

A case of systemic allergic dermatitis caused by inhaled budesonide: cross-reactivity in patch tests with the novel inhaled corticosteroid ciclesonide

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Ciclesonide is a novel non-halogenated synthetic inhaled corticosteroid that has been widely used in the treatment of asthma (1, 2). Like other corticosteroids, ciclesonide is likely to cause immediate and delayed allergic hypersensitivity reactions (3, 4). We present a patient with a systemic type of allergic dermatitis caused by inhaled budesonide and a positive patch test reaction showing additional cross-reactivity to ciclesonide, and a series of 9 patients with positive patch test reactions to ciclesonide.

Case Report

A 63-year-old Caucasian female with a past medical history of asthma experienced an eczematous eruption 10 days after the initiation of inhalation treatment with budesonide. The patient developed a symmetrical and itching eruption, beginning on her décolleté chest and spreading over the trunk and the proximal extremities over 1–2 days. The eruption cleared completely with scaling 2 weeks after discontinuation of the drug. Budesonide was reintroduced after 6 weeks, owing to progression of the asthmatic symptoms, and after 1 day of use a similar, more severe eruption occurred. Inhalation treatment with budesonide was consequently stopped, and the patient was referred for allergy testing, with the object of finding a tolerable inhaled corticosteroid. Treatment with the novel inhaled corticosteroid ciclesonide (Alvesco®) was planned, but the final decision was left until after allergy testing.

Patch tests, including the baseline series and steroid series, were carried out on Finn Chambers® on Scanpor® tape. The series included budesonide (0.1% in pet.), desonide (0.1% and 1.0% in ethanol), ciclesonide (0.1% and 0.5% in pet. and ethanol), fluticasone propionate (0.1% and 0.5% in pet. and ethanol), mometasone furoate (0.1% and 1.0% in ethanol), and beclomethasone dipropionate (0.05% and 0.5% in ethanol), which also are used in inhaled corticosteroids. The steroid patch tests were read on the second, third, fifth and eighth days, and showed positive reactions to budesonide (+) and ciclesonide (+), but negative results for fluticasone propionate and beclomethasone dipropionate. The intracutaneous test for late (48 hr) reactions to hydrocortisone gave a negative result (patient 1 in Table 1). The patient's inhalation corticosteroid treatment was switched to fluticasone propionate, and a good response was achieved during maintenance therapy for asthma. The use of budesonide and ciclesonide was prohibited, and the patient did not show any further skin reactions during the follow-up of 8 months.

Discussion

We screened the patient data and results of testing with the steroid patch test series of all patients who were tested with ciclesonide (Alvesco®) in the Skin and Allergy Hospital, Helsinki University Central Hospital, Finland. In our baseline patch test series, tixocortole pivalate (0.1% in pet.) and budesonide (0.1% in pet.) are incorporated. The steroid series included 14 test substances. Additionally, ciclesonide was included in the steroid patch test series during the period 2009–2011. The steroid patch test series included an intracutaneous test for late (48 hr) reactions with hydrocortisone and, in the case of a positive reaction, an additional intracutaneous test with dexamethasone or methylprednisolone. A total of 79

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Table 1. Results of steroid patch test series and intracutaneous tests

Patient	CIC	BUD	HC17B	TIX	HC	HCA	FLU	DES	BEC	MOM	I.C.
1. Female, 64 years	+	+	—	—	—	—	—	++	—	—	HC —
2. Female, 39 years	++	+++	++	—	—	—	+	—	+	+	HC + MP +
3. Male, 50 years	+	+++	++	—	—	—	—	—	—	—	HC —
4. Male, 37 years	+	++	+++	—	—	—	—	—	—	—	HC —
5. Male, 55 years	+	++	—	+	—	++	—	—	—	—	HC + DX —
6. Female, 25 years	+	++	+	—	—	—	—	—	—	—	HC —
7. Female, 27 years	+	+	+	—	—	—	—	—	—	—	HC — DX —
8. Male, 60 years	++	+	—	—	—	—	—	—	—	—	HC —
9. Female, 63 years	++	+	+	—	+	—	—	++	—	—	HC + DX —
10. Female, 72 years	++	+++	++	++	++	—	—	—	—	—	HC +

BEC, beclomethasone dipropionate; BUD, budesonide; CIC, ciclesonide; DES, desonide; DX, dexamethasone; FLU, fluticasone propionate; HC, hydrocortisone; HCA, hydrocortisone acetate; HC17B, hydrocortisone-17-butyrate; I.C., intracutaneous test; MOM, mometasone furoate; MP, methylprednisolone; TIX, tixocortol pivalate.

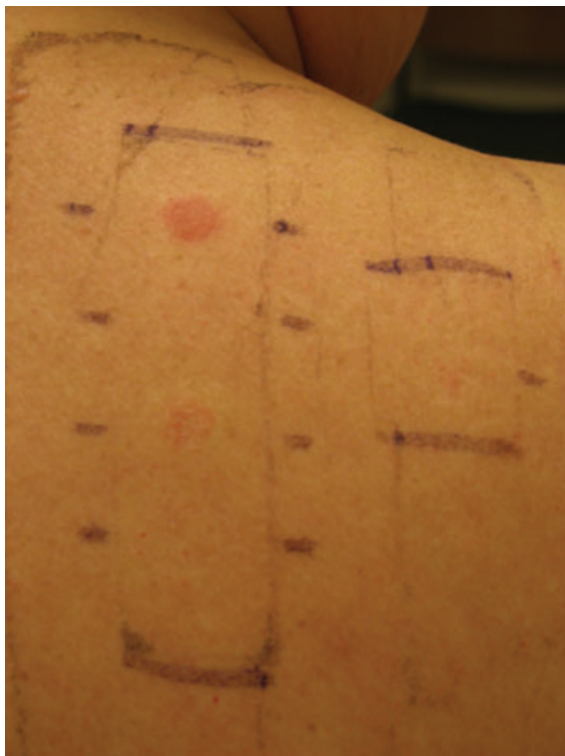


Fig. 1. Patch test with ciclesonide (Alvesco®) and budesonide on the third day. (Left side: ciclesonide, from cranial to caudal, 0.5% in pet., 0.1% in pet., 0.5% aqua, 0.1% aqua. Right side: budesonide 0.1% pet.)

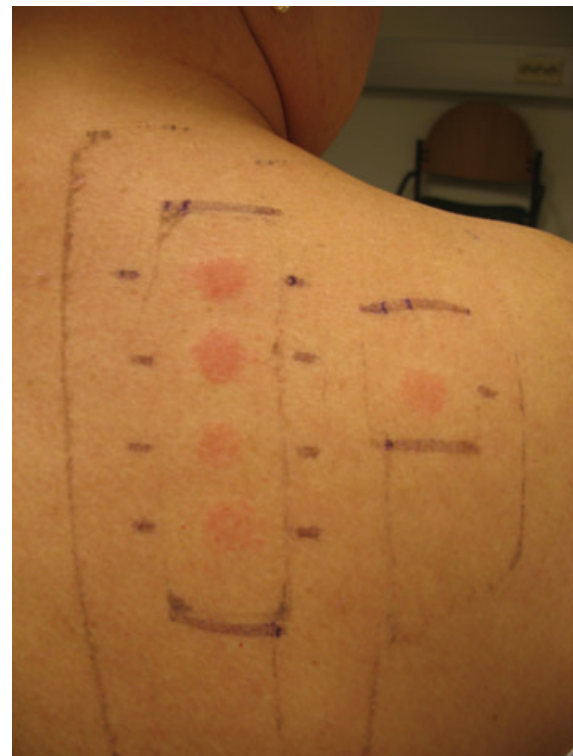


Fig. 2. Same patch test as in Fig. 1 with ciclesonide (Alvesco®) and budesonide on the fifth day; ciclesonide (+) and budesonide (+) are positive.

patients had undergone patch testing with the baseline and steroid series including ciclesonide (0.1% and 0.5% in pet. and 0.1% and 0.5% ethanol), mainly because of eczematous conditions and suspected contact allergy to topical corticosteroids. None of the tested patients had had previous treatment with inhalative ciclesonide (Alvesco®).

Patch testing with inhaled ciclesonide was carried out by means of incorporating the inhalation spray Alvesco® at 160 mg/dose 0.1% and 0.5% in ethanol and 0.1% and 0.5% in pet. and patch testing the mixtures on Finn Chambers® on Scanpor® tape. The patch tests were read on the second, third, fifth and eighth days (Figs. 1 and 2). Testing with the baseline and steroid patch test series

was carried out according to the recommendations of the International Contact Dermatitis Research Group.

Ten (12.7%) of the 79 patch tested patients showed positive reactions to inhaled ciclesonide (Alvesco®). All of these patients showed positive reactions to both 0.1% and 0.5% ciclesonide in ethanol and to 0.1% and 0.5% ciclesonide in pet. Budesonide 0.1% in pet. gave a positive reaction in all patients with a positive reaction to ciclesonide. There were no patients with a positive reaction to budesonide but a negative reaction to ciclesonide. Hydrocortisone-17-butyrate gave positive reactions in 7 of the 10 patients with positive reactions to ciclesonide. Intracutaneous tests for late reactions (48 hr) to hydrocortisone gave positive results in 4 patients. Table 1 shows the results of the steroid patch test series and intracutaneous tests.

Our case indicates a delayed-type allergic reaction to inhaled budesonide with a positive patch test result. Similar cases have been reported in the literature (5, 6). A corticosteroid allergy should be considered in patients

receiving inhalation therapy with corticosteroids and appropriate symptoms (7).

All of our patients with a positive patch test reaction to budesonide also had a positive test reaction to ciclesonide, indicating a cross-reaction pattern. None of our patients had previously used ciclesonide. Cross-reactivity between budesonide and the novel inhaled corticosteroid ciclesonide was shown in 10 of our patients. To our knowledge, this is the first report of cross-reactivity between budesonide and ciclesonide in patch testing. In cases of suspected corticosteroid allergy, patch testing with the active principles diluted in ethanol remains the diagnostic method of choice for the detection of delayed hypersensitivity (8).

Cross-reactivity between budesonide and ciclesonide may have clinical implications for patients with a delayed-type allergic reaction to inhalative budesonide (9). More investigations are necessary to confirm the cross-reaction pattern, to underline the clinical implications, and to determine the correct vehicle and concentrations of ciclesonide for use in patch testing.

References

- 1 Deeks E D, Perry C M. Ciclesonide: a review of its use in the management of asthma. *Drugs* 2008; **68**: 1741–1770.
- 2 Vogelmeier C F, Hering T, Lewin T, Sander P, Bethke T D. Efficacy and safety of ciclesonide in the treatment of 24,037 asthmatic patients in routine medical care. *Respir Med* 2011; **105**: 186–194.
- 3 Isaksson M, Bruze M, Hörnblad Y, Svenonius E, Wihl J A. Contact allergy to corticosteroids in asthma/rhinitis patients. *Contact Dermatitis* 1999; **40**: 327–328.
- 4 Bircher A J, Bigliardi P, Zaugg T, Mäkinen-Kiljunen S. Delayed generalized allergic reactions to corticosteroids. *Dermatology* 2000; **200**: 349–351.
- 5 Pitsios C, Stefanaki E C, Helbling A. Type IV delayed-type hypersensitivity of the respiratory tract due to budesonide use: report of two cases and a literature review. *Prim Care Respir J* 2010; **19**: 185–188.
- 6 Baeck M, Pilette C, Drieghe J, Goossens A. Allergic contact dermatitis to inhalation corticosteroids. *Eur J Dermatol* 2010; **20**: 102–108.
- 7 García A P, Tovar V, de Barrio M, Villanueva A, Tornero P. Contact allergy to inhaled budesonide. *Contact Dermatitis* 2008; **59**: 60–61.
- 8 Soria A, Baeck M, Goossens A, Marot L, Duveille V, Derouaux A S, Nicolas J F, Tennstedt D. Patch, prick or intradermal tests to detect delayed hypersensitivity to corticosteroids? *Contact Dermatitis* 2011; **64**: 313–324.
- 9 Baeck M, Chemelle J A, Goossens A, Nicolas J F, Terreux R. Corticosteroid cross-reactivity: clinical and molecular modelling tools. *Allergy* 2011; **66**: 1367–1374.