

SHORT REPORT

Close association between metal allergy and nail lichen planus: detection of causative metals in nail lesions

A. Nishizawa, T. Satoh,* H. Yokozeki

Department of Dermatology, Graduate School, Tokyo Medical and Dental University, Tokyo, Japan

*Correspondence: T. Satoh. E-mail: tasa-1688.derm@tmd.ac.jp

Abstract

Background Lichen planus (LP) is a common skin disorder of unknown aetiology that affects the skin, mucous membranes and nails. Although metal allergies have been implicated in the development of oral LP (OLP), the contribution of these allergies to nail LP (NLP) has yet to be studied in detail.

Objective To elucidate the link between metal allergy and NLP.

Methods We retrospectively analysed 115 LP patients with respect to the contribution of metals to either NLP or OLP. We also attempted to detect the specific metals involved in these nail lesions.

Results Of the 79 patients that received a metal patch test (PT), 24 (30%) were positive for at least one of the metal compounds tested. Notably, the prevalence of positive reactions to metals in the NLP patients was significantly higher as compared with the OLP patients (59% vs. 27%, $P < 0.05$). Among the 10 PT-positive patients with NLP, improvement of the skin lesions was seen in six of the patients after removal of dental materials containing causative metals or systemic disodium cromoglycate therapy. On the other hand, only 3 of 16 PT-positive patients with OLP exhibited improvement after the removal of dental materials. Causative metals in the dental fillings/braces were detected in the involved nail tissues.

Conclusion This study suggests that metal allergies are more closely associated with NLP vs. OLP, and that deposited metals in the nail apparatus contribute to the development of lichenoid tissue reactions in the nail bed and matrix.

Received: 20 January 2012; Accepted: 4 April 2012

Conflict of interest

We have no conflict of interest in relation to the publication of this article.

Funding source

None.

Introduction

Lichen planus (LP) is a common inflammatory disorder of unknown aetiology that affects the skin, mucous membranes and nails. Hepatitis C virus infection has been proposed to be an increased risk factor for LP.¹ Metal allergies have also been implicated in the development of LP, particularly in oral LP (OLP).²

Nail involvement occurs in 10% of LP patients as an inflammatory onychodystrophy.³ Although the clinical and pathological characteristics of nail LP (NLP) have been previously analysed,⁴ studies on the association of NLP with metal allergies have yet to be performed in detail. Here, we retrospectively analysed LP patients in terms of the contribution of metals to the development of NLP.

Materials and methods**Patients**

We retrospectively analysed the archives of 115 LP patients (43 males; 72 females) who visited our department between January of 1994 and December of 2009 (16 years total). The diagnosis was based on histopathological examinations of biopsied specimens. Patients with drug-induced LP were excluded.

Patch testing

The metal patch test (PT) was performed using Patch test reagents TM (Torii Pharmaceutical Corporation, Tokyo, Japan). Metals tested were as follows:

CuSO₄ 2aq, PdCl₂ 1aq, K₂Cr₂O₇ 0.4aq, NiSO₄ 5aq, CoCl₂ 2aq, HgCl₂ 0.05aq, SnCl₄ 1aq, H₂AuCl₄ 0.2aq, H₂PtCl₆ 0.5aq, FeCl₃ 2aq, InCl₃ 1aq, IrCl₄ 1aq, AgBr 2pet, ZnCl₂ 2pet, MnCl₂ 2pet, CrSO₄ 2aq, Al₂O₃ 2aq.

Skin reactions were determined at 48 and 72 h, and at 7 days using the criteria from the International Contact Dermatitis Research Group.

Detection of metals

Dental fillings and/or braces were analysed for any metals that were present by using an X-ray fluorescence spectroscope (XRSF). Detection of trace metals in the nail matrix and in the bed of the formalin-fixed, paraffin-embedded tissue sections were performed by using field emission scanning electron microscopy (FESEM) in conjunction with energy dispersive spectroscopy (EDS) and/or inductively coupled plasma-mass spectrometry (ICP-MS). Control tissue sections were obtained from normal nail lesions of surgically excised tissues from patients with acral lentiginous melanoma and involved lesions of acrodermatitis continua of Hallopeau.

Results

Prevalence of metal PT-positive results and correlation with clinical courses

Profiles of LP patients included in this study are shown in Table 1. Out of the 115 LP patients, 12 were positive for HCV Ab (6 for OLP alone, 1 for NLP alone, and 5 had two or more affected sites, i.e. OLP, NLP and/or other sites.). In addition, of the 79 total patients who received metal PT, 24 (30%) were positive for at least one of the tested metal compounds. Although the prevalence of positive reactions to metals in the NLP patients was 59% (10 of 17 cases), its prevalence in OLP patients was only 27% (16 of 59 cases). Chi-square analysis of the difference showed the NLP value to be significantly higher than the OLP value ($P < 0.05$; Fig. 1). XRSF analysis for the metal in the dental materials in the 10

PT-positive NLP patients demonstrated that eight were positive, with seven of these patients subsequently undergoing either removal of their dental fillings/braces or oral disodium cromoglycate therapy. As a consequence, six of the seven showed skin

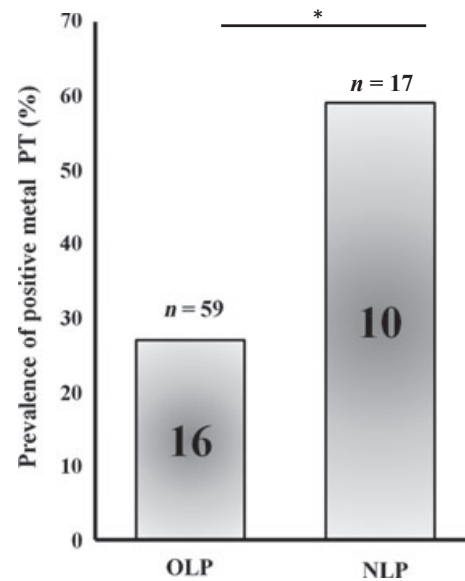


Figure 1 Comparison of metal PT results between OLP and NLP patients. * $P < 0.05$ by chi-square test.

lesion improvements (four after the removal of dental materials and two after the disodium cromoglycate therapy) (Table 2). On the other hand, after XRSF analysis for dental fillings/braces and the subsequent removal of dental braces or oral administration of disodium cromoglycate in 9 of the 16 PT-positive OLP patients, only three patients (one with concomitant NLP lesions) exhibited an improvement of the oral lesions due to the removal of these causative dental metal materials (data not shown).

Detection of metals in nail lesions of NLP

To better understand the aetiological contribution of metals to NLP, we subsequently sought to determine whether the causative metals were deposited within the nail apparatus. In an attempt to detect these trace metals, FESEM in conjunction with EDS were performed in the nail matrix and bed of the biopsied tissue sections. Cr in case 1 and Ni in case 5 were detected in both the dental material and in the respective nail lesions. Also of note was that in the nail tissue specimens from the PT-positive NLP

Table 1 Profile of LP patients

Affected sites	Oral mucosa (OLP)	Genital mucosa	Nails (NLP)	Trunk and extremities
Numbers of cases†	67	9	23	32
Age (years)	62.2 ± 11.84	56.6 ± 14.46	58.5 ± 13.84	59.7 ± 10.88
Gender (M/F)	16/51	5/4	11/12	13/19
HCV (+)	10	1	3	4
Number of metal PT-performed‡	59	5	17	20

†A total of 115 individuals were analysed. Some of the subjects had two or more affected sites.

‡A total of 79 individuals received metal PT. Some subjects had two or more affected sites.

LP, lichen planus; PT, patch test.

Table 2 Link between metals and NLP

Case	Positive PT metal†	Metals detected in dental materials	Therapy‡	Outcome	Metal detected in nail apparatus		
					FESEM/EDS	ICP-MS (ng/0.1 mm ³)	
						Au	Pd
1§	Cr	Cr, Co, Mn, Mo	A	Improved	Cr, Mg, Al, Si, Mo	N.T.	N.T.
2§	Pd, Au, Co	Pd, Au and others	A	Improved	N.T.	N.T.	N.T.
3	Pd	Pd, Ag, Zn, Sn, Ir	A	Improved	Mg, Al, Si, Mo, Ir	0.02	<1.0
4	Au, Ni	Au, Ag, Pd, Pt, In	A	Improved	Mg, Al, Si, Ti, In	0.04	<1.0
5	Au, Ni	Au, Ni, Cr, Cu, Mo, Ag, Pd, Zn, Ir	B	Improved	Ni, Mg, Al, Si, Mo, Ir	0.03	<1.0
6	Au, Cu, Zn, Al	Au, Cu, Zn, Pd, Ag, In, Sn	B	Improved	N.T.	N.T.	N.T.
7	Hg	N.T.	N.P.	Uncertain	N.T.	N.T.	N.T.
8	Pd, Hg, Ni	Pd and others	N.P.	Uncertain	Al, Si, Ti, In	0.02	<1.0
9	Cu, Hg, Sn, Pt, Pd	N.T.	N.P.	Uncertain	N.T.	N.T.	N.T.
10	Cr	Au, Ag, Cu, Pd, Zn, In, Sn	B	Not improved	Al, Si, In	0.02	<1.0

†PT results were assessed on day 7.

‡A, removal of dental materials; B, disodium cromoglycate.

§Cases 15 and 16 had both NLP and OLP.

N.T., not tested; N.P., therapies for metal allergy were not performed.

Au levels higher than 0.03 may be biologically significant.

Table 3 Detection of metals in negative NLP patient PT and in control tissues

Sample	Metal detected in nail apparatus		
	FESEM/EDS	ICP-MS (ng/0.1 mm ³)	
		Au	Pd
NLP11	N.D.	N.T.	N.T.
NLP12	N.D.	N.T.	N.T.
NLP13	N.D.	N.T.	N.T.
NLP14	Mo	0.01	<1.0
ALM1	N.D.	N.T.	N.T.
ALM2	N.D.	N.T.	N.T.
ACH1	Al, Si	0.02	<1.0

NLP11-14, NLP patients with negative metal PT results; ALM, tissues from acral lentiginous melanoma; ACH, tissues from acrodermatitis continua of Hallopeau; N.D., not detected; N.T., not tested.

patients, we detected various kinds of other metals that are commonly included in dental fillings/braces, and which included, Ir, Ti and In. In contrast, these metals were undetectable in the nail tissues of the control samples from the PT-negative NLP ($n = 3$), acral lentiginous melanoma ($n = 2$) and acrodermatitis continua of Hallopeau ($n = 1$) patients (Table 3).

Even though the dental materials in cases 3, 4, 5 and 8 contained either Au or Pd and the patients exhibited positive PT reactions to these materials, FESEM/EDS failed to detect these

metals within the nail tissues. As the possibility existed that the FESEM/EDS assay might not be sensitive enough to detect these metals, we subjected the tissue specimens to a further ICP-MS assay. Although the assay results demonstrated that Au was present in the skin lesions, the ICP-MS assay could not detect Pd in any of the tissues.

Discussion

Although metal allergy has been considered to be one of the precipitating factors in LP,² there are only a few reports^{5,6} that have shown a clinical association between metal allergy and NLP. In the current study, we found that the prevalence of positive metal PT results was higher in NLP as compared with OLP. In addition, 60% of these NLP patients (6 of 10 cases) showed clinical improvement after either removal of the dental materials or systemic disodium cromoglycate therapy. PT-positive metals, such as Cr, Ni and Au, were detected in both the dental fillings/braces and in the nail lesions in some of our NLP patients. These data suggested that metals released from dental materials contributed to the development of NLP via systemic absorption and subsequent deposition in the nail tissues.

In three NLP patients (cases 2, 3 and 8), we failed to detect Pd in their nail tissues even though they had dental fillings/braces containing Pd. As our current analyses found Pd to be entirely undetectable in all of the tissues tested, we were unable to draw any conclusions regarding whether or not Pd was one of the causative agents involved in the development of NLP in these patients.

However, the failure to detect Pd by the ICP-MS method in this study could be related to the assay not being sensitive enough to detect Pd in the nail tissues.

Intriguingly, our results also showed that nail tissues from PT-positive NLP patients generally contained various kinds of dental metals, such as Ir and Ti, in addition to Cr and Ni (Table 2). This was in striking contrast to the results for the PT-negative NLP patients and the other control samples (Table 3). In addition, relatively high levels of Au were detected in cases 4 and 5 as compared with the other patients who were not associated with any Au allergy. Although the actual reason for these findings remains unknown at the present time, it is possible that a continuous release of metal ions from dental fillings/braces followed by a subsequent deposition on the peripheral tissues could potentially lead to an increase in the risk for sensitization for some of these metals.

Data not shown here demonstrated that all three of the OLP patients, including the single patient that had both OLP and NLP, which were successfully treated by simply removing the dental braces, did not have widespread oral lesions, but had localized OLP lesions occurring exclusively adjacent to the dental materials. This suggests that a persistent direct contact between the causative metals and the mucosal tissues may be necessary for the develop-

ment of the LP reaction in the oral mucosa. These results additionally suggest that widespread oral lesions in LP patients may not necessarily be related to a metal allergy.

Overall, metal allergies collectively appear to contribute to the development of LP lesions, with the occurrence more likely to be found in NLP vs. OLP patients.

Acknowledgement

We thank Yu Kawamura for technical assistance.

References

- 1 Lodi G, Giuliani M, Majorana A *et al.* Lichen planus and hepatitis C virus: a multicentre study of patients with oral lesions and a systematic review. *Br J Dermatol* 2004; **151**: 1172–1181.
- 2 Scalf LA, Fowler JF Jr., Morgan KW, Looney SW. Dental metal allergy in patients with oral, cutaneous, and genital lichenoid reactions. *Am J Contact Dermat* 2001; **12**: 146–150.
- 3 Samman PD. The nails in lichen planus. *Br J Dermatol* 1961; **73**: 288–292.
- 4 Tosti A, Peluso AM, Fanti PA, Piraccini BM. Nail lichen planus: clinical and pathologic study of twenty-four patients. *J Am Acad Dermatol* 1993; **28**: 724–730.
- 5 Kato Y, Hayakawa R, Shiraki R, Ozeki K. A case of lichen planus caused by mercury allergy. *Br J Dermatol* 2003; **148**: 1268–1269.
- 6 Yokozeki H, Niiyama S, Nishioka K. Twenty-nail dystrophy (trachyonychia) caused by lichen planus in a patient with gold allergy. *Br J Dermatol* 2005; **152**: 1087–1089.