

Scratch–patch test for the diagnosis of allergic contact dermatitis to aciclovir

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Topical antiviral drugs are frequently used, but although repeated applications can lead to contact reactions (1), adverse cutaneous reactions are not commonly observed. Allergic contact dermatitis caused by aciclovir is rare, with only 20 studies reported (2). We report a patient with acute allergic contact dermatitis of labial and perioral skin following application of a cream containing aciclovir.

Case Report

A 20-year-old non-atopic woman with herpes simplex developed a severe, itching, vesicular eczematous eruption affecting her lips and perioral skin (Fig. 1) on the second day after the application of a cream containing aciclovir 5% (Cycloviran® cream). In recent years, she had used Cycloviran cream for at least three episodes of herpes simplex, with no adverse effect.

She was patch tested with the SIDAPA (Società Italiana di Dermatologia Allergologica Professionale e Ambientale) baseline series (F.I.R.M.A., Florence, Italy and Finn chambers® on Scanpor® tape; Epitest Ltd., Tuusula, Finland) and with the components of Cycloviran cream [aciclovir, cetostearyl alcohol (cetearyl alcohol), propylene glycol, and sodium lauryl sulfate]. Readings were according to International Contact Dermatitis Research Group recommendations. Results are shown in Table 1.



Fig. 1. Contact allergy to aciclovir.

Because of the doubtful reactions with aciclovir and in view of the suggestive clinical history, we performed a scratch–patch test (patch test after scarification of the epidermis by a sterile skin prick lancet) with aciclovir 1% and 5% pet. and with the other components of Cycloviran cream: strong positive reactions at D3 (++), D4 (+++), and D7 (+) to aciclovir 1% and 5% pet. were observed; the other constituents were negative. No positive reactions to aciclovir and components of Cycloviran cream were found in 10 controls, confirming the specificity of the scratch–patch test.

We tested a different class of topical antiviral agent as an alternative drug in the case of recurrence of her herpetic infection. A repeated open application test (ROAT) with a topical 1% foscarnet cream performed on the volar surface of the forearm for 7 days did not produce a reaction.

Comment

Contact allergy to aciclovir appears to be rare and in some cases develops several years after recurrent use of the substance (3).

Although closed patch tests are the mainstay for the evaluation of allergic

contact dermatitis, occasionally, even when appropriate concentrations of allergens are used and contact allergy is strongly suspected, positive reactions are not always obtained (4). As in our case, patch tests with aciclovir may give doubtful results in sensitized patients, possibly due to poor penetration of aciclovir through the epidermis (5). Scratch–patch testing, by compromising epidermal barrier function, enables enhanced penetration of substances into the skin. The method is performed by causing mechanical injury to the epidermis with a sterile skin prick lancet in order to compromise the stratum corneum, which represents the most important barrier limiting hapten penetration (6). The test reactions are usually read after D2 and D3, when possible, also after D4 and D7. The method of grading a positive scratch–patch test is identical to that used for conventional patch testing with no differences.

Cross-reactions between aciclovir, valaciclovir, and famciclovir are documented (5, 7). The chemical structure common to these three antiviral drugs is the 2-aminopurine nucleus, and this is probably the allergenic determinant of the molecules. As this determinant is also

Table 1. Results of scratch–patch test compared with patch test

|           | Concentration/vehicle | p.t. D2 | s.p.t. D2 | p.t. D3 | s.p.t. D3 | p.t. D4 | s.p.t. D4 | p.t. D7 | s.p.t. D7 |
|-----------|-----------------------|---------|-----------|---------|-----------|---------|-----------|---------|-----------|
| Aciclovir | 1% pet.               | ?+      | +         | ?+      | ++        | ?+      | +++       | N       | +         |
| Aciclovir | 5% pet.               | ?+      | +         | ?+      | ++        | ?+      | +++       | N       | +         |

N, negative; p.t., patch test; s.p.t., scratch–patch test.

found in ganciclovir but not in foscarnet or cidofovir, we tested topical 1% foscarnet cream (never previously used by our patient) with a ROAT, both of which were negative.

In conclusion, when contact allergy to aciclovir is suspected and when conventional closed patch test shows negative or doubtful results, scratch-patch testing should be considered. Because of possible cross-reactions, we recommend testing an alternative topical antiviral drug before use.

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