

Dear Editor

Systemic Contact Dermatitis due to Zinc Successfully Treated with a Zinc-Restricted Diet: A Case Report

Metal allergies may result in allergic contact dermatitis and also systemic contact dermatitis.¹ Metals such as nickel and chromium are well known allergens that cause systemic contact dermatitis, but such zinc allergies are less common.² We herein report a case of systemic contact dermatitis due to zinc that was successfully treated with a zinc-restricted diet.

A 58-year-old female experienced multiple pruritic eruptions covering her entire body in June 2010. Although several therapies, including the application of steroid ointment and administration of anti-allergic drugs and cyclosporine were performed at another hospital, the eruptions were not improved. She visited our hospital in January 2011. Red papules and

plaques with lesions 2-15 mm in diameter were distributed over her entire body (Fig. 1a, b). On a histological examination of the lower leg, there was noted to be vacuolar alterations and many lymphocytic infiltrations surrounding the vessels and appendages of skin. Few eosinophils were observed in the dermis (Fig. 1c, d). We performed a patch test with a metal series (Torii Pharmaceutical Co., Ltd., Tokyo, Japan) consisting of aluminum chloride, gold chloride, tin chloride, iron chloride, platinum chloride, palladium chloride, indium chloride, manganese chloride, silver bromide, cobalt chloride, potassium dichromate, nickel sulfate, chromium sulfate, copper sulfate, and zinc chloride. She developed a highly positive reaction to only zinc chloride on day 2 (++), day 3 (+++), and day 7 (+++) (ICDRG criteria, Fig. 1e). In addition, flare-ups of the original eruptions occurred around the area of zinc patch test. A lymphocyte stimulation test (LST) revealed a reaction to zinc chloride (20 µg/ml), with a stimulation index (S.I.) of 985% in this patient. This value was much higher than those of

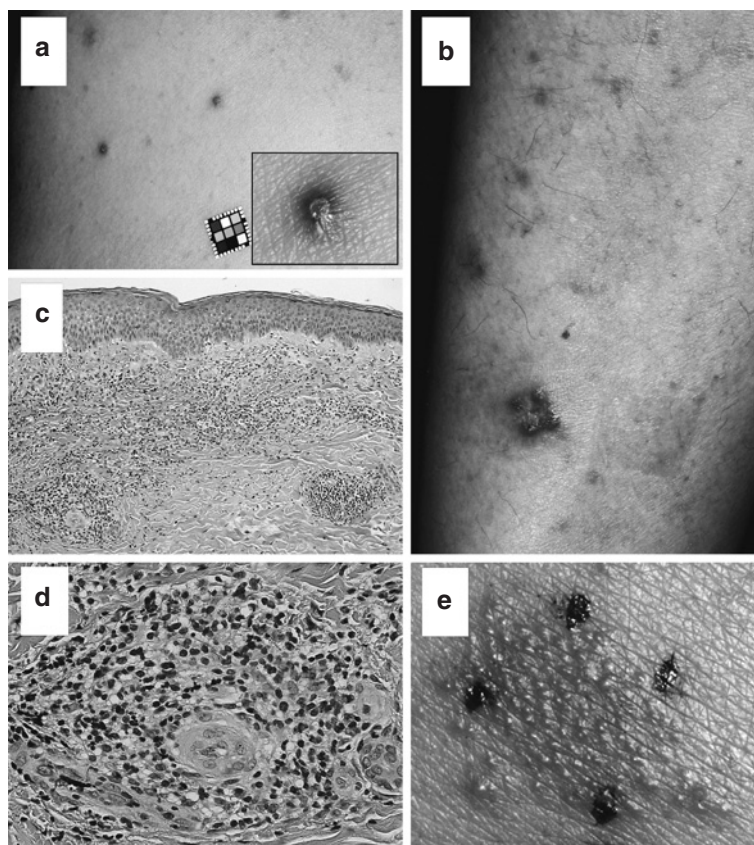


Fig. 1 Pruritic papules and plaques developed over her entire body (a, b). Basal vacuolopathy was observed, and inflammatory cells had infiltrated around the appendages and blood vessels (c). There were a lot of lymphocytes and few eosinophils (d). The findings of the patch test. Many papules and vesicles with erythema developed (Day 3; Zinc chloride, e). (c, d); Hematoxylin and Eosin staining. Original magnification; (c) $\times 100$, (d) $\times 400$.

Table 1 Cases of zinc allergy diagnosed by the LST

Reference	Age/sex	Clinical features	S.I. (%)
2	37/M	Systemic dermatitis	518
5	59/F	Palmoplantar pustulosis	1880
6	62/F	Disseminated lichen planus	2742 (222 ± 64) [†]
7	49/F	Systemic dermatitis	396
10	52/F	Stomatitis	883 (127 ± 32) [†]
Present case	58/F	Systemic dermatitis	985 (222 ± 64) [†]

[†] values in parenthesis are the average of four or six healthy volunteers.

four age-matched healthy volunteers (average of S.I., 222 ± 64%). Systemic contact dermatitis due to zinc in foods was suspected, because she had daily eaten a lot of almonds, chocolates and cheeses, which include high levels of zinc. She started avoiding of foods that have high levels of zinc, such as those foods, liver and oyster.³ The eruptions gradually started improving two or three weeks later, and she no longer needed treatment four months after starting the zinc-restricted diet. In addition, the eruptions flared up after she ate chocolate cake. According to these clinical and laboratory findings, we concluded that the refractory eruptions were systemic contact dermatitis due to dietary zinc, although a provocation test by the ingestion of zinc was not allowed.

Metals that are electrophilic have the ability to ionize and react with proteins, thus forming complexes that can be recognized by dendritic cells, which allows for sensitization to occur.⁴ It is recognized that the metals present in foods and dental fillings can induce several types of systemic skin inflammation. Zinc is an essential trace element involved in many physiological functions, and is included in many foods and widely used in dental restoration.¹ Although zinc allergy is rare, palmoplantar pustulosis,⁵ lichen planus⁶ and systemic dermatitis^{2,7} due to zinc were reported previously. The main cause of these cases was dental fillings containing zinc, and the symptoms improved after removal of the dental fillings. In terms of dietary metal allergies, nickel and cobalt are well known causes,¹ but, this is the first report of systemic contact dermatitis due to zinc, in which the patient was successfully treated with a zinc-restricted diet alone, without the removal of any dental fillings. Naturally, the patient could not completely avoid all foods including zinc, because zinc is an essential trace element included in many foods.^{1,3} However, a study of systemic nickel allergy found a dose-response relationship between nickel ingestion and the occurrence of dermatitis flare-ups.⁸ Therefore, the patient's eruptions might have improved, since

the ingested dose of zinc decreased. The levels of zinc in the peripheral blood were not examined in the present case. Therefore, whether the efficacy of the zinc-restricted diet was associated with an alteration of the levels of zinc in the peripheral blood remains unclear.

We performed a LST to zinc for the evaluation of allergic reaction to zinc. Basically, LST is not recommended for the diagnosis of contact allergies to the metals; gold, palladium and nickel, since a large number of false-positive results (S.I. >200%) can be obtained in patients with negative patch test reaction,⁹ although some metal allergy patients who demonstrated negative patch test reactions for the causative metals might be included in the false-positive group.^{3,9} In addition, the reaction of the LST to zinc in healthy controls has not been fully assessed. Therefore, we performed the LST for zinc in healthy volunteers under the same experimental conditions as in the patient's case. In fact, some positive reaction to zinc was detected in our four healthy volunteers (S.I., 222 ± 64) as well as in six subjects (S.I., 127 ± 32) in another report,¹⁰ suggesting that false-positive results can be frequently obtained in the reaction to zinc (Table 1). However, it should also be noted that the value of S.I. in each case of zinc allergy, including our present case, was much higher than the values in healthy volunteers (Table 1). These results suggest that the LST for zinc could be useful if the values are evaluated with reference to those of healthy volunteers, although a larger scale assessment should be performed to conclude about the false-positive in LST for zinc.

Finally, we could not completely exclude an involvement of allergy to other metals such as nickel, because a patch test is not always positive in cases of systemic metal allergy.³ Moreover, chocolate and almonds include many metals.^{1,3} On the other hand, flare-ups of the original eruptions emerged in accordance with the occurrence of the positive patch test reaction to zinc in the present case. In addition to the result of the LST, this finding strongly suggests that the eruptions were associated with zinc, rather than other metals, and that a provocation test by ingestion of zinc is not necessarily essential to indicate the involvement of a zinc allergy in the present case. In fact, a similar case of exacerbation of systemic allergic dermatitis due to the zinc patch test was reported previously.²

Takashi Sakai¹, Yutaka Hatano¹ and Sakuhei Fujiwara¹

¹Department of Dermatology, Faculty of Medicine, Oita University, Oita, Japan

Email: t-sakai@oita-u.ac.jp

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