Pustular Allergic Contact Dermatitis to Isoconazole Nitrate

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The topical imidazole antimycotics are widely used and are an infrequent cause of contact allergy. We report on a woman, who developed an unusual clinical picture of allergic contact dermatitis, namely papulo-pustular reaction, evoked by an isoconazole nitrate-containing cream. The histopathologic changes included subcorneal pustules, spongiosis, and an inflammatory infiltrate composed mainly of lymphocytes and some eosinophils and neutrophils. The patient demonstrated a severe vesicular reaction to isoconzole nitrate as is and at an imidazoles concentration of 0.5%. No cross-reactivity with other imidazole antimycotics was noted.

IMIDAZOLE ANTIMYCOTICS were first introduced in 1969, and, consequently, a wide range of these antimycotics has been developed. Although they are extensively used for topical treatment, because of their high antimycotic activity and lack of side effects, contact allergy from topical imidazoles appears to be infrequent.[1-5]

We report on a female patient, who developed allergic contact dermatitis to an isoconazole nitrate-containing cream.

CASE REPORT

A 57-year-old patient presented with a long standing, severely itchy papular and pustular eruption on the extremities (Fig 1). The lesions appeared after treatment for eczematized tinea pedis that was initiated with a cream containing 0.1% diflucortolone valerate and 1% chlorquinaldol (Multiderm, Agis, Israel), followed by 1-month application of a 1% isoconazole nitrate cream (Isogen, Pharma Clal, Israel), and a cream containing 1% isoconazole nitrate and 0.1% diflucortolone valerate (Isocort, Pharma Clal, Israel). Contact dermatitis from one of the topical drugs was suspected, and patch tests with the TRUE Test, isoconazole nitrate, and related antimycotics were performed. The results from the patch testing are listed in Table 1. The patient demonstrated a severe vesicular reaction to isoconazole nitrate as is and at a concentration of 0.5%. No cross-reactivity with other imidazole antimycotics was noted. Patch tests with isoconazole nitrate cream as is and in a concentration of 0.5%, applied to 10 healthy volunteers were negative.

The histopathologic changes seen in a biopsy from a papulo-pustular lesion included subcorneal pustules, acanthosis, and mild spongiosis in the epidermis. In the upper and lower dermis, a perivascular and interstitial infiltrate, composed mainly of lymphocytes and some neutrophiles and eosinophiles was observed (Fig 2). The periodic acid-Schiff stain (PAS) did not reveal the presence of fungi. The bacteriological and mycological tests from the pustular contents were all negative, demonstrating sterile pustules.

All the topical medications used by the patient were withdrawn, and she was treated further with bifonazole and ketoconazole creams. The treatment lead to control of the mycotic infection without any evidence of allergic reaction to these topical antimycotics.

COMMENTARY

Allergic contact dermatitis to isoconazole nitrate appears to be rare compared with the wide use of the antifungal agent. There are only several reports in literature concerning contact allergy to isoconazole nitrate.[1,5,6] Our case is another example of this infrequent reaction. The contact allergy to isoconazole nitrate was proved by the strongly positive patch tests with different dilutions of the incriminated substance and by the negative results to the patch testing with the vehicle of the cream. The positive reaction to quinoline mix had also present relevance because there was chlorquinaldol in the first cream used by the patient. This cream produced erythematous reaction on the dorsal aspects of the feet.

An unusual clinical picture of allergic contact dermatitis, namely papulo-pustular reaction, evoked by isoconazole nitrate was observed in our patient. The significance of such pustular reaction remains speculative. Sterile pustular eruptions have been related mainly to primary irritation[7] and rarely to allergic contact dermatitis.[8,9] The pustular reaction in our case was demonstrated to be an expression of contact allergy through positive patch tests with isoconazole nitrate, the clinical course of the disease, and the observed histopathologic changes.

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1046-199X/97/0804-0008$3.00/0

Table 1. Patch Tests Results

Allergen	Concentration	Results Day 2	Results Day 4
1% Isoconazole nitrate and vehicle (Isogen cream)	as is	3+	3+
Isoconazole nitrate	0.5% pet	2+	2+
Isoconazole nitrate	0.1% pet	2+	2+
Vehicle of isoconazole nitrate cream	as is	−	−
Isocort	as is	+	+
Bifonazole	1%	−	−
Ketoconazole	2%	−	−
Clotrimazole	1%	−	−
Miconazole	2%	−	−
TRUE Test	quinoline mix	+	+

Abbreviation: pet, petrolatum.

Fig 1. Papulo-pustular eruption on the shins after treatment with isoconazole nitrate.

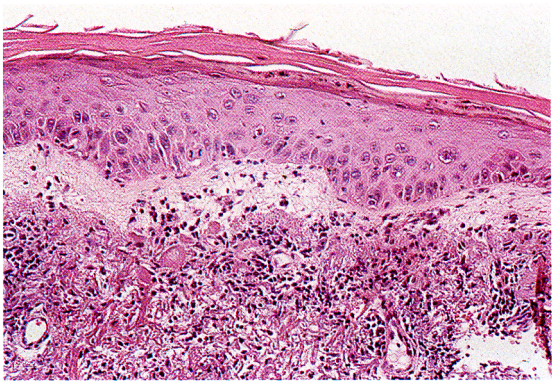

Fig 2. Histopathologic findings of pustular allergic contact dermatitis.

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