

Allergic contact dermatitis from oleyl alcohol in Elidel[®] cream

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We report an atopic dermatitis patient with recurrent hand dermatitis who developed a severe allergic contact dermatitis from the use of Elidel[®] cream. Diagnostic patch tests showed an isolated contact allergy to the emulsifier oleyl alcohol present in the product. Pimecrolimus appeared to have had an aggravating effect on the dermatitis in spite of its immunosuppressive effects. The initial clinical appearance of the patient's widespread dermatitis was atypical with resemblance to subacute cutaneous lupus erythematosus. Even though emulsifiers are widely used in topical products, contact allergic reactions to these are relatively uncommon.

Key words: allergic contact dermatitis; Elidel[®]; emulsifiers; oleyl alcohol; pimecrolimus. © Blackwell Munksgaard, 2006.

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Introduction

Allergic contact dermatitis from cosmetics and topical drugs is a well-recognized complication of dermatological therapy. Contact allergy to anti-inflammatory drugs including topical corticosteroids is well described (1–3). The clinical appearance of an allergic contact dermatitis is sometimes atypical and may in rare cases resemble lupus erythematosus or acute generalized exanthematous pustulosis (4, 5).

Calcineurin inhibitors are new topical drugs. Even though used increasingly, there has so far been only one report of allergic reactions to topical treatment with tacrolimus (6), but none to pimecrolimus. Here, we report a patient who developed a severe acute allergic contact dermatitis from treatment with Elidel[®] cream, caused not by the active drug but an emulsifier in the cream vehicle.

Case Report

A 20-year-old woman was referred with a suddenly developed widespread rash. She had a history of childhood atopic dermatitis, which healed in the early school years, followed by moderate, recurring vesicular hand dermatitis from her late teens. Diagnostic patch tests with the European standard series had been negative in dermatology practice. She had been treated with mometasone

furoate cream effective for the hand dermatitis, but because of recurrence on withdrawal, the treatment was changed to Elidel[®] cream 4 months earlier. It was well tolerated in the beginning, but treatment effect abated over time.

On referral, the patient had a widespread symmetrically located erythematous, edematous, sharply defined rash affecting hands, forearms, and neck. The clinical appearance had resemblance to subacute cutaneous lupus erythematosus (Fig. 1)

Topical treatment was changed to a betamethasone valerate cream, and the dermatitis healed. A 4-mm punch skin biopsy showed histologically a spongiotic dermatitis and negative immunofluorescence. Blood samples were unremarkable including negative antinuclear antibodies.

Diagnostic patch test was performed weeks later with the European standard series (TRUE[®] test, panels 1 and 2), supplemented with petrolatum-based preparations, a corticosteroid series, own topical products and Protopic[®] 0.1% ointment (Finn chambers[®] on Scanpor[®]). The reactions were read on day 3 and day 7.

The only positive reaction was a strong (2+) reaction to Elidel[®] cream.

A repeated open application test (ROAT) (7) with Elidel[®] cream was performed, and after just 2 applications to the 1 elbow flexure, she developed a widespread itchy rash on the back and



Fig. 1. Sharply demarcated acute dermatitis on dorsal aspect of hand and forearm.

forehead and initially a minimal reaction on the arm, which became clearly positive on day 9.

The patient agreed to subsequent patch tests with ingredients of Elidel[®] cream, and 4 months after the initial testing, a repeated patch test with Elidel[®] cream and a pimecrolimus-free placebo cream, provided by Novartis (Basel, Switzerland), was performed. She had positive reactions (2+) to both products, but the reaction was stronger to Elidel[®] cream. A ROAT with Elidel[®] and placebo cream was performed showing reactions to both products, but again stronger to the Elidel[®] cream.

Novartis supplied all the ingredients of Elidel[®] cream including pure pimecrolimus. Repeated patch tests with Elidel[®] cream, Protopic[®] 0.1% ointment, and the separate ingredients of Elidel[®] cream were performed. Pimecrolimus as such was tested in an ethanol-based dilution series (5%, 2.5%, 1%, 0.1%, 0.01%, 0.001%). As expected, a strong (2+) reaction to Elidel[®] cream was reproduced, and all other tests were negative except a strong (2+) reaction to oleyl alcohol 10% in petrolatum. Both reactions were seen already on day 2 (Fig. 2).

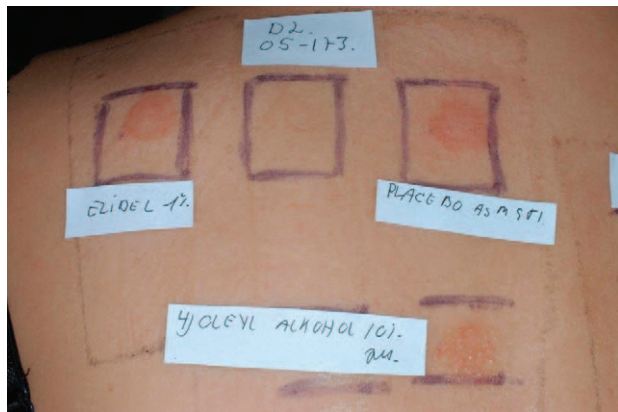


Fig. 2. Strong patch test reactions on day 2 to Elidel[®] cream, placebo cream and oleyl alcohol 10% pet.

All other tests including pimecrolimus and stearyl alcohol 30% in petrolatum were negative also on day 7.

The ROAT was repeated with placebo cream on one side and pimecrolimus 0.1% ethanol on the other. A strong reaction was seen to the placebo cream after 2 applications, with an itchy rash affecting not only the site of application at the forearm but also the shoulder and back on the same side. The ROAT with pimecrolimus was continued for 14 days and was negative, even though the concentration was increased to 2.5% ethanol after 1 week.

A total of 25 consecutive suspected contact dermatitis patients acted as controls and were patch tested with Elidel[®] cream as marketed and oleyl alcohol 10% in petrolatum, and they were all negative.

Discussion

To our knowledge, this is the first report of an acute allergic contact dermatitis to Elidel[®] cream. The active compound, pimecrolimus, was not the contact allergen but appeared to have an aggravating effect on the contact allergic reaction to oleyl alcohol used as emulsifier in the vehicle. This was evident from both patch tests and ROAT. The explanation for this clinical finding is dubious, and the initial clinical appearance was atypical for an allergic contact dermatitis with an erythematous, edematous rash with a sharply defined border, suggesting a combination effect with pimecrolimus. The patient did not consume alcohol during the test period, which has been reported causing application site erythema after pimecrolimus use (8).

Curry and Warshaw recently reported a patient with long-standing, persistent, stasis dermatitis, who on patch testing showed contact allergy to benzyl alcohol (9). The patient had used several topical products containing this allergen including Elidel[®] cream. Compared with our patient, however, the clinical picture in this case was a chronic dermatitis, worsened by the use of numerous benzyl-alcohol-containing products, and not that of an acute contact dermatitis elicited by a single product (Elidel[®]).

Even though emulsifiers are widely used in cosmetics and topical products, contact allergic reactions to these are relatively uncommon (10, 11). Among allergic reactions to emulsifiers, reaction to oleyl alcohol seems to be more common (12). Oleyl alcohol is a long-chain fatty alcohol often used as an emulsifier in the production of lubricants, papers, printing inks, cutting fluids, and cosmetics but only rarely used in topical drugs. Lipstick dermatitis resulting from oleyl alcohol

was first described in 1960 (13), and since then there have been scattered reports of allergic reactions to oleyl alcohol, primarily in cosmetics (14, 15). Oleyl alcohol might be a more common allergen than the relatively few reports indicate, as it is not tested on a routine basis. In 1996, Tosti et al. (12) tested 146 patients with suspected allergy to topical preparations with 5 fatty alcohols and found 34 positive reactions, of which 33 were due to oleyl alcohol 30% in petrolatum. We tested with 10% in petrolatum, and all the controls were negative.

Our case report illustrates the importance of a patient giving consent to repeated diagnostic tests, collaboration with the product manufacturer, and thorough investigation to identify the final allergen, because the primary tests were inconclusive.

Acknowledgement

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