

CONTACT POINT

Contact allergy caused by methylisothiazolinone in a mouthwash as the likely trigger of oral pemphigus vulgaris

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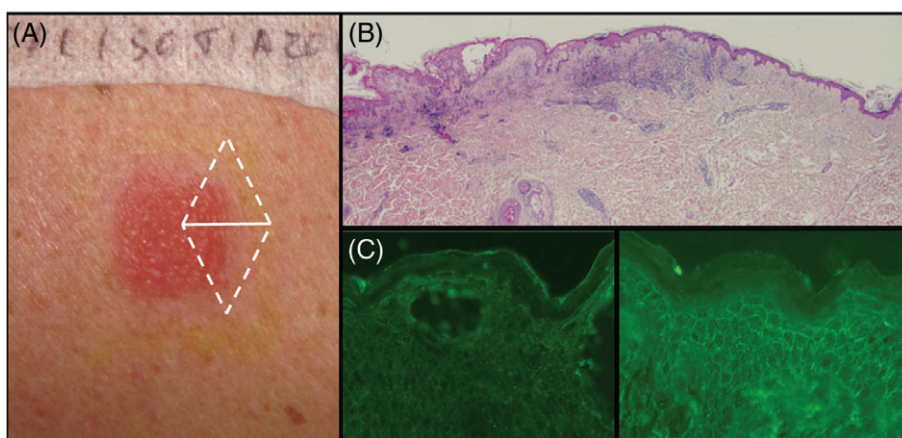
Following an epidemic of allergic contact dermatitis, the preservative methylisothiazolinone (MI) was recently banned from use in leave-on cosmetics and limited to 15 ppm in rinse-off cosmetics in Europe.¹ Medical devices and products which may contain MI do not have to comply with these regulations.² Pemphigus vulgaris (PV) is a chronic inflammatory autoimmune bullous disease affecting the skin and mucous membranes. It is caused by autoantibodies directed against desmosomal glycoproteins as a result of the interaction of endogenous and exogenous factors, including contact allergy.³

CASE REPORT

A 79-year-old woman with an 8-year-history of recurrent ulcerations of the oral mucosa was referred for patch testing shortly after the sudden onset of severe stomatitis. She denied having any previous symptoms suggestive of contact allergy. She was patch tested

according to ESCD guidelines with the Italian baseline series, a dental screening series, and her oral hygiene products, including, in particular, Buccagel Afte collutorio, a mouthwash that she had started using 1 month before her oral symptoms worsened. She had ++ reactions on day (D) 3 and D4 to MI, and a ?+ reaction on D3 and a + reaction on D4 to the mouthwash tested "as is". The latter is a medical product that, according to the label, contains MI. The patient stopped using the mouthwash, and her stomatitis slightly improved but did not resolve. A further diagnostic workup showed high levels of circulating anti-desmoglein 3 autoantibodies, compatible with oral PV. Patch testing with MI and with the mouthwash was repeated, and histopathology plus direct immunofluorescence (DIF) of lesional and perilesional skin of the ensuing reactions were performed. Histology showed acute spongiotic dermatitis and some areas of suprabasal acantholysis. DIF showed a typical pemphigus pattern with IgG and C3 deposits (Figure 1).

FIGURE 1 A, Vesicular patch test reaction to MI. The dotted line shows that the biopsy included both lesional and perilesional skin. B, Histology showing intraepidermal blistering and a dense dermal inflammatory infiltrate in the area of the positive patch test reaction. C, Direct immunofluorescence showing IgG autoantibodies bound to the surface of epidermal keratinocytes both in the area of the vesicular patch test reaction and in the apparently normal epidermis, where they are more evident



DISCUSSION

This case shows that sensitization to MI can be triggered in the oral cavity by contact with a mouthwash. It also shows that the restrictions concerning MI should be extended to medical products and devices. In our patient, contact allergy to MI was associated with oral PV. Whether it induced PV or, rather, aggravated subclinical PV is debatable. The pathogenetic relationship between the 2 events is supported by the following facts: PV was restricted to the oral cavity where sensitization to MI occurred; the patient had circulating autoantibodies against desmoglein 3, an antigen that is mainly present in mucous membranes; DIF of the biopsy taken at the site of the MI patch test reaction showed a typical pemphigus pattern; and finally, although oral ulcers may constitute the initial presentation of oral PV, in our patient they were mild and recurrent, whereas severe stomatitis developed only after contact with the mouthwash, and did not resolve after its discontinuation. Rare cases of "contact pemphigus" have already been reported.³ It has been suggested that some contact allergens may induce direct superficial acantholysis. This, together with the allergic inflammatory reaction, may, in turn, favour the expression of desmosomal neo-antigens, producing a specific autoantibody response.

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REFERENCES

1. Aerts O, Goossens A, Lambert L, Lepoittevin J-P. Contact allergy caused by isothiazolinone derivatives: an overview of non-cosmetic and unusual cosmetic sources. *Eur J Dermatol*. 2017;27:115-122.
2. Schliemann S, Isaksson M, Persson C, Bruze M, Tittelbach J, Elsner P. Allergic contact dermatitis caused by methylchloroisothiazolinone/-methylisothiazolinone in a medical device. *Contact Dermatitis*. 2016;75:312-314.
3. Gallo R, Massone C, Parodi A, Guarrera M. Allergic contact dermatitis from thiurams with pemphigus-like autoantibodies. *Contact Dermatitis*. 2002;46:364-365.

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