

Contact allergy to dibromopropamide cream

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Key words: allergic contact dermatitis; medicaments; dibromopropamide; over-the-counter antimicrobials; herpes genitalis. © Munksgaard, 1999.

Case Report

A 40-year-old man, with herpes genitalis for 10 years, presented at the polyclinic for venereal diseases in the Municipality of Oslo. On average, he had 1 outbreak every 6 months, and therefore chose not to use systemic antiviral treatment. Instead, he had long used an over-the-counter cream, as suggested by a general practitioner. On examination, he had an acute edematous vesiculobullous dermatitis of the penile shaft. 1 week previously, for an outbreak of herpes genitalis, he had started applying Brulidine® cream, containing dibromopropamide 0.15%, as usual. The cream was withdrawn and the dermatitis treated with topical corticosteroids, with clearance in 2 weeks.

3 months later, the patient was patch tested with the ingredients of the cream (dibromopropamide isethionate, methyl-parahydroxybenzoate, aroma ingredients, oleum ricini, cetostearyl, macrogol stearate, and silicone M.S. antifoam), and the cream itself, using Finn Chambers® on Scanpor® tape, the active ingredient, dibromopropamide, being kindly supplied by the pharmaceutical company. At D3, there was an eczematous

reaction to Brulidine®, which was somewhat less intense to dibromopropamide 5%, 1%, 0.5% and 0.15% pet. He showed no reaction to the other ingredients.

Discussion

Contact allergy to dibromopropamide was first described in 1983 (1). Over-the-counter antimicrobials are among the medicaments most often causing contact allergy (2). Development of medicament dermatitis is especially common in patients with stasis dermatitis and leg ulcers (3, 4). Perturbation of the epidermal barrier, during vesiculation, may have similarly encouraged sensitization in this case. Contact dermatitis due to dibromopropamide is rare in comparison to its wide use.

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Allergic and systemic contact dermatitis from estradiol

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Key words: estrogen transdermal therapeutic system; estradiol; systemic contact dermatitis; allergic contact dermatitis; medicaments; patch testing technique; adverse drug reactions. © Munksgaard, 1999.

Several cases of allergic contact reactions from estradiol transdermal therapeutic systems (TTS) have been published, mostly due to the delivery system (1) or to a component of the gel (2), namely hydroxypropyl cellulose (3) or ethanol (4, 5). Estradiol was the probable cause in half a dozen cases (1, 6, 7), but confirmed only in 2 where patch testing with estradiol was performed (8, 9).

Case Reports

We recently observed 2 women, aged 42 and 52 years, who were treated with Estraderm TTS 50™ (Ciba-Geigy) 2 × weekly after oophorectomy. Under the 6th and

8th patch, respectively, they developed acute vesicular eczema, limited to the areas of the TTS but increasing on subsequent patch applications. Patient no. 1 next had acute eczema from Estronar-gel™ (a topical gel containing 6% 17-β-estradiol) and, on the 5th day of oral estrogen therapy (Premarin Plus™), she developed a symmetrical pruritic maculopapular rash, mainly localized on the trunk, neck and limb girdles, which regressed with oestrogen suspension and an oral anti-H1.

Both patients were patch tested with the standard series of the Portuguese Contact Dermatitis Group (GPEDC), a vehicles and preservatives series, 96% ethanol and with the Estraderm TTS 50™ as is, the gel con-

Table 1. Positive patch test results

	Patient no. 1		Patient no. 2	
	D 2	D 4	D 2	D 4
Estraderm TTS 50 TM as is	++	++	++	++
Estraderm TTS 50 TM gel of the reservoir	++	++	++	++
Dermestril TTS TM	+	NT	+	++
Estronar-gel TM	+++	+++	++	++
17- β -estradiol				
pet. 1%	—	—	—	—
5%	—	—	—	—
10%	—	?+	—	+
acet. 1%	+	NT	—	—
10%	++	NT	—	—
96% eth. 1%	++	NT	+	+
5%	++	NT	++	++
10%	++	NT	++	++

Estradiol at 5% in ethanol was negative in 10 controls.

tained in its reservoir, with a matricial oestrogen TTS (DermestrilTM), and Estronar-gelTM as is; patient no. 2 was also tested with Progenar-gelTM (a 1% progesterone gel). Pure 17- β -estradiol, kindly supplied by the pharmaceutical industry and freshly prepared at 1, 5 and 10% in pet., acet. and 96% eth., was patch tested with Finn Chambers on Scanpor tapeTM. The patients reacted only to estradiol and estradiol-containing products (Table 1).

Despite positive reactions to estradiol, patient no. 2 was treated with oral EstrofemTM (estradiol 2 mg/tablet) and, on the 16th day of treatment, she developed an erythematopapular generalized pruritic eruption, mainly localized on the trunk and limbs, with no fever or systemic symptoms, that progressed despite oral anti-H1 and regressed only after oestrogen suspension.

We thus interpreted both rashes as cutaneous delayed-type hypersensitivity reactions to the systemic administration of oestrogen, after topical sensitization to the oestrogen in the TTS, a form of systemic contact dermatitis.

Discussion

Considering the wide use of estrogen TTS, allergic contact dermatitis from 17- β -estradiol is not frequent. This is probably because, according to the pharmacokinetic principles of transdermal drug delivery, the active drug should not bind to skin proteins in order to improve transcutaneous absorption, and, on the other hand, interaction with skin proteins is an important step in antigen presentation and skin sensitization for the development of allergic contact dermatitis. Furthermore, as an endogenous molecule, the immune system might be less reactive to estradiol, although several cases of immune or autoimmune reactions to estrogen (10), as well as to other steroid molecules (progesterone, testosterone and corticosteroids), have been described (11, 12). Cross-reactions between steroid molecules have been suspected (13), but our patients had negative tests to a progester-

one gel and to the corticosteroid mix used in the GPEDC standard series, which contains budesonide, tixocortol pivalate and hydrocortisone 17-butyrate.

The ideal vehicle for testing estradiol is not ascertained, but it is probably ethanol. Petrolatum was effective for estradiol patch testing in only 1 report (8), and in our patients, only the highest concentration gave a moderate (+) reaction, while in ethanol, we had ++ reactions with lower concentrations, as in the Boehncke & Gall patient (9).

Although not frequently, patients sensitized to the active drug of the TTS may suffer reactivation of previous eczema at the site of the patch, vesicular hand dermatitis or maculopapular generalized rash on systemic drug administration, as in our 2 patients. Systemic contact dermatitis from estrogen, after allergic contact dermatitis from topical estradiol, has previously been reported only once (8). Thus, estrogen replacement therapy may still be worth trying in such patients, as most will tolerate the drug well (9, 11) and a reaction is not life-threatening. Nevertheless, we should be aware of this possibility, so as to suspend systemic medication as soon as any reaction develops.

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