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LETTER TO THE EDITOR

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Severe pustular lesions induced by topical immunotherapy with squaric acid dibutylester for alopecia totalis

Dear Editor,

Case 1: A 41-year-old female visited our department complaining of diffuse alopecia unresponsive to topical therapies. On physical examination, the patient had almost no scalp hair, and bilateral eyebrows had fallen off. Half of the patient's eyelashes, as well as all of her axillary and pubic hair, were also absent. She had allergic rhinitis, and serum IgE was slightly elevated (247 IU/mL, normal <169). Methylprednisolone half-pulse therapy (500 mg/d for 3 days) was administered, but had no effects. After obtaining informed consent, topical application of squaric acid dibutylester (SADBE) solution was started after a positive patch test reaction (2%). Initially, we applied SADBE with a concentration between 10^{-6}% and 0.1% on the small areas of the scalp using a fin chamber, among which 0.1% showed erythema. We then started application of SADBE solution (0.05%); however, itchy erythema appeared at that night, and pustular lesions appeared on the next day. After 3 days, diffuse erythema and a number of tiny pustules had appeared on the scalp (Figure 1A). She was successfully treated with oral prednisolone (30 mg/d) within 2 weeks. Thereafter, she tried SADBE therapy again at a concentration of 0.01%, which showed a dramatic effect within 9 months (Figure 1B).

Case 2: A 39-year-old female with atopic dermatitis and bronchial asthma presented with total hair loss, involving the scalp, eyebrows, eyelashes, axillae, and pubic region. Various therapies, including methylprednisolone pulse therapy, resulted in no effects. Serum IgE was elevated (1975 IU/mL). We applied between 10^{-6}% and 10^{-2}% SADBE, and 10^{-2}% caused erythema. Next, we started application of SADBE solution (10^{-3}%) to the whole scalp. However, itchy erythema appeared at that night, and pustular lesions appeared the next morning. On the next day, diffuse erythema, a number of tiny pustules on the scalp, and slight edema of the bilateral upper eyelids had appeared (Figure 1C). She was successfully treated with oral prednisolone (30 mg/d).

The most common adverse effect of topical immunomodulatory therapy is eczema, and other rare forms include local irritation, blister formation, persistent dermatitis, lymphadenopathy, generalized eczema, urticarial reaction, and vitiliginous depigmentation.[1–4] We herein reported two cases of alopecia totalis, who developed a severe pustular reaction on the total scalp after topical application of 0.05% and 0.001% SADBE, respectively. Case 1 showed lymphadenopathy on the postauricular areas, and Case 2 developed upper eyelid edema. Systemic prednisolone was required in both cases. The mechanism of contact immunotherapy has been suggested to modulate cytokine gene expression balance, and interferon-γ expression was reduced while IL-2, IL-8, IL-10, and TNF-α levels were increased in the lesional skin.[5] Furthermore, recent studies have demonstrated that Th17 cells are involved in the pathogenesis of contact hypersensitivity. The mechanism underlying severe pustulation is uncertain; however, IL-8 and IL-17 are known to attract neutrophils and thus may have played a role in the induction of pustular conditions. Our patients had allergic conditions that may be associated with the development of severe adverse events. Careful attention should be paid when carrying out contact immunotherapies for patients with allergic predisposition.

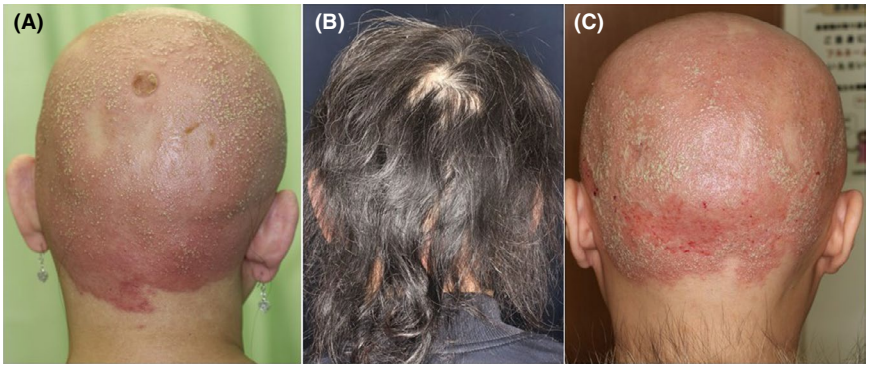

FIGURE 1 A, Diffuse well-circumscribed erythema with a number of pustular lesions on the occipital scalp (Case 1). B, Successful treatment with 0.01% SADBE 9 mo later. C, Diffuse erythema with a number of pustular lesions on the occipital scalp (Case 2)

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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