled corticosteroids are first-line agents for patients with persistent asthma. They may cause local adverse effects, mainly mucosal irritation or oropharyngeal candidiasis. Contact mucositis because of type IV hypersensitivity has rarely been reported.

Case Story

A 49-year-old man, with a history of pollen allergy, was treated for seasonal respiratory symptoms with oral ebastine and inhaled budesonide/formoterol. 1 D after starting treatment, he experienced oropharyngeal itching, erythema, dysphonia, tongue oedema, and dysphagia. Budesonide/formoterol was discontinued. 1 week later, budesonide/formoterol was restarted and symptoms recurred.

Methods and Results

Single-blind challenge test (SBCT) with inhaled budesonide was performed. 6 hr later, the patient experienced oropharyngeal erythema and inflammation. A pharyngeal exudate culture was negative for *Candida* and other fungi. A subsequent patch test with budesonide (0.1% in pet.) was performed using Leukotest[®] (Beiersdorf AG, Hamburg, Germany) and a hypoallergenic tape applied to the upper back. The occlusion time was 2 D. Readings were taken on D2, D4, and D7 according to the recommendations from the International Contact Dermatitis Research Group (ICDRG). It tested positive (++) on D2. An exposure test to inhaled formoterol and oral ebastine was well tolerated.

In order to investigate cross-reactivity, patch tests were performed in the same manner using a standard series of corticosteroids (Bial-Aristegui, Bilbao, Spain): triamcinolone acetonide (5%), tixocortol pivalate (0.1%),

Contact allergy to inhaled budesonide*

Contact Dermatitis 2008; 59: 60–61

Alicia Prieto García, V. Tovar, M. de Barrio, A. Villanueva and P. Tornero

*Financial Disclosure: The authors have no relevant commercial interests to declare in conjunction with this report.

prednisolone (5%), betamethasone dipropionate (0.5%), betamethasone-17-valerate 5%, betamethasone 1%, clobetasone-17-propionate (1%), fluocinolone acetonide (0.25%), dexamethasone-21-acetate (1%), dexamethasone-21-disodium-phosphate (1%), dexamethasone (1%), hydrocortisone acetate (25%), and hydrocortisone (12.5%), all in pet., with negative results. SBCT with inhaled fluticasone propionate and oral methylprednisolone and betamethasone was also negative.

Discussion

There are many reports of contact dermatitis caused by budesonide contained in topical skin medications. Yet allergic contact mucositis caused by inhaled budesonide is uncommon, despite its widespread use.

Kilpio et al. (1) and Isaksson et al. (2) found the rates of type IV hypersensitivity to corticosteroids of 3.9% and 2.9%, respectively, in 2 series of 51 and 34 patients with asthma or rhinitis who referred side-effects from inhaled or nasal corticosteroids, as assessed by patch test to a corticosteroid series.

There are some reports of allergic contact mucositis induced by corticosteroids in patients with asthma/rhinitis. The causative corticosteroids most commonly involved are budesonide and tixocortol pivalate, both by nasal and by inhaled routes.

Local allergic side-effects of inhaled corticosteroids include pruritus, dryness, mouth erythema and oedema, dry cough, andodynophagia (3). Systemic signs consisting of eczematous lesions particularly on the face and sometimes affecting trunk and flexures have also been reported (1, 3). Allergic side-effects often occur within a very short latent period, as in the patient described here (4-6).

Our patient showed hypersensitivity to budesonide only, as in other publications (4, 6, 7). Bircher et al. (7) suggested that most of these patients appear to be allergic to a single corticosteroid molecule, unlike patients with skin contact allergy, who often show multiple sensitizations (8). However, there are also cases of cross-reactivity between budesonide and corticosteroids of group D2 (1, 5) and group A (5) in asthma patients. Cross-reactivity should therefore be individually assessed to find a therapeutic alternative for these patients.

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Address:

Dr Alicia Prieto García
Servicio de Alergia
Hospital General Universitario
Gregorio Marañón
C/Dr Esquerdo, 46 28007 Madrid
Spain
Tel: 915868268
Fax: 915868268
e-mail: aprieto.hgugm@salud.madrid.org