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Contact dermatitis caused by efinaconazole solution for treatment of onychomycosis

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Key words: alkyl lactate; CAS no. 164650-44-6; efinaconazole; topical antifungal agents.

Efinaconazole 10% topical solution was introduced as the first topical treatment for onychomycosis in Japan in September 2014. We report the first case of allergic contact dermatitis caused by efinaconazole 10% topical solution.

Case Report

A 64-year-old Japanese man presented with itchy, scaly erythema of both great toes in October 2014. The patient had suffered from ungual hyperkeratosis and itchy, scaly erythema of the interdigital web spaces for 5 years, for which he had consulted our department in September 2014. On that occasion, onychomycosis and interdigital erythrasma was diagnosed, and efinaconazole 10% topical solution (Kaken Pharmaceutical Company Limited, Tokyo, Japan) and ketoconazole cream (Janssen Pharmaceuticals Inc., Tokyo, Japan) were prescribed.

At the current presentation, scaly erythema with microvesicles, erosions and crusts in the subungual area and web space and around the toenails were observed, which had started 1.5 months after treatment initiation (Fig. 1). Repeat direct microscopic examination of a skin sample on potassium hydroxide mounts did not show any fungal infection. Therefore, we diagnosed contact dermatitis caused by efinaconazole 10% topical solution, as the patient applied the solution not only to the nail but also to the skin around the nail and the web space.

Patch testing was performed with the Japanese standard series supplemented with efinaconazole 10% topical



Fig. 1. Clinical appearance 1.5 months after the start of treatment with efinaconazole 10% topical solution.

Table 1. Patch test results

Allergens	D2	D3
Japanese baseline allergens		
Potassium dichromate 0.5% aq.	+	+
Formaldehyde 1% aq.	+	+
Ketoconazole cream	–	–
Luliconazole cream	–	–
Terbinafine cream	–	–
Efinaconazole 10% topical solution	+	+
Individual ingredients of efinaconazole 10% topical solution		
Efinaconazole 10% pet. or ethanol	+	++
Alkyl lactate pet. or in ethanol	?+	+
Decamethyl cyclopentasiloxane pet. or ethanol	–	–
Diisopropyl adipate pet. or ethanol	–	–
Dibutylhydroxytoluene, anhydrous citric acid pet. or ethanol	–	–
Anhydrous citric acid aq.	–	–
Disodium EDTA aq.	–	–
Ethanol	–	–

Concentrations of all antifungal agents and individual ingredients of efinaconazole 10% topical solution are 'as is'. The concentration of ingredients is proprietary.

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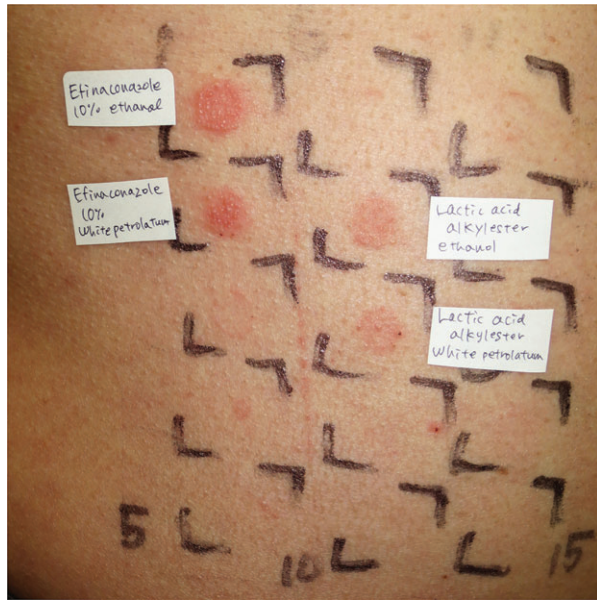


Fig. 2. Positive patch test reaction to efinaconazole and alkyl lactate on D3.

solution, ketoconazole cream, luliconazole cream (Pola Pharma Inc., Tokyo, Japan), and terbinafine cream (Novartis Pharmaceuticals Japan, Tokyo, Japan). Patch test units were applied on the patient's back with Patch Tester Torii® (Torii Pharmaceutical, Tokyo, Japan), and left occluded for 2 days. Readings were taken on day (D)2 and D3 according to ICDRG criteria; the results

are summarized in Table 1. Efinaconazole 10% topical solution elicited a positive reaction. Thus, additional patch testing was performed with the individual ingredients of efinaconazole 10% topical solution, including efinaconazole, alkyl lactate, decamethylcyclotrisiloxane, diisopropyl adipate, dibutylhydroxytoluene, anhydrous citric acid, disodium edentate, and ethanol (concentrations as in the product, provided by Kaken Pharmaceutical Company Limited; the concentration is proprietary); efinaconazole and alkyl lactate elicited positive reactions (Fig. 2). Patch testing of 9 healthy controls with efinaconazole 10% topical solution, efinaconazole 10% pet. and 10% ethanol, and alkyl lactate, white petrolatum and ethanol all gave negative results on D2 and D3. Contact dermatitis resolved within 2 weeks after the prescription of topical betamethasone butyrate propionate.

Discussion

The mechanism of action of efinaconazole (CAS No. 164650-44-6) – a lipophilic triazole antifungal – is blockage of ergosterol biosynthesis by inhibition of 14 α -demethylase; its low keratin affinity may contribute to its efficacy in onychomycosis (1, 2). Alkyl lactate – an emollient and solvent – is an ingredient in cosmetics formulations (3). The possibility of efinaconazole 10% topical solution-induced contact dermatitis, possibly because of the stronger penetration of skin and nails than occurs with other topical antifungal agents, needs to be considered.

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