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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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Induction of leukoderma following allergic contact dermatitis to FreeStyle Libre

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Isobornyl acrylate (IBOA) is a potent contact sensitizer contained in the glucose sensor FreeStyle Libre.¹ Many cases of allergic contact dermatitis (ACD) have already been described in this regard. We herein describe a case of ACD caused by IBOA and followed by hypopigmentation in the application areas of this sensor.

1 | CASE REPORT

A 35-year-old woman with diabetes mellitus type 1 was referred to our department with pruritic annular erythematous dermatitis under an adhesive patch of the glucose sensor FreeStyle Libre fixed to the inner side of her arm. These lesions occurred following 5 months of sensor use. Approximately 6 months later, hypopigmentation appeared on the periphery of the area of dermatitis, where sensors had been applied, and on the inner side of both arms (Figure 1A, B). There was no hypopigmentation on any other part of her body, and there was no personal or family history suggesting an autoimmune disease, such as vitiligo. She had never applied corticosteroid

cream or hydrocolloid dressings between the sensor and skin. She was patch tested with the European baseline series, an acrylate, plastic, and glue series (Chemotechnique Diagnostics, Vellinge, Sweden; and Trolab; Almirall Hermal, Reinbek, Germany, respectively), a piece of the adhesive patch of the glucose sensor "as is"; IBOA (Sigma-Aldrich, Steinheim, Germany, 0.1% pet. and prepared by the hospital pharmacy [Saint-Luc]); and *N,N*-dimethylacrylamide (DMAA; Sigma-Aldrich and prepared by the Department of Occupational and Environmental Dermatology in Malmö) 0.1% pet. Patch tests were performed using IQ Ultra test chambers (Chemotechnique Diagnostics) and fixed with Fixomull stretch (BSN Medical, Hamburg, Germany) on the upper back. Readings were performed on day (D) 2 and D4. The patch test reactions were classified according to ESCD criteria.² A positive reaction was observed for both IBOA (+/++) and DMAA (+/+), as well as for the adhesive part of FreeStyle Libre (+/?+; Figure 1C). A biopsy of the depigmented area showed a complete absence of epidermal melanocytes, which was confirmed via immunohistochemistry using SOX10 labeling.

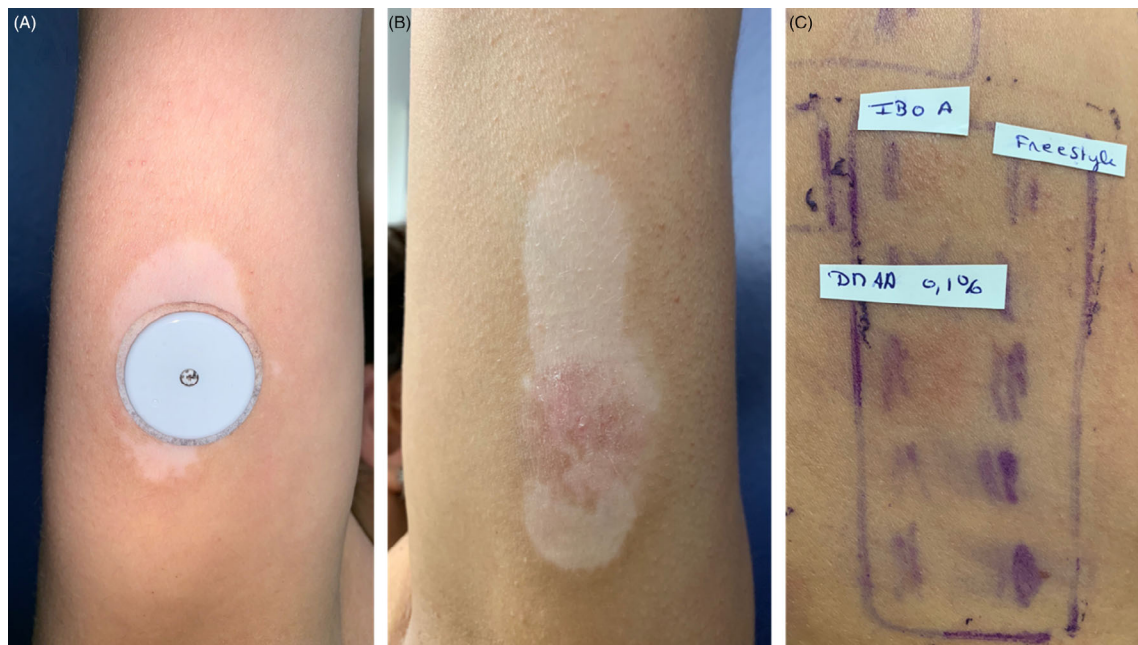


FIGURE 1 (A,B) Hypopigmentation area on the periphery of the allergic contact dermatitis caused by FreeStyle Libre on the inside of both arms. (C) Positive patch test reaction to isobornyl acrylate (IBOA) 0.1% (++) and adhesive part of FreeStyle Libre (?+) (Day 4 reading)

2 | DISCUSSION

Several cases of ACD due to the glucose sensor FreeStyle Libre have previously been reported.^{1,3,4} To our knowledge, this is the first case of acquired leukoderma following sensitization to FreeStyle Libre. Acquired leukoderma may occur in an area previously affected by ACD. Several chemicals have been reported to cause depigmentation. Hitherto, neither IBOA¹ nor DMAA,⁴ the two potent sensitizers used in the glucose sensor, have been described as causing depigmentation. However, medical devices with adhesives have been reported to cause hypopigmentation,⁵ as have some acrylates.⁶ It should be noted that hydroquinone monomethyl ether (HMME) is also known to cause depigmentation.⁷ This agent was present, at concentrations varying from 100 to 300 ppm, in the IBOA purchased from Sigma-Aldrich and applied for patch testing on this patient. Therefore, we can assume that it may have also been contained in the IBOA used in the sensor. HMME acts as inhibitor to prevent the inadvertent IBOA polymerization. Once polymerization of IBOA has started, at temperatures above 80°C, HMME is mostly degraded.⁸ However, it has already been reported that the IBOA contained in the sensor's plastic part is also present in the sensor adhesive, though in smaller quantities, due to substance migration.¹ We hypothesized that HMME similarly may have migrated during one of the steps, thereby contaminating the adhesive patch. Incomplete polymerization could also be responsible. HMME was previously reported to have caused depigmentation of the forehead skin of two workers in a vinylidene chloride plant.⁹ Of note, both hydroquinone monobenzyl ether and hydroquinone monoethyl ether¹⁰ act as very potent depigmenting agents due to their direct toxicity on melanocytes, potentially resulting in subclinical

inflammation via melanocyte destruction. As these two molecules are chemically similar to HMME, we assume that HMME acts in the same way, thereby accounting for the histological characteristics identified on this patient. In conclusion, we have reported the first case of acquired leukoderma following ACD to FreeStyle Libre, with a potential role of HMME present in IBOA.

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Patch testing with formaldehyde 2% aq. – A multicenter study in Spain

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The prevalence of formaldehyde sensitization differs between regions. The concentration of formaldehyde used in the patch test has been controversial, but the latest European recommendations¹ suggest that formaldehyde 2% aq. is the optimal concentration because clinically relevant contact allergy to formaldehyde may be missed by testing with formaldehyde 1% aq. For this reason, the Spanish baseline series was updated by the Spanish Contact Dermatitis and Skin Allergy Research Group (GEIDAC), and the concentration of formaldehyde increased to 2% aq. in

2016.² The aims of this descriptive one-year prospective study were to determine the prevalence of sensitization to formaldehyde and assess the features of patients with sensitization to formaldehyde in Spain.

METHODS

In 14 Spanish hospitals, 2971 patients were patch tested in 2017 with the Spanish baseline series. Formaldehyde 2% aq. was supplied by