

Contact dermatitis from Zovirax cream

HERMAN BAES¹ AND ERIC VAN HECKE²

¹Department of Dermatology, H. Serruys Hospital, Kairostraat, 84, 8400 Ostend, and ²Department of Dermatology, University Hospital, De Pintelaan 185, 9000 Ghent, Belgium

Key words: acyclovir; Zovirax; allergic contact dermatitis; compound allergy; medicaments.

Only 2 cases of contact allergy to acyclovir have so far been published (1, 2). Very recently, 2 cases of contact allergy to Zovirax cream, with negative patch tests to its constituents, were reported (3).

Case Reports

Case no. 1

A 25-year-old woman presented with an acute dermatitis of the lips and surrounding skin, starting a few days after applying Zovirax cream for recurrent herpes infection. She also used a lipstick: Labello Sun. She had used Zovirax cream 5 times in the past year.

After clearance of the dermatitis, repeated patch tests (up to 15 months later) in several sessions demonstrated contact allergy to nickel sulphate, balsam of Peru, butylated hydroxyanisole and isopropyl dibenzoylmethane. Strongly positive reactions were obtained after 2 and 4 days to Labello Sun lipstick and Zovirax cream (Table 1). Out of the constituents supplied, the base of Zovirax cream was made up by a local pharmacist. Patch tests with this base, with and without 5% acyclovir, remained negative.

Her nickel and balsam of Peru allergies were of past relevance. The allergies to butylated hydroxyanisole and isopropyl dibenzoylmethane were attributable to Labello Sun lipstick, from which both chemicals have recently been omitted.

Case no. 2

A 59-year-old woman presented with an acute eczema of the lips and surrounding skin, after using Zovirax cream for herpes simplex. She regularly had herpes and had used Zovirax cream in the past without any problem.

Patch tests were performed on 3 occasions, the 1st after clearance of the dermatitis, the 2nd and the 3rd, 3 and 4 months after its onset, respectively. Contact allergy to nickel and fragrance-mix was detected. Zovirax cream gave a very strong reaction. No reaction was obtained with Zovirax ointment, nor with any of the constituents of Zovirax cream.

Since the company gave us only very little acyclovir (25 mg), and we knew that acyclovir aq. or pet. was negative in Case no. 1, we diluted acyclovir to 2.5% in Carbopol (water-soluble vinyl polymer) gel. Still, no reaction was obtained (Table 1).

Discussion

Both patients had positive patch test reactions to Zovirax cream, but were negative to its constituents as well as to Zovirax ointment (paraffin as base). Unfortunately, we were unable to obtain the acyclovir-free cream-base from the company.

Although allergy to acyclovir has been reported in 2 patients, using acyclovir 5% pet. (1) and aq. (2), testing with acyclovir in different concentrations and vehicles (aq., pet., Carbopol gel) was negative in our patients. This does not necessarily disprove contact allergy to acyclovir. Penetration of acyclovir into the epidermis is probably optimal in the commercial cream base and could be marginal in petrolatum, water or a water-based vehicle like Carbopol gel.

As both patients were allergic to several allergens, the possibility of angry back syndrome was considered. However, all positive reactions persisted on retesting (up to 15 months later in the 1st case).

Moreover, since testing with a home-made Zovirax base with and without acyclovir remained negative in our 1st case, a hidden source also had to be

Table 1. Results of patch testing at 2 days

	Case no. 1	Case no. 2
European standard series:		
nickel sulphate	++	++
balsam of Peru	++	—
fragrance-mix	—	+
butylated hydroxyanisole 2% pet.	++	—
butylated hydroxytoluene 2% pet.	—	—
isopropyl dibenzoylmethane 2% pet.	++	—
Labello Sun lipstick	++	NT
Zovirax cream	++	+++
Zovirax ophthalmic ointment	—	—
Zovirax cream constituents:		
acyclovir 5%, 10% aq. and pet.	—	NT
acyclovir 2.5% Carbopol gel	NT	—
propylene glycol 10% aq.	—	—
cetostearyl alcohol 30% pet.	—	—
sodium lauryl sulphate 1% aq.	—	—
liquid paraffin as is	—	—
Poloxamer 407 10% pet.	—	—
petrolatum	NT	NT

considered as an explanation for these discrepant allergic results. We suspected butylated hydroxyanisole. However, we could demonstrate no traces of it in Zovirax cream by gas chromatography with mass spectrometry. Besides, the 2nd patient did not react to it.

Compound allergy was proposed as an explanation by Goh (3), who recently published 2 similar cases. However, proof for this assumption was not given.

Acknowledgements

We thank Wellcome Belgium for kindly supplying Zovirax cream and its constituents.

Allergic contact dermatitis due to p-nitrobenzyl bromide

M. PAMBOR AND M. WIESNER

Department of Dermatology, Ernst Moritz Arndt University, Fleischmannstraße 42/44, Greifswald 2200, DDR

Key words: allergic contact dermatitis; p-nitrobenzyl bromide; bromomethyl-4-nitrobenzene; occupational; laboratory chemist; lack of cross-sensitivity.

Halogenated organic compounds are chemically highly reactive and are powerful irritants; they can also be potent sensitizers (1-3). Pickering & Ive (1) reported 3 cases of allergic contact dermatitis due to bromomethyl-4-nitrobenzene. p-nitrobenzyl bromide and bromomethyl-4-nitrobenzene are synonyms for the chemical structure shown in Fig. 1.

Case Report

A 22-year-old female chemistry student was assigned the synthesis of p-nitrobenzyl bromide (PNBB). Carrying this out for the first time, she had no trouble with her skin. Working once more on synthesizing PNBB 2 months later for 4 days, she developed a papular vesicular dermatitis of the hands, face, chest and upper thighs. On treatment with topical corticoids, the dermatitis resolved within a few days.

After exclusion from PNBB contact, she had no more trouble, until 3 months later she had a further episode of hand dermatitis, after cleaning test tubes that other students had used for their experiments with PNBB. Additional inquiries ascertained that several students annually had synthesized PNBB, but not until this patient had any skin problems occurred.

Skin tests were carried out on the patient 9 months later, with the following results.

References

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	D1	D2	D3
<i>Open tests</i>			
p-nitrobenzyl bromide			
1% ac.	++	++	++
0.1% ac.	++	++	++
0.01% ac.	-	-	-
<i>Patch tests</i>			
p-nitroaniline 0.1% aq.	-	-	-
p-nitrophenol 5% aq.	-	-	-
p-nitro-toluol 1% aq.	-	-	-
m-nitrobenzoic acid 10% aq.	-	-	-
acetone	-	-	-
bromhexine hydrochloride			
0.8% aq.	-	-	-

The standard series, including further para-substituted compounds (parabens 5%, benzocaine 1%, p-

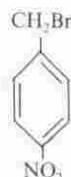


Fig. 1. Chemical structure of p-nitrobenzyl bromide.

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