

## CONCISE COMMUNICATION

# Hypohidrosis and metal allergy: Trigger factors for unilateral lichen planus

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## ABSTRACT

Unilateral lichen planus (LP) is a rare clinical variant of LP. The etiology of unilateral LP has not been clarified, although various causes have been reported because of the characteristic distribution. We focused on the contribution of metal allergy and sweating in the development of unilateral LP in this case. To confirm the presence of metal allergy, patch tests with metal allergens were performed. To investigate the cause of the unilateral distribution in unilateral LP, the function of sweating and sweat leaking in the dermis was assessed by a thermoregulatory sweat test and immunohistochemical staining of dermcidin. The patch tests with  $\text{SnCl}_2$ ,  $\text{H}_2\text{PtCl}_6$ ,  $\text{ZnCl}_2$  and  $\text{MnCl}_2$  were positive. The thermoregulatory sweat test using the starch–iodine method (Minor test) with sweating provoked by heat stimulation revealed hypohidrosis of the affected area, whereas no skin lesions were observed on the dorsal hand and wrist where sweating was normal. Histopathological examination showed keratin plugging of the acrosyringium and lymphocytic infiltrations in the papillary and subpapillary dermis around the intraepidermal and intradermal eccrine duct in the affected area. The immunohistochemical staining of dermcidin confirmed sweat leakage in the subpapillary dermis in the affected area. The symptoms refractory to the topical steroids were markedly improved after removal of the dental metals. The coexistence of metal allergy and sweat leakage in the hypohidrotic area may be involved in the development of unilateral LP.

**Key words:** dermcidin, hypohidrosis, metal allergy, sweat, unilateral lichen planus.

## INTRODUCTION

Lichen planus (LP) is a common inflammatory dermatosis that involves the skin, mucous membranes and nails.<sup>1</sup> The contribution of metal allergies to the development of LP has been proposed.<sup>2,3</sup> A report suggested that abnormalities of the sweat glands contribute to lichenoid dermatosis, including LP.<sup>4</sup> Many morphological variants have been described,<sup>1</sup> and unilateral LP is a rare clinical variant.<sup>5,6</sup> The etiology of unilateral LP has not been clarified, although drug, genetic, infectious, pharmacological, neurological and psychological causes have been reported.<sup>1,5,6</sup> Here, we report a case of unilateral LP whose patch tests revealed positive reactions to metal including  $\text{SnCl}_2$ ,  $\text{H}_2\text{PtCl}_6$ ,  $\text{ZnCl}_2$  and  $\text{MnCl}_2$ . A thermoregulatory sweat test for investigation of the causative factor for the unilateral lesions demonstrated hypohidrosis of the affected area. Moreover, histological analysis of the lesion suggested leakage of sweat into the dermis. The symptoms were markedly improved after removal of the dental metals. This is the first report of the association between metal allergies and hypohidrosis in unilateral LP.

## CASE REPORT

A 62-year-old woman presented with a 32-year history of pruritic, violaceous to brown, polygonal plaque or flat-topped

papules that coalesced on the right arm (Fig. 1a). She had no history of drug intake prior to development of the eruption. Physical examination revealed no abnormal findings of the nails or oral mucosa apart from the skin lesions on the right arm, and no neurological abnormality. Laboratory tests showed no abnormal findings. The histological examination revealed a lichenoid tissue reaction in the affected area. It showed basal liquefaction, Civatte body formation, a lichenoid inflammatory infiltrate and pigmentary incontinence (Fig. 2a). On the basis of clinical and histopathological findings, the lesions were diagnosed as unilateral LP. Because her symptoms were refractory to topical steroids and we suspected the involvement of metal allergies with the development of LP, we performed patch tests with metal allergens (Torii Pharmaceutical, Tokyo, Japan). A positive patch test was identified by the presence of erythema, papules and vesicles, and the results were interpreted according to the recommendations of the International Contact Dermatitis Research Group. In our case, patch tests with  $\text{SnCl}_2$ ,  $\text{H}_2\text{PtCl}_6$ ,  $\text{ZnCl}_2$  and  $\text{MnCl}_2$  were positive at days 2, 3 and/or 7 (Fig. 3a,b). To study the cause of the unilateral lesions, a thermoregulatory sweat test using the starch–iodine method (Minor test) with sweating provoked by heat stimulation was carried out on both arms. This examination revealed no or low perspiration on the affected right arm compared with the left arm, confirming hypohidrosis of the

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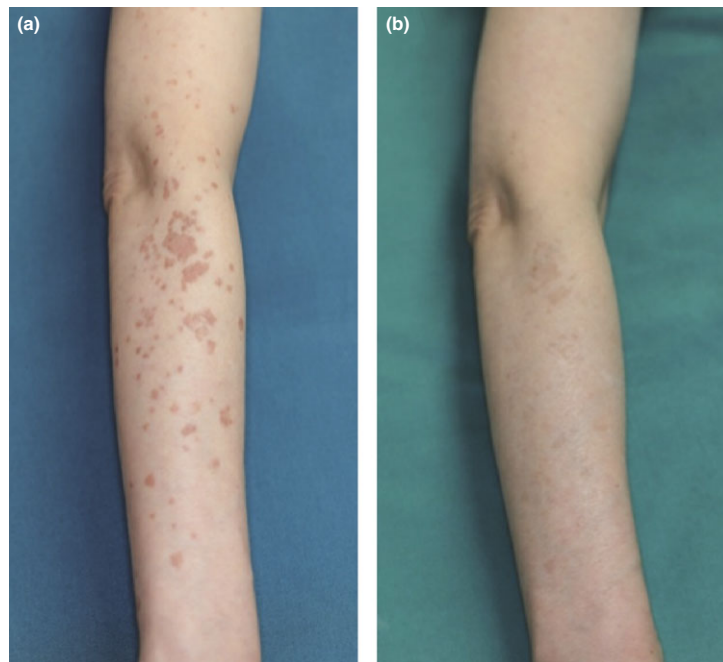


**Figure 1.** Clinical manifestations of the disease. (a) Violaceous, brownish and coalescing papules were distributed on the right arm and did not follow the lines of Blaschko. (b) Clinical appearance at 10 months after avoidance of metal allergens.

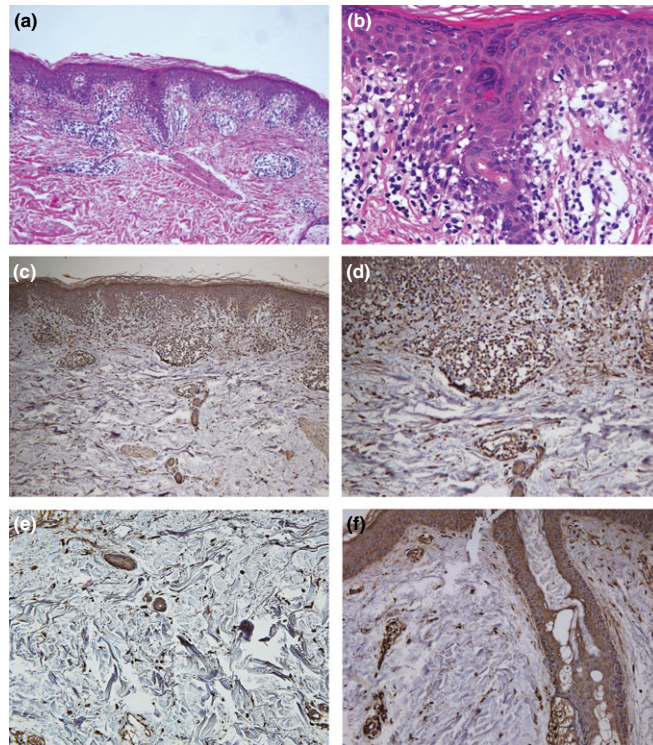


**Figure 2.** Histopathology and immunohistochemical staining of the lesions. (a,b) The histopathological examination revealed wedge-shaped hypergranulosis, destruction of the basal layer and lymphocytic infiltrate in the papillary dermis (hematoxylin–eosin [HE], original magnifications: [a]  $\times 100$ ; [b]  $\times 400$ ). (c,d) Immunohistochemical staining of dermcidin confirmed the presence of sweat leakage in the subpapillary dermis around the eccrine sweat duct in the affected area ([c]  $\times 100$ ; [d]  $\times 200$ ). (e,f) Dermcidin was positive only in the intradermal eccrine sweat ducts in the unaffected area ( $\times 200$ ).

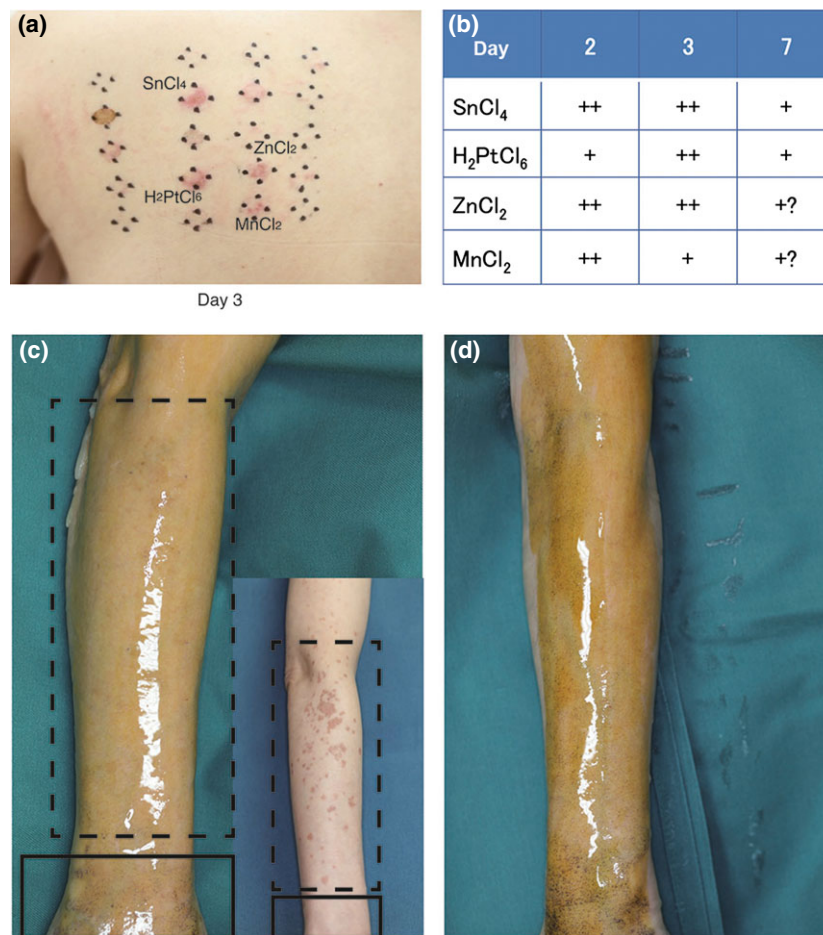


**Figure 3.** Results of patch tests and thermoregulatory sweat test. (a,b) Positive skin reactions in the epicutaneous patch test. (a) Patch tests with SnCl<sub>2</sub>, H<sub>2</sub>PtCl<sub>6</sub>, ZnCl<sub>2</sub> and MnCl<sub>2</sub> were positive at day 3. (b) Summary of the results of the patch tests. (c,d) Thermoregulatory sweat test using the starch-iodine method. (c) Almost no black dots (perspiration points) on the affected area (right forearm). Skin lesions are consistent with the area of few perspiration points (broken line). No skin lesions were observed at the sweating area (solid line). (d) Many black dots on the unaffected area (left forearm).

affected arm (Fig. 3c,d). On the right arm, the hypohidrotic area was consistent with the existence of skin lesions, whereas no skin lesions were observed on the dorsal right hand and wrist where perspiration points were detected (Fig. 3c). Histopathological examination of high-power fields showed keratin plugging of the acrosyringium and lymphocytic infiltrations in the papillary and subpapillary dermis around the intraepidermal and intradermal eccrine duct in the affected area (Fig. 2b). It has been reported that metals in sweat may play a role in the exacerbation of intrinsic atopic dermatitis.<sup>7</sup> Therefore, we hypothesized that metals in the sweat and in the leakage of sweat into the dermis were associated with the development of unilateral LP in this case. Interestingly, immunohistochemical staining of dermcidin (mouse monoclonal antibody to dermcidin [G-81]; Santa Cruz Biotechnology, Dallas, TX, USA) confirmed sweat leakage in the subpapillary dermis in the affected area (Fig. 2c,d).<sup>8,9</sup> In contrast, dermcidin was detected in the eccrine sweat duct and

eccrine sweat glands but not in the dermis in the unaffected area (Fig. 2e,f). Because her condition was refractory to the topical steroids, she eliminated dental metals containing materials such as Sn, Pt and Zn to which she was sensitive. Subsequently, the subjective symptom of itch disappeared within 1 week and the lesions started to improve within 3 weeks. Finally, all lesions disappeared within 10 months after instruction for avoidance of metal allergens (Fig. 1b).

## DISCUSSION

Unilateral LP is a rare form of LP and is characterized by violaceous, polygonal, flat-topped papules and plaques with a unilateral distribution. Its distribution usually follows the lines of Blaschko, and the condition is named as linear LP in less than 0.2% of LP patients.<sup>10</sup> Unilateral LP that does not follow the lines of Blaschko is much less frequent than linear LP that follows the lines of Blaschko.

Metal allergy is implicated in the pathogenesis of LP. There is a report of three cases of linear LP caused by dental metal compounds.<sup>11</sup> One of the three cases was cured after removal of the dental metals, although the contribution of metal allergies to the development of unilateral LP is not clarified. Based on this information, we performed patch tests with metal allergens and confirmed that allergies to dental metals were involved in this case. Despite the lack of response to other treatments, the removal of the dental metal compounds was effective in alleviating her objective and subjective symptoms.

However, it is insufficient to state that metal allergy is the sole cause of the unilateral lesions. Because metals in sweat may play a role in the exacerbation of intrinsic atopic dermatitis,<sup>7,12</sup> we next focused on the function of sweating. Interestingly, a thermoregulatory sweat test revealed hypohidrosis of the affected arm but not the unaffected arm. To investigate the involvement of sweat histologically, we performed immunohistochemical staining for dermcidin. Dermcidin is the major sweat antimicrobial peptide with broad antibacterial activity. This protein is specifically and constitutively expressed in the sweat glands and secreted into sweat.<sup>8,13–15</sup> Murakami *et al.*<sup>9</sup> studied the sweat secretion in the pathomechanism of palmoplantar pustulosis by using dermcidin as a marker for sweat. In our case, immunohistochemical staining of dermcidin was positive in the subpapillary dermis of the affected area, possibly around the eccrine sweat duct, indicating sweat leakage in the dermis of the affected area. Although the elimination of dental metals resulted in improvement of the lesions, the unilateral hypohidrosis persisted after disappearance of the lesions (data not shown). These observations suggest that the coexistence of metal allergy and sweat leakage in the hypohidrotic area may be necessary for the onset of unilateral LP. The etiology of unilateral LP, however, should be investigated further in the future.

**CONFLICT OF INTEREST:** None declared.

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