Allergic Contact Dermatitis from Calcipotriol

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Sir,

Calcipotriol (Daivonex®) is a vitamin D derivative that is efficacious in the treatment of psoriasis and disorders of epidermal hyperproliferation (1). It may cause irritant contact reactions, particularly on the face and intertriginous areas, but allergic reactions have also been reported. However, it has been difficult to confirm whether these are true allergic or irritant reactions. Allergic contact dermatitis can be diagnosed by patch testing with a concentration of 2 μg/ml in isopropanol (2), and by the positive repeated open application test (ROAT) (3). A few reports have demonstrated true allergic reactions to calcipotriol and here we present a further case of allergic contact dermatitis from calcipotriol.

CASE REPORT

A 31-year-old man with psoriasis for 10 years had previously received psoralen-UVA (PUVA) therapy three times a week for 2 years. He had also been treated with topical calcipotriol (Daivonex) ointment and scalp solution for several weeks. Following a short break, calcipotriol was restarted. A pruritic papulovesicular eruption developed on the psoriatic lesion of the upper and lower extremities, where the calcipotriol had been applied for one week. The patient had multiple tense bullae and vesicles with surrounding erythematous papules (Fig. 1). Laboratory examinations, including calcium, phosphate, urine analysis, liver and renal function test, were within normal limits. Histological examination revealed spongiosis of the epidermis with several vesicles and marked perivascular infiltration of lymphocytes, histiocytes and eosinophils. Eosinophils were also present in the vesicles of epidermis as well as within areas of spongiosis (Fig. 2). Patch testing with the Korean standard series (Chemotechnique Diagnostics, Sweden) was negative, but testing with Daivonex demonstrated a strong positive (++) reaction. A ROAT was performed and Daivonex ointment produced an itchy papulovesicular dermatitis on the forearm after five applications on the third day. The calcipotriol-free base used as a negative control did not induce dermatitis. Three months later, the patient was tested with commercial Daivonex ointment, Daivonex solution, and serial diluted calcipotriol in isopropanol (0.08, 0.4, 2.0, 5.0, 10, 50 μg/ml) using Finn Chambers® (Table I). The patient showed strong positive reactions (++) to 0.4, 2.0, 5.0, 10, 50 μg/ml and positive reactions (+) to 0.08 μg/ml on the fourth day of patch testing. Reactions to the vehicle, including isopropanol, menthol, sodium citrate, were negative.

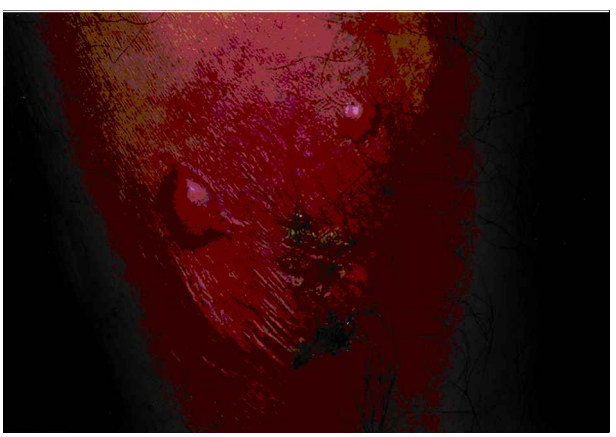

Fig. 1. Multiple bullae and tiny vesicles with surrounding erythematous papules on the left lower leg.

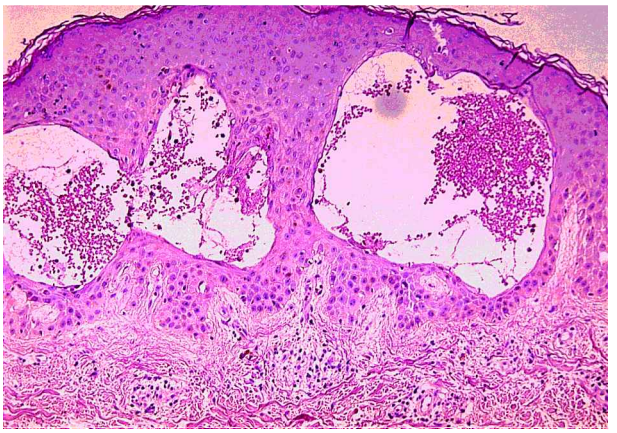

Fig. 2. Histopathological examination demonstrated spongiosis of the epidermis with several vesicles with perivascular infiltration with lymphocytes, histiocytes and eosinophils.

Table I. *The result of patch test with dilutions of calcipotriol*

Patch test materials		Patch test reactions	
		2 days	4 days
Korean standard series		–	–
–			
Daivonex® ointment (as is)		++	++
Daivonex® solution (as is)		++	++
Calcipotriol	50 μg/ml	+++	++
in isopropanol	10 μg/ml	++	++
	5 μg/ml	++	++
	2 μg/ml	++	++
	0.4 μg/ml	++	++
	0.08 μg/ml	+	+
75% isopropanol		–	–
Menthol	–	–	
Sodium citrate		–	–

DISCUSSION

Calcipotriol is a vitamin D derivative that is as potent as $1,25(OH)_2D_3$ in inhibiting epidermal proliferation, inducing differentiation and reducing inflammation, but has a markedly less hypercalcemic effect (4). Calcipotriol has demonstrated effects on various types of psoriasis, pityriasis rubra pilaris, inflammatory linear verrucous epidermal nevus, ichthyosis, and morphea (1). Moreover, calcipotriol has greater efficacy than tars, dithranol and topical corticosteroid in the treatment of psoriasis (5–7).

The toxicity of calcipotriol is low but human trials have shown that it may elevate the serum calcium levels (8).

Local cutaneous irritations may commonly occur as an adverse effect, whereas allergic contact dermatitis from calcipotriol has rarely been reported. Acute irritant reactions to calcipotriol are similar to allergic reactions in the clinical picture, and it is therefore difficult to differentiate between irritant and allergic contact dermatitis.

Yip & Goodfield (9) reported the first case of contact dermatitis from calcipotriol, and Frosch & Rustemeyer (10) concluded that contact allergy should be suspected if a severe dermatitis develops. Patch testing is non-conclusive, and serial dilution patch testing down to 0.08 μg/ml calcipotriol in isopropanol is necessary. If a strong positive reaction is observed with the reproduction at a concentration of 2 μg/ml after several weeks, it is most likely to be contact allergy.

Fullerton et al. (2) recommended that in the case of suspected allergy to calcipotriol the patient should be patch-tested with calcipotriol 2 μg/ml citrate-buffered isopropanol solution applied under occlusion for 48 h using small Finn Chambers. Another method to prove contact allergy to calcipotriol is a positive ROAT. De Groot (11) recommended 2–10 μg/ml calcipotriol in isopropanol for ROAT. Frosch & Rustemeyer (10) stated that ROAT with commercial materials for 7 days is useful in confirming the suspicion of an allergic sensitization. Zollner et al. (12) confirmed contact allergy to calcipotriol by a positive lymphocyte transformation test.

In our case, the patient clearly demonstrated contact allergy with sensitization to calcipotriol, because the reactions occurred during re-application of the ointment and solution. In patch testing, the patient had strong positive reactions down to the concentration of 0.4 μg/ml calcipotriol after 3 months in a non-dermatitis phase. In addition, ROAT was positive to the commercial ointment (50 μg/ml) within 3 days. Clinically, the lesions showed severe papulovesicular dermatitis at the site of calcipotriol application, which is consistent with allergic contact dermatitis; the histology revealed compatible with allergic contact dermatitis.

It was doubtful at first whether UV light had contributed to the contact dermatitis as a photoallergic or phototoxic reaction because the patient was treated with combined therapy with topical calcipotriol and systemic PUVA therapy. However, the patch test and the ROAT demonstrated positive reactions without UV.

Of previous case reports on contact allergy to calcipotriol, several could be interpreted as irritant dermatitis. The cases reported by Zollner et al. (12) and Frosch & Rustemeyer (10) are clearly contact allergy to calcipotriol. This report adds a typical case of allergic contact dermatitis from calcipotriol, and emphasizes the importance of considering calcipotriol as an allergic sensitizer, although the incidence of allergic reactions is low.

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