

Severe allergic contact dermatitis to two different continuous glucose monitoring devices in a patient with glycogen storage disease type 9b

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Abstract

Continuous glucose monitoring (CGM) systems are of great value for patients with disorders of impaired glucose homeostasis, including glycogen storage diseases. We report on an 8-year-old girl with glycogen storage disease type 9b who developed severe allergic contact dermatitis to two different continuous glucose monitoring systems, FreeStyle[®] Libre and Dexcom[®] G6. Our case highlights the impact of sensitization for pediatric patients, the urgent need for open labeling of components by pharmaceutical and device manufacturers, and the need for avoidance of skin sensitizers in medical devices.

KEYWORDS

allergic contact dermatitis, continuous glucose monitoring, dexcom[®], freeStyle[®], glycogen storage disease

1 | INTRODUCTION

Continuous glucose monitoring (CGM) systems are increasingly implemented in patients with diabetes and other disorders with disturbed glucose homeostasis to promote good metabolic control. However, shortly after their appearance on the market, the first concerns about adverse skin reactions were raised.¹ CGM devices are usually combined with a subcutaneous catheter and a transmitter for blood glucose sensors applied to the skin by an adhesive patch for a period of 3-14 days.² Dermatological complications are especially common in children and adolescents using GCM devices.³ Herman et al have recently identified isobornyl acrylate as the main culprit allergen to cause allergic contact dermatitis (ACD) in patients using the FreeStyle[®] Libre device.² Interestingly, isobornyl acrylate was the American Contact Dermatitis Society Allergen of the Year in 2020.⁴

We herein report on a girl with glycogen storage disease (GSD) type 9b who developed severe ACD to both FreeStyle[®] Libre and Dexcom[®] G6 devices. Our case highlights the severe consequences of sensitization for pediatric patients and the urgent need for open labeling as well as the use of less allergenic adhesives and components in medical devices.

2 | CASE PREPORT

This 8-year-old girl is the third child of non-consanguineous parents with no family medical history of allergies. At the age of 4 years, she was diagnosed with GSD 9b after presenting with recurrent hypoglycemia. Genetic panel diagnostics yielded two mutations in the *PHKB* gene (c.2540C>T (p. Val847Ala); c.2309A>T (p. Lys770Ile)).

Abbreviations: ACD, allergic contact dermatitis; CGM, continuous glucose monitoring; DKG, German Contact Allergy Group; GCMS, gas chromatography-mass spectrometry.

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A high-protein diet with supplementation of uncooked corn starch and reduction of simple sugars was initiated. Due to recurrent episodes of hypoglycemia, continuous glucose monitoring was started at the age of 4 years using a FreeStyle® Libre 1 device. The sensor was positioned alternately on both upper arms. Within the following two years, she developed severe skin reactions beneath the attached glucose sensor, which on three occasions led to wound infections and abscesses requiring oral antibiotic treatment. Due to these dermatologic complications, the CGM system was changed to the Dexcom® G6 device, which was initially tolerated well. After 1 year, however, she again showed progressively worsening severely itching eczema with blistering and skin detachment at the adhesion site (Figure 1).

Patch testing was performed using the modified standard patch test series for children according to the DKG recommendations along with the synthetic resins and adhesive series and both of the culprit CGM patch systems. The patch tests with the adhesive plasters of Dexcom® G6 and FreeStyle® Libre 1 devices showed a strongly positive reaction with infiltration, erythema, papules, and vesicles and a positive reaction with erythema and infiltration to isobornyl acrylate but no reaction to 2-hydroxyethylmethacrylate. All other patch test allergens were negative (Table 1).



FIGURE 1 Severe allergic contact dermatitis caused by a Dexcom® 6 device. Panel A-B, skin lesions on the upper arm of the patient

TABLE 1 Patch test results

Substance/Allergen	Result at 48 h	Result at 72 h
Plastic and glues series	negative	negative
Adhesive dressing of FreeStyle®	++	+++
Adhesive dressing of Dexcom® G6	++	+++
Isobornyl acrylate 0.1%	+	+
2-hydroxyethyl methacrylate 1%;	negative	negative
p-tert-butylphenyl-glycidyl-ether 0.25%	negative	negative

Note: The patient showed a strong reaction to the adhesive dressing of both the FreeStyle and the Dexcom device and a mild reaction to isobornyl acrylate.

Abbreviation: h, Hour.

According to the manufacturer of the Dexcom® G6 device, neither isobornyl acrylate nor 2-hydroxyethylmethacrylate is present in the adhesive of the device. No further information could be obtained on the incorporated adhesives or the devices themselves from the manufacturers of both systems.

3 | DISCUSSION

Dermatological complications associated with the use of CGM devices can be a serious problem, especially in pediatric patients. However, only limited information exists on how many patients using CGM devices for longer periods of time actually develop ACD.⁵ Berg et al performed an online questionnaire study to address dermatological complications related to the use of CMG devices in diabetic children.³ In this cohort of 83 children and adolescents between 2 and 20 years, who were currently using or had previously used CGM, 79.5% had experienced dermatological complications. Itching (70%), eczema (46%), and wounds (33%) were the most frequently reported complications.³ Interestingly, atopy was not associated with dermatological complications in individuals using CGM.³ Skin reactions have been found to constitute one of the main causes of treatment discontinuation.^{6,7}

Herman et al have recently identified isobornyl acrylate as the main allergen in the FreeStyle® Libre device causing ACD.² Of 15 patients with skin reactions caused by a FreeStyle® Libre sensor, 12 were sensitized to isobornyl acrylate.² The acrylate was detected by gas chromatography-mass spectrometry (GCMS) of the sensor. Oppel et al consequently performed GCMS of the Dexcom® sensor and did not detect isobornyl acrylate in this device.⁸ Five diabetic patients between 11 and 54 years who presented with ACD caused by FreeStyle® Libre were included in their study. The onset of ACD was between 5 months and 1 year after the first use of FreeStyle® Libre. Patch tests were performed and showed that all patients were sensitized to isobornyl acrylate. In parallel, patients were provided with a Dexcom® CGM sensor, which was fixed on their skin for 2 days. None of the patients had skin reactions to the Dexcom® sensor, and the authors therefore postulated that the Dexcom® device is a possible alternative for CGM in patients with ACD.⁸ This recommendation was supported by a second study that analyzed the plastic material

and adhesives of three different CGM systems, the FreeStyle® Libre, the Dexcom® G6, and the Enlite®. Isobornyl acrylate was found in the housings of Freestyle® Libre and Enlite® sensors, but not in the Dexcom® G6. In contrast to these findings, a more recent study by Svedman et al found small amounts of isobornyl acrylate also in the Dexcom® G6 device. Using GCMS, the authors detected isobornyl acrylate in both the adhesive patches removed from the sensors and the sensors themselves.⁹ They also report several cases of ACD in diabetic patients using the Dexcom® G6 device, similar to our patient.⁹

While initially, components of the adhesives have been considered the culprit, there is now evidence that the sensor itself may contain the allergen. Kamann et al performed patch tests in a 10-year-old boy using three different adhesive components of the FreeStyle® Libre device that were provided by the manufacturer of the adhesives (Adhesive Research Glen Rock).⁵ Surprisingly, these patch tests showed no skin reaction. The authors therefore hypothesized that isobornyl acrylate is possibly not a component of the adhesive, but may be part of the polymerized plastic material of the glucose sensor itself.⁵ In this case, skin reactions could be explained by monomer leak when the device comes into contact with substances in the adhesive having high extraction properties. This has already been described for alkyl glucosides that have been detected in foam wound dressings and may also occur in CGM system adhesive plasters.^{10,11}

As no therapy exists for ACD, the only way to prevent dermatological symptoms is to avoid exposure to the allergen. Hydrocolloid plates or stoma plates underneath the sensors have been recommended and may help some patients tolerate the CGM system for a while,¹² but these plasters are not a good long-term solution for most patients as their use is usually perceived as cumbersome. In addition, the patches have poorer resistance to water contact, requiring more frequent replacement of the sensor. In our case, in which CGM is mandatory to enable good metabolic control, the off-label use of a long-term implantable CGM system (Eversense XL) remains the only option.¹³ Apart from the fact that these devices have not yet been approved for children and adolescents, the need for periodic general anesthesia for sensor replacement poses additional risks and burdens for the patient. Since sensitization to an allergen lasts a lifetime and cross-reactivity to chemically related substances is possible, the prevention of ACD is of particular importance in pediatric patients. It is therefore problematic that materials contained in medical devices, such as glucose sensors, are not declared. In addition, manufacturers tend to be reluctant to communicate this information and address skin problems caused by their products adequately.^{2,5,14} There is accumulating evidence that adverse skin reactions to these devices affect a significant number of patients. Cooperation from the pharmaceutical and medical device industry is urgently needed, and effort should be made to avoid skin sensitizers provoking ACD, such as isobornyl acrylate in medical devices, especially if such devices are to be used in children.

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