Angioedema, Stomatitis, and Urticaria Caused by Contact Allergy to Invisalign

Olabola Awosika, MD, MS,* Stephanie Kao, BS,†
Monica Rengifo-Pardo, MD,*†
and Alison Ehrlich, MD, MHS*†

PRECÍS

We report a case of angioedema, urticaria, and stomatitis caused by a potential isocyanate allergy resulting from Invisalign application.

DISCUSSION

A 23-year-old healthy white woman was referred to our dermatology clinic for patch testing. One month before presentation, the patient developed intermittent urticaria on her extremities and flanks 2 days after application of Invisalign clear aligners (Align Technology, Santa Clara, CA). Subsequent development of facial and periorbital swelling and redness with burning/stinging of the lips and oral mucosa prompted the patient to present to an urgent care facility. She was treated with oral prednisone and advised to remove her aligners, leading to resolution of her symptoms. The patient's medical history was significant for allergy to penicillin and amoxicillin and a family history of asthma.

Patch testing was performed with the North American Contact Dermatitis Group standard tray, dental screening series, and isocyanate series (Chemotechnique MB Diagnostics AB, Vellinge, Sweden), and Invisalign clear aligners (Fig. 1). At 96 hours, strong positive reactions (2+) to Invisalign (Figs. 2A, B) and questionable reactions (+/−) to formaldehyde, cobalt, copper sulfate, diaminodiphenylmethane (MDA), and hexamethylene diisocyanate (HDI) were observed. These findings were consistent with contact sensitization to Invisalign and concerning for sensitivity to isocyanates.

Isocyanates are highly reactive, low–molecular-weight compounds that react exothermically with hydroxyl groups to form polyurethane products.[1] Isocyanates are a known culprit in occupational contact dermatitis, particularly for workers in the polyurethane industry.[2] Similar to our observation, Lammintausta and Liippo[2] reported a man who developed periorbital and lip dermatitis and was patch tested positive for MDA from occupational isocyanate exposure. Our patient was highly sensitive to Invisalign clear aligners and questionably sensitive to MDA and HDI. Invisalign is composed of polyurethane from 4,4′-methylene diphenyl diisocyanate (4,4′-MDI) and 1,6-hexanediol precursors (including HDI).[3] However, patients have been shown to test positive for MDA without reacting to 4′4-MDI. This discrepancy is thought to be due to exclusive sensitization to 4,4′-MDI–derived MDA after contact with water.[1]

Invisalign wraps around the teeth and is worn continuously throughout the day. When isocyanates come into contact with mucosal tissues, they bind to proteins forming immunogenic haptens that enter the epithelium and may lead to systemic or localized sensitization.[4] Leaching of isocyanates from clear aligners may lead to systemic exposure through ingestion and mucosal absorption inducing type 1 hypersensitivity, which may manifest as angioedema and urticaria as seen in our patient.[4] Interestingly, Premaraj et al[4] demonstrated increased membrane permeability and decreased adhesion of gingival epithelial cells after exposure to Invisalign plastic that was reversible upon removal. However, saliva was found to confer a protective effect against isocyanates by maintaining epithelial cell integrity and neutralizing potential adverse effects of wearing Invisalign.[4]

Reported adverse events associated with clear aligners include angioedema, acute urticaria on the neck and face, and ulcerations of the oral mucosa, equivalent to the hypersensitivity observed in

Figure 1. Invisalign clear aligners worn by the patient during her reactions.

*From the *Department of Dermatology, The George Washington Medical Faculty Associates; and †The George Washington University School of Medicine & Health Sciences, DC.*

Address reprint requests to Alison Ehrlich, MD, MHS, Department of Dermatology, The George Washington University Medical Faculty Associates, 2150 Pennsylvania Ave NW, Suite 2B-430, Washington, DC 20037. E-mail: aehrlich@mfa.gwu.edu.

O.A.'s fellowship is funded by Janssen Biotech, Inc.

The authors have no conflicts of interest to declare.

DOI: 10.1097/DER.0000000000000314

© 2017 American Contact Dermatitis Society. All Rights Reserved.

Copyright © 2017 American Contact Dermatitis Society. Unauthorized reproduction of this article is prohibited.

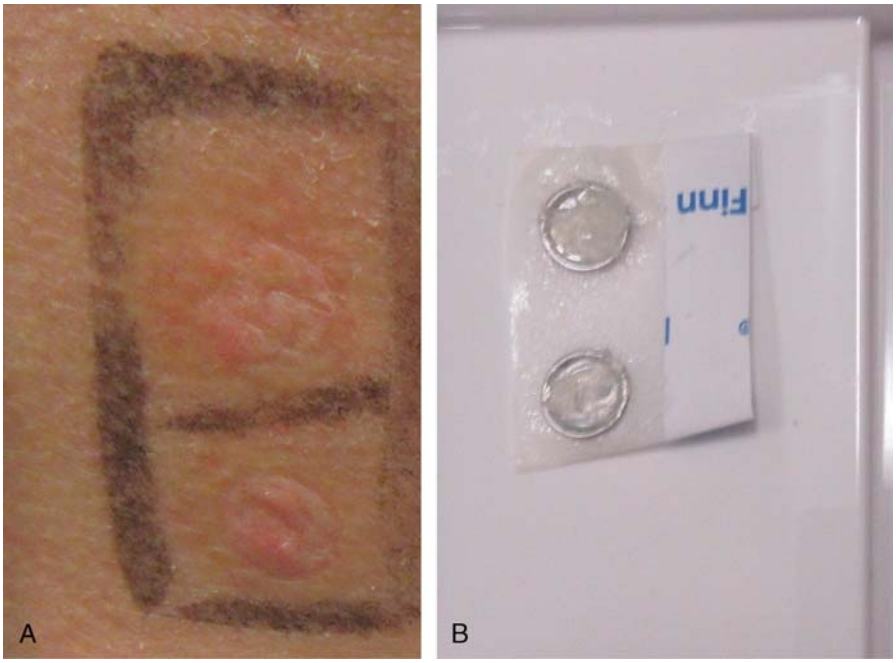

Figure 2. A, 2+ positive reactions to 2 separate Invisalign clear aligners in petrolatum. B, Two separate aligners in petrolatum affixed to a Finn chamber used in patch testing.

our patient.[5] Additional reports include nausea, headaches, muscle cramping, and anaphylaxis.[5] Recently, the conditional probability of having an adverse event (such as inflammation/swelling of the oral and pharyngeal mucosa) with Invisalign was found to be increased by 10-fold compared with the general population.[5] Given the increasing use of clear aligners in orthodontics, it is prudent for practitioners to be aware of the potential for isocyanate allergic reactions associated with these products.

ZEBRA

Invisalign is composed of polyurethane plastic, and persistent contact of the oral mucosa with this plastic may lead to contact sensitization to isocyanates.

REFERENCES

1. Wenk KS, Ehrlich A. Isocyanates. *Dermatitis* 2012;23(3):130–131.
2. Lammintausta K, Liippo J. Contact sensitization to 4,4′-diaminodiphenylmethane and to isocyanates among general dermatology patients. *Contact Dermatitis* 2008;59:109–114.
3. Ryokawa H, Miyazaki Y, Fujishima A, et al. The mechanical properties of dental thermoplastic materials in a simulated intraoral environment. *Orthodontic Waves* 2006;65:64–72.
4. Premaraj T, Simet S, Beatty M, et al. Oral epithelial cell reaction after exposure to Invisalign plastic material. *Am J Orthod Dentofacial Orthop* 2014;145(1):64–71.
5. Thavarajah R, Thennukoda RA. Analysis of adverse events with use of orthodontic sequential aligners as reported in the manufacturer and user facility device experience database. *Indian J Dent Res* 2015;26(6):582–587.

Lichen Planus Pigmentosus Inversus Caused by Occupational Systemic Sensitization to Metals in a Semiconductor Factory Worker

Che-Yuan Hsu, MD,* Donald Liu, MD,*
Woan-Ruoh Lee, MD, PhD,*†‡
and Yi-Hsien Shih, MD*†‡

PRECÍS

Lichen planus pigmentosus inversus is an uncommon variant of lichen planus and has never been reported with occupational systemic sensitization to metals.

DISCUSSION

Lichen planus pigmentosus inversus (LPPI) is a variant of lichen planus characterized by subtle onset of asymptomatic or mildly pruritic hyperpigmented macules affecting the intertriginous areas. Up to date, approximately 50 cases of LPPI have been reported.[1]

*From the *Department of Dermatology, Taipei Medical University Shuang Ho Hospital; and †Department of Dermatology, School of Medicine, and ‡Graduate Institute of Medical Sciences, College of Medicine, Taipei Medical University, Taiwan.*

Address reprint requests to Yi-Hsien Shih, MD, Department of Dermatology, Taipei Medical University-Shuang Ho Hospital, No. 291, Zhongzheng Rd, Zhonghe District, New Taipei City 23561, Taiwan. E-mail: 13263@s.tmu.edu.tw.

The authors have no funding or conflicts of interest to declare.

DOI: 10.1097/DER.0000000000000292

© 2017 American Contact Dermatitis Society. All Rights Reserved.

Copyright © 2017 American Contact Dermatitis Society. Unauthorized reproduction of this article is prohibited.