

LETTER TO THE EDITOR

Disseminated lichen planus due to a zinc allergy

Dear Editor,

Although lichen planus is one of the cutaneous inflammatory dermatoses in which the involvement of metal allergy has been considered,¹ to the best of our knowledge, there has been no previous report of disseminated lichen planus due to zinc allergy, and only two cases of oral lichen planus due to zinc have been reported.^{2,3} A T-helper (Th)1-predominant immunological status is considered to be one of the most important aspects of the pathogenesis of lichen planus.⁴

A 62-year-old woman was referred to us with a 6-week history of multiple, pruritic, dark-red plaques, which emerged initially on the dorsal surface of her hands and gradually progressed up her limbs and face (Fig. 1a,b). Subsequently, a white, atrophic, linear lesion on the right oral mucosa appeared (Fig. 1c). A skin biopsy revealed an apparent lichenoid reaction (Fig. 1f) with CD8-positive cell infiltration at the interface between the dermis and epidermis (data not shown). Conventional therapies, such as topical corticosteroids and p.o. administration of an anti-histamine (olopatadine hydrochloride), were administered for 5 months, but they did not demonstrate any beneficial effect.

The patient had a history of ingesting a large quantity of oysters 2 weeks before the onset of the symptoms and her dental examination revealed that she had a total of 14 metallic crowns. Therefore, a patch test with a metal series (Torii Pharmaceutical, Tokyo, Japan) consisting of 16 metals was performed. The patient developed a highly positive (++) reaction (International Contact Dermatitis Research Group criteria) to zinc chloride on days 2 and 3, a positive (+) reaction to manganese chloride on day 2, and a (+?) reaction to platinum chloride on day 2. Notably, her skin manifestations worsened after the patch test (Fig. 1d,e). Concomitant narrowband ultraviolet (UV)-B irradiation therapy showed some therapeutic benefit, but the skin manifestations were still refractory. The metal analysis of some of the patient's crowns revealed that all of them contained zinc, but not manganese or platinum. Removal of all of her dental metallic crowns and concomitant therapies for dental caries were started, and were continued for 5 months. The restriction of excess dietary zinc, by prohibiting or limiting the consumption of oysters, processed cheese, milk chocolate, black soybean cocoa and so on, was also started. Finally, her oral and skin symptoms disappeared after the removal of the metallic crowns was completed, even though the narrow band UV-B irradiation therapy was discontinued due to its insufficient effect. Complete remission has been maintained since then without any treatment. The patient was negative for both serum hepatitis B virus antigens and antibodies for hepatitis C virus.

A lymphocyte stimulation test (LST) revealed a reaction to zinc chloride (20 µg/mL), with a stimulation index (SI) of 2742% in the present patient. This value was much higher than those of four

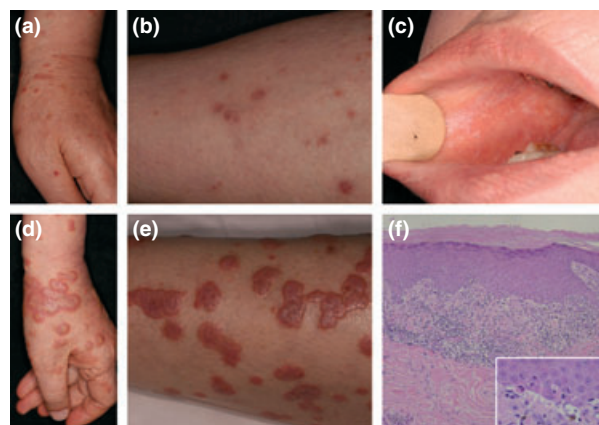


Figure 1. Multiple dark-red plaques were observed on (a) the dorsal surface of the patient's hands, and also on (b) the extensor surfaces of the lower extremities at the initial presentation. (c) A white, atrophic, linear lesion on the right oral mucosa was also found. (d,e) The multiple dark-red plaques became raised and expanded after the patch test with the metal series. (f) A histological examination of the skin obtained from the lateral side of her right lower leg showed irregular acanthosis, hypergranulosis and dense band-like infiltration of lymphocytes in the upper dermis, with prominent vacuolization of the basal cell layer and some necrotic keratinocytes (hematoxylin–eosin, original magnification $\times 100$ [inset $\times 400$]).

age-matched healthy volunteers (average of SI, $222 \pm 64\%$). The reactions of her lymphocytes to manganese chloride and platinum chloride were within the stimulation indices of non-stimulated negative controls (data not shown).

We next examined the interferon (IFN)- γ /interleukin (IL)-4 ratio in the supernatants harvested during the LST with zinc chloride in the patient and two age-matched healthy volunteers to assess the involvement of the Th1-predominant immunological status. The IFN- γ /IL-4 ratio in the patient was increased compared to those in the healthy volunteers, both before (IFN- γ /IL-4 ratio: the patient, 0.74; one healthy volunteer, 0.49; another healthy volunteer, 0.34) and after (IFN- γ /IL-4 ratio: the patient, 0.95; one healthy volunteer, 0.51; another healthy volunteer, 0.42) the stimulation with zinc chloride. The LST in healthy volunteers were performed under approval of the Ethics Committee of Oita University.

The patient's entire clinical course and laboratory examinations suggest that a zinc allergy with a Th1-predominant immunological status was strongly involved in the emergence of lichen planus in the present case, although an oral provocation test with zinc was not permitted by the patient.

Notably, the level of SI of the LST in our present case was very high. It should therefore be addressed in the future whether such a

high reactivity to zinc was involved in the dissemination of the lesions, in contrast to cases in which the lesion was localized in the oral cavity.^{2,3} Interestingly, a relatively high reactivity to zinc (an SI of 518% [normal, <180%]) was observed by LST in a case which displayed exacerbation of systemic allergic contact dermatitis due to zinc, even though zinc has generally been recognized only extremely rarely as an allergen.⁵

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