

Contact allergy to isoconazole nitrate with unusual spreading over extensive regions

Leonardo Bianchi, Katharina Hansel, Elettra Antonelli, Veronica Bellini and Luca Stingeni

Department of Medicine, Section of Clinical, Allergological and Venereological Dermatology, University of Perugia, 06156, Perugia, Italy

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Allergic contact dermatitis caused by imidazole antimycotics is comparatively rare, considering their high prescription rates. Among these, isoconazole nitrate was one of the most frequently reported imidazole derivative

allergens in the 1990s (1); however, the last published report of contact allergy to isoconazole nitrate dates back to 1997 (2).

Correspondence: Luca Stingeni, Department of Medicine, Section of Clinical, Allergological and Venereological Dermatology, University of Perugia, 06156 Perugia, Italy; Polo Ospedaliero, Universitario Santa Maria della Misericordia, Sant'Andrea delle Fratte, 06156 Perugia, Italia. Tel: +39 0755783452; Fax: +39 0755783498. E-mail: luca.stingeni@unipg.it

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Fig. 1. Erythematous and oedematous dermatitis involving the trunk, limbs, and neck; (a) site of application of Travocort® cream

Case Report

A 65-year-old female had itchy, erythematous and oedematous diffuse dermatitis involving the upper and lower limbs, abdomen, chest, and neck (Fig. 1). Two weeks before, eczematous dermatitis began on the right thigh, where she had applied Travocort® cream (Bayer, Milano, Italy) containing diflucortolone valerate (CAS no. 59198-70-8) 0.1% and isoconazole nitrate (CAS no. 24168-96-5) 1% for suspected tinea corporis. At consultation in our department, she was still applying this topical medication. She denied previous use of topical imidazoles. The cream was withdrawn, and the dermatitis disappeared within 2 weeks with the use of topical zinc oxide and oral cetirizine.

Patch testing with the SIDAPA baseline series and the patient's own product 'as is' was performed 2 months later on the upper back with Hayes Test Chambers (Hayes Service, Alphen aan den Rijn, The Netherlands) on Soffix tape (Artsana, Grandate, Italy). The readings on day (D) 2, D4, and D7, according to ICDRG criteria, showed a ++ reaction to Travocort® cream (Table 1). The patient was subsequently tested with the

Table 1. Patch test results

	Concentration (%)	D2	D4	D7
Travocort® cream	'as is'	++	++	++
Diflucortolone valerate	1	–	–	–
Phenethyl imidazoles				
Econazole nitrate	2	–	–	–
Fenticonazole nitrate	2	–	–	–
Isoconazole nitrate	2	+++	+++	+++
Ketoconazole	2	–	–	–
Miconazole nitrate	2	+++	+++	+++
Sertaconazole nitrate	2	–	–	–
Tioconazole	2	–	–	–
Phenmethyl imidazoles				
Bifonazole	2	–	–	–
Clotrimazole	2	–	–	–
Triazoles				
Fluconazole	2	–	–	–
Itraconazole	2	–	–	–
Nitroimidazoles				
Albendazole	5	–	–	–
Mebendazole	5	–	–	–
Metronidazole	5	–	–	–
Tinidazole	5	–	–	–

All allergens in pet.

two active ingredients of the cream, showing a +++ reaction to isoconazole nitrate 2% pet., and with an extended antimycotic and antiparasitic azole series,

showing a +++ reaction to miconazole nitrate 2% pet. (Table 1).

Discussion

In recent years, contact allergy to imidazoles has been reported only twice and has been limited to clotrimazole (3, 4), probably depending on the local prescribing habits. Herein, contact sensitivity to isoconazole nitrate with extensive spreading is reported: although our patient applied the topical medication to an extremely limited area, the eruption enlarged extensively to areas where it had not been applied at all. This dissemination to distant regions was first described as 'autoeczematization' by Whitfield in 1921 (5), and then termed 'auto-allergy' by Parish in 1965 (6). Spreading has been sporadically reported in patients with imidazole contact allergy (Table 2), mostly involving regions adjacent to application sites and with eczematous features (2, 7–10). In our case, in contrast, unusually extensive and non-eczematous spreading was observed. The particular erythematous and oedematous clinical picture could be related to the anti-inflammatory properties of the corticosteroid present in the topical combination drug.

Moreover, in our patient, among the set of agents tested, we found cross-reaction only to miconazole, which is a phenethyl imidazole (as isoconazole nitrate). Cross-reactions have not been extensively and systematically investigated in patients with contact allergy

Table 2. Reports of allergic contact dermatitis caused by imidazoles with spreading

Author	Year	Imidazole sensitizer	Site of sensitization	Spreading	
				Involved site(s)	Clinical picture
Raulin et al.* (7)	1988	Miconazole	Axillae	Trunk	Eczematous
Baes (8)	1991	Miconazole	Genital area	Thighs, perineal and pelvic regions, chest	Eczematous
Valsecchi et al. (9)	1994	Clotrimazole	Genital area	Abdomen, thighs	Eczematous
Lazarov et al. (2)	1997	Isoconazole nitrate	Foot	Lower limbs	Papular and pustular eruption
Erdmann et al. (10)	1999	Clotrimazole	Genital area	Abdomen, thighs	Eczematous

*One of a 9-patient series.

to imidazoles. Probably, their chemical structures may fail to explain cross-sensitization, and stereochemical studies are therefore needed, as previously stated (1). In our opinion, an extensive antimycotic and antiparasitic azole series should be tested, also including triazoles and nitroimidazoles, in order to fully diagnose the individual spectrum of contact allergy and thereby prevent inadvertent systemic contact dermatitis (4).

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