



Contents lists available at ScienceDirect

Allergology International

journal homepage: <http://www.elsevier.com/locate/alit>

Letter to the Editor

Patch testing in patients with recurrent vesicular hand eczema

Dear Editor,

Hand eczema is an inflammation of the skin of the hands; some people with hand eczema may also have foot eczema.¹ Recurrent vesicular hand eczema, also known as pompholyx or dyshidrotic eczema, is cutaneous inflammatory disease of the palmoplantar regions characterized clinically by appearance of small tense vesicles and histologically by spongiotic vesicles. Previous reports have shown a dysfunction of the acrosyringium, debunked, hyperhidrosis.² Furthermore, several previous reports have suggested the influence of metal in food or dental alloy and contact sensitivities on the course of patients with recalcitrant vesicular hand and foot eczema.^{2–7} The purpose of this study was to investigate the frequency of contact hypersensitivity in patients with recurrent vesicular hand eczema and the relationship between metal allergy and recalcitrant eczema in the patients.

We conducted a retrospective study from January 2008 to December 2015 in the Department of Dermatology, University Hospital, Kyoto Prefectural University of Medicine, on a total of 48 patients (21 men, 27 women; median age: 56 years old; range: 15–79 years old) with recalcitrant vesicular hand and foot eczema had received patch testing, as previously reported.⁸ The diagnosis of recurrent vesicular hand eczema was made on the basis of clinical presentation and history. Skin biopsies were performed in 14 patients to distinguish eczema from other palmoplantar diseases. These findings showed spongiosis and vesiculation in the epidermis and perivascular infiltration of lymphocytes in the upper dermis. The patients suffered from vesicular eczematous lesions on only hands ($n = 23$), only feet ($n = 3$), or both hands and feet ($n = 22$). The study protocol was approved by the university ethics committee and was conducted in accordance with the Declaration of Helsinki.

Patch testing was performed in the patients with metal series, dental material series, the Japanese standard series (Supplementary Table 1), and/or suspected products, on normal looking skin of the back with aluminum cups (Finn Chamber®, SmartPractice, Phoenix, AZ, USA). No patients had been treated with systemic steroids or immune suppressive agents. Patches in the tests were removed at 2 days, and the results were assessed after 2, 3, and 7 days, based on the recommendations of the International Contact Dermatitis Research Group. Results classified as +, ++, or +++ were defined as positive for an allergic reaction in contrast to all other results (negative, doubtful or irritative) which were not regarded as positive.

A total of 18 (37.5%) patients had a positive patch test reaction to at least one substance or product (Table 1). The prevalence was

33.3% ($n = 7$) in men and 40.7% ($n = 11$) in women. This difference was mostly due to nickel (9.5% versus 22.2%) and cobalt (4.7% versus 11.1%). Five patients with atopic dermatitis were included. Two patients with atopic dermatitis had a positive patch test reaction to paraben and antiseptic, respectively.

With regard to metal allergy, 14 patients (29.2%) had a positive patch test reaction to at least one metal. The prevalence was 36.8% ($n = 14$) in 38 patients with dental alloy and 0% ($n = 0$) in 10 patients without dental alloy. According to previous studies, the occurrence of metal allergy in patients with recurrent vesicular hand eczema ranges between 20% and 25%.^{3,4} In 4 patients with a positive patch test reaction to metal, dental alloy containing allergenic metal was removed. However, skin symptoms of all the patients were not improved at one to three years after removal of dental alloy (Table 2). These findings imply that dental alloy may be not always associated with the development of vesicular eczematous lesions, although the relationships between recalcitrant eczema and dental alloy were reported.⁵

A metal-free diet was done in 6 patients with a positive patch test reaction to metal and 3 patients with no patch test reaction to metal. Eczematous lesions and itching were partially reduced in only one patient with no patch test reaction to metal at about

Table 1

The prevalence of contact sensitizations in patients with recurrent vesicular hand eczema.

	Concentration and vehicle	Contact sensitization prevalence% (n/n _{total})
Metals		
Nickel sulfate	5% aq.	16.7% (8/48)
Cobalt chloride	2% aq.	8.3% (4/48)
Gold sodium thiosulfate	0.25% pet.	6.3% (3/48)
Potassium dichromate	0.5% aq.	4.2% (2/48)
Manganese chloride	2% pet.	4.3% (2/47)
Palladium chloride	1% aq.	2.1% (1/47)
Silver bromide	2% pet.	2.1% (1/47)
Amalgam	5% pet.	5.0% (1/20)
Fragrances		
Balsam of Peru	25% pet.	4.8% (1/21)
Preservations		
Paraben mix	15% pet.	9.5% (2/21)
Kathon CG	0.01% aq.	4.8% (1/21)
Rubber accelerators		
Thiuram mix	1.25% pet.	9.5% (2/21)
Topical drugs		
Antifungal drug	as is	20.0% (2/10)
Antiseptic	as is	10.0% (1/10)
Other chemicals		
Caine mix	7% pet.	4.8% (1/21)
p-Phenylenediamine	1% pet.	4.8% (1/21)

Peer review under responsibility of Japanese Society of Allergy.

<http://dx.doi.org/10.1016/j.alit.2017.03.006>

1323–8930/Copyright © 2017, Japanese Society of Allergy. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Table 2
Clinical information and prognosis of the patients after avoidance of causative factors.

Age/Gender	Location	Positive results of patch testing	Guidance	Results of avoidance
73/F	Hands	None	Metal-free diet	Partial improvement
56/M	Hands	Paraben mix	Metal-free diet	No change
			Avoidance of moisturizer containing parabens	Improvement
42/F	Hands and feet	Nickel sulfate, gold sodium thiosulfate, and silver bromide	Metal-free diet	No change
			Removal of dental alloy	No change
71/F	Hands and feet	Nickel sulfate, cobalt chloride, balsam of Peru, Kathon CG, and <i>p</i> -phenylenediamine	Metal-free diet	No change
			Avoidance of shampoo and rinse containing Kathon CG	No change
46/M	Hands and feet	Gold sodium thiosulfate	Metal-free diet	No change
71/F	Hands and feet	Nickel sulfate and cobalt chloride	Metal-free diet	No change
			Removal of dental alloy	No change
29/M	Hands	Nickel sulfate	Metal-free diet	No change
34/M	Hands	None	Metal-free diet	No change
71/F	Hands and feet	Potassium dichromate and antifungal drug	Metal-free diet	No change
			Avoidance of antifungal drug	Improvement
68/F	Hands and feet	Potassium dichromate and manganese chloride	Removal of dental alloy	No change
33/M	Hands	Manganese chloride	Removal of dental alloy	No change
71/F	Hands and feet	Antifungal drug	Avoidance of antifungal drug	Improvement
67/F	Hands	Antiseptic	Avoidance of antiseptic	Improvement
57/M	Hands	Nickel sulfate, cobalt chloride, potassium dichromate, parabens mix, and thiuram mix	Avoidance of topical drugs and moisturizer containing parabens and rubber gloves	No change
78/M	Hands and feet	Caine mix	Avoidance of topical drugs containing local anesthetic	No change
64/F	Hands	Cobalt chloride	Avoidance of clay	No change

a week after starting a metal-free diet (Table 2). The symptoms of other 5 patients had not improved during 4 weeks' metal-free diet. Veien *et al.* have reported that skin test reactivity to metal correlated poorly to the results of oral metal challenge.⁶ Oral challenge can induce the flare of dermatitis in patients with recurrent vesicular hand eczema who have negative patch tests. Therefore, we need to think the possible involvement of oral metal in the flare of vesicular eczematous lesions despite patch test results.

We advised the patients with positive patch test reactions ($n = 8$) to avoid the products containing allergenic substances (Table 2). The avoidance of topical drugs and moisturizer improved skin eruptions on their hands and feet within 2 weeks in 4 patients. Of these patients, two patients and one patient who had positive patch test reactions to antifungal drug and antiseptic respectively, had used these topical drugs. The other patient who tested positive for parabens had used moisturizer containing parabens. Other patients' symptoms did not improve at least 1 month after the avoidance of products including allergens. Guillet *et al.* have demonstrated the importance of contact vesicular dermatitis in which cosmetic and hygiene products play a preponderant role compared with metals.³ These findings suggest that contact allergens may be important factors causing eczematous lesions in patients with recurrent vesicular hand eczema. In this study, a limitation was the small number of subjects. Therefore, further study is needed to clarify the relationships between vesicular hand and foot eczema and allergic reactions to metal or other allergens.

In conclusion, our study indicates that more than one-third of the patients with recurrent vesicular hand eczema had contact sensitivities to metals, topical medicaments, and other chemicals. This study also shows that the removal of dental alloy did not improve the vesicular eczematous lesions. Therefore, we should carefully advise the patients whether or not they remove dental alloy. Furthermore, avoidance of contacting products including allergenic substances improved skin symptoms in the half of patients with positive patch test reactions to the products. Therefore, we should regard not only metal but also contact products including topical drugs and moisturizer as factors that can worsen recurrent vesicular hand eczema.

Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.alit.2017.03.006>.

Conflict of interest

The authors have no conflict of interest to declare.

Risa Tamagawa-Mineoka*, Naomi Nakamura, Sachiko Ueda, Koji Masuda, Norito Katoh

Department of Dermatology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan

* Corresponding author. Department of Dermatology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, 465 Kajii-cho, Kawaramachi-Hirokoji, Kamigyo-ku, Kyoto 602-8566, Japan.
E-mail address: risat@koto.kpu-m.ac.jp (R. Tamagawa-Mineoka).

References

- Coenraads PJ. Hand eczema. *N Engl J Med* 2012;**367**:1829–37.
- Yokozeki H, Katayama I, Nishioka K, Kinoshita M, Nishiyama S. The role of metal allergy and local hyperhidrosis in the pathogenesis of pompholyx. *J Dermatol* 1992;**19**:964–7.
- Guillet MH, Wierzbicka E, Guillet S, Dagregorio G, Guillet GA. 3-year causative study of pompholyx in 120 patients. *Arch Dermatol* 2007;**143**:1504–8.
- Lodi A, Betti R, Chiarelli G, Urbani CE, Crosti C. Epidemiological, clinical and allergological observations on pompholyx. *Contact Dermat* 1992;**26**:17–21.
- Nakayama H. New aspects of metal allergy. *Acta Dermatovenerol Croat* 2002;**10**:207–19.
- Veien NK, Kaaber K. Nickel, cobalt and chromium sensitivity in patients with pompholyx (dyshidrotic eczema). *Contact Dermat* 1979;**5**:371–4.
- Nishizawa A. Dyshidrotic eczema and its relationship to metal allergy. *Curr Probl Dermatol* 2016;**51**:80–5.
- Tamagawa-Mineoka R, Masuda K, Ueda S, Nakamura N, Hotta E, Hattori J, et al. Contact hypersensitivity in patients with recalcitrant atopic dermatitis. *J Dermatol* 2015;**42**:720–2.

Received 24 December 2016

Received in revised form 20 February 2017

Accepted 13 March 2017

Available online xxx