

### Fixed Drug Eruption Due to Chlorhexidine Mouthwash Confirmed by Lesional Patch Testing



Timothy J. Watts, MRCP, David Thursfield, DipHE, and Rubaiyat Haque, FRCP *London, United Kingdom*

A 69-year-old woman used a chlorhexidine-containing mouthwash (as chlorhexidine digluconate 0.2%) for oral rinsing and 48 hours later developed a solitary erythematous oval-shaped macular patch on her lower back that evolved over the next 72 hours into a partly violaceous hyperpigmented well-defined plaque (Figure 1). The plaque-like lesion improved over the course of 7 days with potent topical corticosteroids. A skin biopsy for histologic analysis was not performed and clinically a fixed drug eruption (FDE) was diagnosed. She had no prior history of atopic disease, drug hypersensitivity, or autoimmune diseases. She avoided further use of the mouthwash and no further skin eruptions developed.

In our allergy clinic 3 months later there was evidence on physical examination of a residual pigmented macular lesion at the site of the original eruption on her lower back. Patch testing was performed using IQ Ultra chambers and chlorhexidine digluconate (0.5% aqueous) (Chemotechnique Diagnostics, Vellinge, Sweden), with both control (uninvolved upper back skin) and lesional (residual pigmented lesion) patch test application. The control patch testing was read on day 2 (D2) and day 4 (D4) and the lesional patch testing was read on day 1 (D1) and day 2 (D2), in accordance with International Contact Dermatitis Research Group criteria and European Society of Contact Dermatitis guidance. To exclude immediate hypersensitivity, skin prick testing to chlorhexidine digluconate 0.5% (undiluted) was also performed, and this was negative when read at 15 minutes against a positive (histamine) and negative (0.9% NaCl) control.

Patch testing to chlorhexidine digluconate 0.5% was completely negative at the control testing site at D4. However, patch testing was strongly positive (++) to chlorhexidine digluconate 0.5% at the lesional testing site at D2, with reactivation of the residual FDE lesion (Figure 2). There was a demonstrable crescendo effect at the lesional testing site from



**FIGURE 1.** Partly violaceous hyperpigmented well-defined plaque-like fixed drug eruption after use of a chlorhexidine mouthwash.

D1 to D2. The reactivated FDE faded over the course of 7 days to a pigmented state without treatment. Given the positive lesional patch test result and the suggestive clinical features she was diagnosed with an FDE due to a chlorhexidine mouthwash. She was advised to avoid all chlorhexidine-containing mouthwashes and other products (due to risk of delayed-type hypersensitivity) and use chlorhexidine-free alternatives (which she later tolerated).

An FDE is a delayed-type cutaneous hypersensitivity reaction to medication that recurs at the same site on further administration or exposure. Commonly implicated drugs include antimicrobials, nonsteroidal anti-inflammatory drugs, analgesics, and anticonvulsants. The pathogenesis is believed to involve both CD8<sup>+</sup> effector/memory T cells and IFN- $\gamma$  release. Lesional patch testing and/or provocation studies are useful tools to aid with its diagnosis.<sup>1</sup>

Chlorhexidine is a widely used bisbiguanide antimicrobial agent that has been previously associated with both immediate

Department of Adult Allergy, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom

No funding was received for this work.

Conflicts of interest: R. Haque is on the Allergy Therapeutics board; and has received travel support from Allergy Therapeutics and ALK Abello. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication July 12, 2018; revised July 19, 2018; accepted for publication July 21, 2018.

Available online September 8, 2018.

Corresponding author: Timothy J. Watts, MRCP, Department of Adult Allergy, Guy's and St Thomas', NHS Foundation Trust, London SE1 9RT, United Kingdom. E-mail: [Timothy.Watts2@gstt.nhs.uk](mailto:Timothy.Watts2@gstt.nhs.uk).

J Allergy Clin Immunol Pract 2019;7:651-2.  
2213-2198

© 2018 American Academy of Allergy, Asthma & Immunology  
<https://doi.org/10.1016/j.jaip.2018.07.038>



**FIGURE 2.** Lesional reactivation of the fixed drug eruption by lesional patch testing with chlorhexidine digluconate 0.5% (photo taken at D2 reading). The arrow indicates the site of the lesional patch test.

and delayed-type hypersensitivity reactions.<sup>2,3</sup> Allergic reactions to mouthwashes containing chlorhexidine are uncommon, although immediate hypersensitivity (urticaria) after oral rinsing has been reported with confirmation via skin prick testing.<sup>4</sup> Delayed-type hypersensitivity to chlorhexidine-containing mouthwashes has been rarely reported; however, allergic contact dermatitis to chlorhexidine after oral sensitization has been described.<sup>5</sup> Only 1 prior report of an FDE to a chlorhexidine mouthwash has been published in the literature, although placebo-controlled oral-mucosal provocation studies were used instead of patch testing to achieve the diagnosis.<sup>6</sup> To our knowledge we describe the first report of an FDE induced by a chlorhexidine mouthwash that has been confirmed by lesional patch testing. Overall, we highlight the importance of a comprehensive approach to evaluating and diagnosing an FDE and the utility of lesional patch test studies.

#### REFERENCES

1. Shiohara T. Fixed drug eruption: pathogenesis and diagnostic tests. *Curr Opin Allergy Clin Immunol* 2009;9:316-21.
2. Spoerl D, Jandus P, Harr T. Pitfalls and peculiarities in chlorhexidine allergy. *J Allergy Clin Immunol Pract* 2016;4:991-2.
3. Watts TJ, Li PH, Ue KL, Haque R. Chronic allergic contact dermatitis due to chlorhexidine. *J Allergy Clin Immunol Pract* 2018;6:254-5.
4. Sharma A, Chopra H. Chlorhexidine urticaria: a rare occurrence with a common mouthwash. *Indian J Dent Res* 2009;20:377-9.
5. McEnery-Stonelake M, Silvestri DL. Allergic contact dermatitis to chlorhexidine after oral sensitization. *Dermatitis* 2013;24:92-3.
6. Moghadam BK, Drisko CL, Gier RE. Chlorhexidine mouthwash-induced fixed drug eruption. Case report and review of the literature. *Oral Surg Oral Med Oral Pathol* 1991;71:431-4.