

Allergic Contact Dermatitis Syndrome Due to Tocopherol Acetate, in Addition to Glycyrrhetic Acid

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Received December 18th, 2011; revised December 30th, 2011; accepted January 13th, 2012

ABSTRACT

Natural vitamin E is suggested to have an antioxidant function. However, the synthetic form of vitamin E, *DL*-tocopherol, which has been widely used in topical ointments, may cause allergic contact dermatitis. Here, we report a case of allergic contact dermatitis with erythema multiforme-like eruption caused by a topical ointment. Patch testing indicated a positive allergic reaction to an anti-inflammatory ointment the patient had been using and its ingredient, *DL*-alpha-tocopheryl acetate (vitamin E). In addition, a positive reaction to glycyrrhetic acid was observed. Both vitamin E and glycyrrhetic acid are useful ingredients of topical applications. However, the possibility that both can cause contact dermatitis, albeit rarely, should be considered.

Keywords: Allergic Contact Dermatitis; Tocopheryl Acetate; Vitamin E; Enoxolone; 18-Glycyrrhetic Acid

1. Case Report

A 39-years-old woman without any notable medical history had been using a skin lotion on her face, neck and arms for about 7 months without any problems. However, itchy erythema developed on the bilateral cubital fossae, and for this the patient began to apply an anti-pruritic and anti-inflammatory ointment that is widely used in Japan. Two weeks later, the rash had spread to her neck and upper extremities, and she stopped applying her skin lotion, while continuing with the ointment. She visited a local dermatologist and was prescribed topical corticosteroids (deprodone propionate for the trunk and extremities, and alclometasone dipropionate for the face). After two days, an erythema multiforme-like eruption and bullae spread to both extremities, pustules developed on the neck, and the patient became febrile. Therefore she visited our hospital and was admitted (**Figure 1**). Her con-

dition was finally improved after administration of a short course of oral corticosteroid (prednisolone 30 mg/day for three days, followed by gradual tapering). Patch testing demonstrated a positive allergic reaction to the anti-inflammatory ointment itself, its ingredients including *DL*-alpha-tocopheryl acetate 5% pet, glycyrrhetic acid 2% pet, and glycyrrhetic acid 0.2%, and the skin lotion (containing 0.002% *D*-gamma-tocopherol) based on the criteria of the International Contact Dermatitis Research Group. However, there was no reaction to *DL*-alpha-tocopheryl acetate 0.5% pet (**Table 1**). Control patch tests were performed on 5 healthy volunteers using *DL*-alpha-tocopheryl acetate and glycyrrhetic acid, but no allergic or irritant reaction was elicited.

2. Discussion

Both vitamin E and glycyrrhetic acid are widely used

Table 1. Patch test results.

		day 2	day 3	day 7
Ointment (she used)	as is	++	++	++
glycyrrhetic acid	0.2% pet	+	++	++
glycyrrhetic acid	2.0% pet	+	++	++
<i>DL</i> - α -tocopheryl acetate	0.5% pet	-	-	-
<i>DL</i> - α -tocopheryl acetate	5.0% pet	++	++	++
skin lotion (containing 0.002% <i>D</i> - γ -tocopherol)	as is	++	++	++
petroleum jelly		-	-	-

Readings were performed according to the International Contact Dermatitis Research Group criteria on day 2, day 3 and day 7; + is weak (nonvesicular) positive reaction; erythema, infiltration, possibly papules; ++ is strong (vesicular) positive reaction; erythema, infiltration, papules, vesicles.



Figure 1. Erythema and bullae on both arms.

in topical ointments. Natural vitamin E is suggested to have an antioxidant function. Several forms of vitamin E exist, and non-esterified *D*-alpha-tocopherol has the greatest biologic activity. The synthetic form, *DL*-tocopherol is a mixture of eight stereoisomers, and the esterified forms (usually the acetate ester) are more stable, although their antioxidant potential is minimal [1]. Furthermore, the *DL*-form of vitamin E has been reported to cause allergic contact dermatitis when applied topically [2-9], and only tocopherol causes an erythema-multiforme-like eruption [4]. Our patient showed no allergic reaction to *DL*-alpha-tocopheryl acetate 0.5%, which was an ingredient of the cream she was using. This was compatible with the fact that a 10% pet patch-test concentration of tocopheryl acetate has been recommended [10]. However, Matsumura [8] has reported a case of allergy elicited by much lower concentrations (0.5%, 0.25%). Enoxolone (18-glycyrrhetic acid), on the other hand, a metabolite of glycyrrhizinic acid, is a widely used ingredient of topical anti-inflammatory preparations [11], and some cases of sensitization to it have been reported [11-13].

We suspect that our patient had become sensitized to *DL*-alpha-tocopheryl acetate and glycyrrhetic acid in-

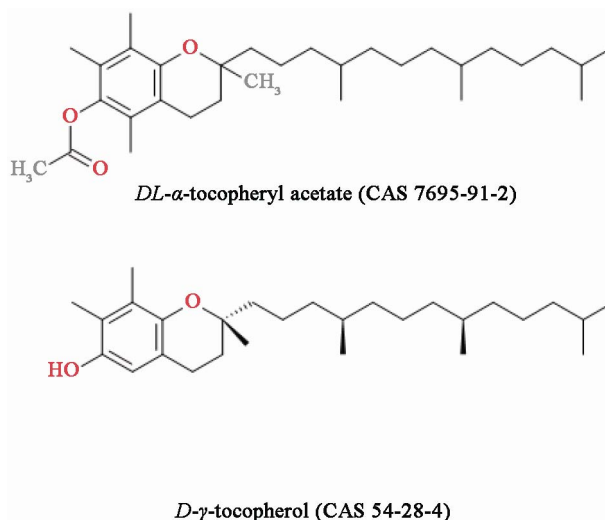


Figure 2. Chemical structure of *all-rac*-alpha-tocopheryl acetate (*DL*-alpha-tocopheryl acetate) and *D*-gamma-tocopherol.

dependently, as their chemical structures are quite different. On the other hand, the chemical structures of the two tocopherol forms are quite similar (**Figure 2**). Although vitamin E and glycyrrhetic acid are widely used in ointments and cosmetics, and are useful ingredients, the present case suggests that both can cause contact dermatitis, albeit rarely.

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