

Ulcerative contact dermatitis caused by benzethonium chloride

Yu Hirata, Teruki Yanagi, Yasuyuki Yamaguchi, Kazumasa Sato, Satoru Shinkuma, Hiroo Hata and Hiroshi Shimizu

Department of Dermatology, Hokkaido University Graduate School of Medicine, 060-8638 Sapporo, Japan

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Quaternary ammonium compounds, such as benzethonium chloride (BEC) (CAS no. 121-54-0), are widely used as disinfectants. BEC is a well-characterized skin irritant, but it rarely causes sensitization (1). Previously, Dao et al. reported patch test results with the quaternary ammonium compounds BEC and benzalkonium chloride (BAK) in 142 patients, confirming that sensitization to BEC and BAK is rare (2). Herein, we report a case of contact dermatitis with ulceration caused by BEC.

Case Report

A 31-year-old Filipino woman presented with a 3-month history of erythema on the right big toe. Before onset, she had been suffering from dyshidrotic eczema on the soles for 4 months. The eczematous lesion on the big toe gradually worsened, showing exudative erythema. The patient had applied the topical disinfectant MakironS® (Daiichi Sankyo Healthcare, Tokyo, Japan), with 0.10% BEC as an active ingredient, to the right big toe three

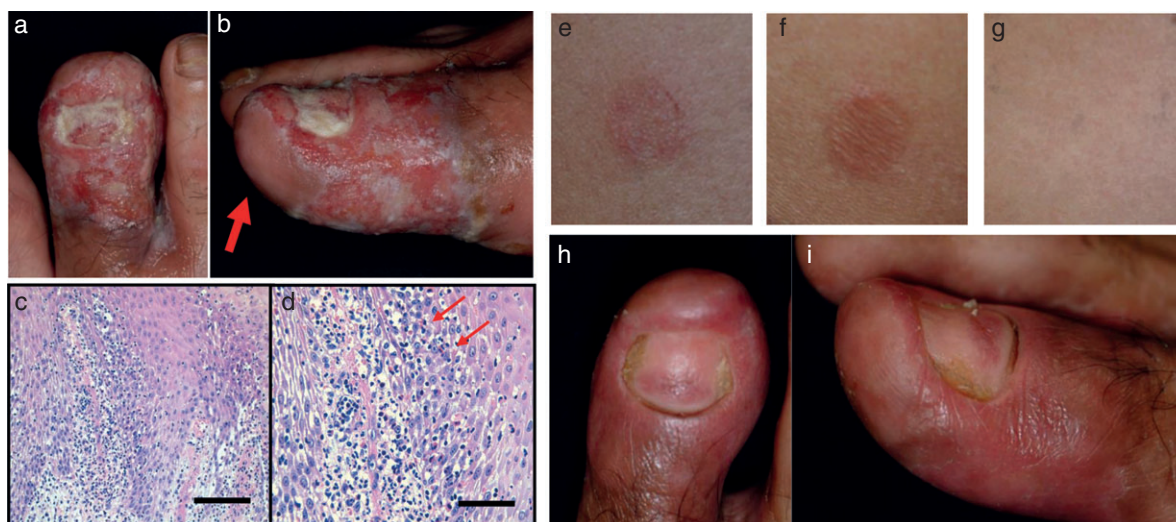


Fig. 1. (a, b) ulcer with surrounding erythema on the right big toe. The tip remained intact (b, red arrow). (c, d) A skin biopsy from the right big toe shows liquefaction degeneration and eosinophilic spongiosis (haematoxylin and eosin stain). Scale bars: 100 μ m (c) and 50 μ m (d). Original magnification: $\times 100$ (c) and $\times 200$ (d). Infiltrated erythema was observed on the patch test areas on day 3: (e) benzethonium chloride (0.1%); (f) MakironS® ('as is'). There was no reaction on the negative control area [(g) white pet.]. After 1 week treatment with topical steroid ointment, the ulcerative and erythematous lesion rapidly improved (h, i).

Correspondence: Teruki Yanagi, Department of Dermatology, Hokkaido University Graduate School of Medicine, N15 W7, 060-8638 Sapporo, Japan. Tel: +81 11 706 7387; Fax: +81 11 706 7820. E-mail: yanagi@med.hokudai.ac.jp

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Table 1. Clinical features of patients with contact dermatitis caused by benzethonium chloride (BEC); scoring of test reactions according to ICDRG criteria

Case no.	Sex	Age (years)	Duration of disinfectant treatment	Location	Clinical features	Causative agent(s)	Patch test with BEC (0.1%), day 3	Vehicle	References
1	M	55	3 months	Left index finger	Ulcer	BEC	Positive (++)	Not described	(3)
2	F	45	6 months	Right sole	Erosion/ulcer	BEC; dibucaine hydrochloride; chlorpheniramine maleate	Positive (++)	Not described	(4)
3	F	2	6 days	Head	Erythema/erosion	BEC	Positive (+)	pet.	(5)
4	M	20	3 weeks	Right dorsum of the hand	Erythema	BEC; dibucaine hydrochloride	Positive (+)	aq.	(5)
5	F	51	2 months	Both lower legs	Ulcer	BEC	Positive (++)	Not described	(6)
Present case	F	31	3 months	Right big toe	Ulcer/erythema	BEC	Positive (+)	aq.	–

F, female; M, male.

times daily for 3 months. At initial examination, a skin ulcer with surrounding itchy erythema was observed on the right big toe (Fig. 1a,b). The lesion was in the shape of a band around the toe, with the tip remaining unaffected (Fig. 1b, arrowheads). Laboratory data and complete blood counts were within normal limits. The skin biopsy specimen from the edge of the ulcer showed infiltration of eosinophils in the epidermis, with severe spongiosis (eosinophilic spongiosis) (Fig. 1c,d). Clinical and histopathological findings were suggestive of contact dermatitis; therefore, patch testing was performed on the back with MakironS® 'as is', BEC (0.10% aq. wt/vol), and chlorpheniramine maleate (1% aq. wt/vol, another component of MakironS®). Skin reactions were assessed on day (D) 2, D3, and D7, according to ICDRG criteria. At all readings, infiltrated erythematous lesions (+) were observed on the patch test areas that had been exposed to BEC (0.1%) and MakironS® (Fig. 1e–g). Excipients included fragrances, allantoin, and menthol; however, these components were not tested. From these results, contact dermatitis caused by BEC was finally diagnosed (see Discussion). The patient stopped using MakironS®, and the lesion was treated with topical clobetasol propionate ointment, yielding marked improvement within 1 week (Fig. 1h,i).

Discussion

To our knowledge, there have been only 5 reported cases of contact dermatitis caused by BEC (Table 1)

(3–6). Our review shows that 5 of 6 patients showed positive reactions to BEC in patch tests. Clinically, 4 of 6 patients showed ulcerative skin lesions. The patient with long-term (>3 months) use of BEC showed severe skin ulceration. In general, the common features of contact dermatitis are well-demarcated erythema and/or vesicle formation with itching, but not ulcer formation. Thus, ulcer formation is a characteristic feature of contact dermatitis caused by BEC administration.

We speculate that both irritant and allergic mechanisms were involved in the present case. In the previous study, Dao et al. used a patch test series (BAK 0.15% aq., BAK 0.15% pet., BEC 0.15% aq., and BEC 0.5% aq.) in 142 patients to assess the prevalence of sensitization to these quaternary ammonium compounds. This study suggested that a reaction present on D7 can be defined as allergic (2), which would confirm an allergic reaction in our patient, who had a positive reaction on D7. Basically, BEC irritates the skin; thus, we think that irritant dermatitis occurred first, after which the patient became sensitized to BEC because of long-term use.

In summary, the present case and the cases reviewed suggest that the use of a BEC-containing disinfectant should be suspected when a refractory ulcerative lesion is seen.

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