

Generalized Urticaria Caused by a Glycerin Enema in an Infant

Kajita N¹, Kanamori K², Yamamoto S³, Yoshida K¹

¹Division of Allergy, Tokyo Metropolitan Children's Medical Center, Tokyo, Japan

²Division of Neurology, Tokyo Metropolitan Children's Medical Center, Tokyo, Japan

³Division of General Pediatrics, Tokyo Metropolitan Children's Medical Center, Tokyo, Japan

J Investig Allergol Clin Immunol 2022; Vol. 32(4): 318-319
doi: 10.18176/jiaci.0760

Key words: Glycerin enema. Allergy. Basophil activating test. Skin prick test. Contact urticaria.

Palabras clave: Enema de glicerina. Alergia. Test de activación de basófilos. Prick test. Urticaria de contacto.

Glycerin (C₃H₈O₃) is a trihydric alcohol that is used in cosmetic and noncosmetic applications [1]. In cosmetics, glycerin acts as a denaturant, fragrance ingredient, and hair conditioning agent. In noncosmetic applications, it is used in food packaging and medications, such as anorectal drug products, dermal protectants, ophthalmic products, and oral health care products. Few cases of hypersensitivity to glycerin have been reported [2-5], and the substance is generally considered to be hypoallergenic, since it is reported to be nonsensitizing [1]. Although the clinical picture of patients with allergy to glycerin and the utility of allergy testing for this condition are not fully understood, most patients with glycerin allergy present adult-onset contact eczema caused by creams or cosmetics containing glycerin. We report the case of an infant who developed generalized erythema and hives immediately after receiving a glycerin enema. Immunological contact urticaria was diagnosed based on the results of a skin prick test (SPT), basophil activating test (BAT), and drug provocation test (DPT). Informed consent to publish the details of the case was obtained from the patient's parents.

A female infant with a history of severe neonatal asphyxia (Apgar score 3 at 5 minutes), hypoxic ischemic encephalopathy, and infantile spasms started to receive daily glycerin enemas (GLYCERIN ENEMA 50%; Kenei Pharmaceutical Co., Ltd) to manage constipation during the neonatal period. The enemas did not contain polyethylene glycol. At age 8 months, she experienced generalized erythema and hives without respiratory or gastrointestinal symptoms on 2 occasions immediately after receiving a glycerin enema (Figure). Neither she nor her family had a history of allergic disease (eg, food allergy, bronchial asthma, or atopic dermatitis).

An SPT with 50% glycerin (concentration as described in a previous report [2]) produced a wheal measuring around 3 mm in diameter. Saline was negative, and histamine (Torii Pharmaceutical Co, Ltd) elicited wheals measuring about 5 mm in diameter. Activation >5% in the BAT (BML) is

considered positive. In the present case, basophil activation was 6.5% (in 0.048 g/mL of glycerin); in the negative and positive controls, it was 0.7% and 21.1%, respectively.

The patient's parents gave their written informed consent for the patient to undergo a DPT, in which she received 15 mL of a 50% glycerin enema solution under medical supervision. Thirty minutes later, she developed erythema and hives on her chest and thighs without perianal skin symptoms. Based on the results of the allergy tests, she was diagnosed with glycerin enema-induced immunological contact urticaria. After glycerin enemas and dietary glycerin were discontinued, the patient experienced no further allergic events.

Contact urticaria is characterized by the immediate onset of contact skin reactions, consisting mainly of wheals and flares [6]. The severity of contact urticaria can be classified into 4 stages: localized urticaria (stage 1), generalized urticaria (stage 2), extracutaneous involvement (stage 3), and generalized anaphylactoid reactions (stage 4) [6]. According to the classification, the case we present, which involved generalized urticaria, was considered stage 2 contact urticaria.

Of 6 previously reported cases of hypersensitivity to glycerin, 5 involved contact dermatitis, and only 1 involved contact urticaria (the patient was an 81-year-old woman [2] who had taken glycerin enemas on a regular basis to prevent constipation, as in the case we report). Interestingly, both patients had glycerin enema-induced immunological contact urticaria but no history of contact eczema and no further allergic symptoms after discontinuing glycerin. Glycerin in enema solutions is not absorbed by the rectal mucosa [7], although anorectal injuries incidental to frequent



Figure. Generalized urticaria after administration of a glycerin enema.

administration [8] may increase the risk of sensitization and even introduce antigens into the blood via the rectal venous plexus, thus leading to general symptoms.

In clinical practice, skin tests are often used to determine whether immunological mechanisms are involved, and the DPT is considered the gold standard in the diagnosis of drug hypersensitivity. However, these *in vivo* tests tend to be avoided, as in a previously reported case in which an intradermal test and a DPT were ruled out [2] owing to the risk of triggering allergic symptoms, such as anaphylaxis. The utility of the BAT has been shown in patients with drug allergy and food allergy and might reduce the need for DPTs [9]. Moreover, basophil activation triggered by diethyltoluamide has been reported in a patient with diethyltoluamide-induced contact urticaria [10]. The utility of BAT for diagnosing contact urticaria and glycerin allergy has not been established. However, in the present case, basophil activation was observed in response to glycerin; therefore, BAT may be useful for diagnosing contact urticaria and reducing the need for DPTs in patients with contact urticaria. This approach is expected to undergo further examination in future clinical studies.

IgE-induced basophil degranulation has been well documented for several allergens. However, with regard to pseudoallergens, such as nonsteroidal anti-inflammatory drugs, basophil activation does not seem to increase the expression of cell membrane markers [10]. The basophil response to glycerin seen on the BAT in the present case may suggest that the pathophysiology of the glycerin hypersensitivity reaction was IgE-mediated.

In conclusion, we report the case of an infant with generalized urticaria caused by a glycerin enema solution. This is the first report to describe SPT, BAT, and DPT-proven, glycerin-induced immunological contact urticaria. Glycerin enema solution was found to be capable of causing an allergic reaction. Further investigation is needed to understand the pathophysiology of hypersensitivity to glycerin and the differences between this condition and glycerin-induced contact dermatitis.

Acknowledgment

We thank Mr James Robert Valera for his assistance with editing this manuscript.

Funding

The authors declare that no funding was received for the present study.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

1. Becker LC, Bergfeld WF, Belsito DV, Hill RA, Klaassen CD, Liebler DC, et al. Safety Assessment of Glycerin as Used in Cosmetics. *Int J Toxicol*. 2019;38:6-22.
2. Suzuki R, Fukuyama K, Miyazaki Y, Namiki T. Contact urticaria syndrome and protein contact dermatitis caused by glycerin enema. *JAAD Case Reports*. 2016;2:108-10.
3. Tamagawa-Mineoka R, Katoh N, Kishimoto S. Allergic contact dermatitis due to 1,3-butylene glycol and glycerol. *Contact Dermatitis*. 2007;56:297-8.
4. Hannuksela M, Förström L. Contact hypersensitivity to glycerol. *Contact Dermatitis*. 1976;2:291.
5. Preston PW, Finch TM. Allergic contact dermatitis from glycerin in a moisturizing cream. *Contact Dermatitis*. 2003;49:221-2.
6. Tlanusta Garret M, Borders LD, Cruchfield LB, Torres-Rivera E, Brotherton D, Curtis R. Contact urticaria. *J Multicult Couns Devel*. 2001;29:147-58.
7. Wan B, Zhang H, Yin J, Fu H, Chen Y, Yang L, et al. Rhubarb vs. Glycerin enema for treatment of critically ill patients with intra-abdominal hypertension. *Exp Ther Med*. 2017;14:855-61.
8. Saltzstein RJ, Quebbeman E, Melvin JL. Anorectal injuries incident to enema administration. A recurring avoidable problem. *Am J Phys Med Rehabil*. 1988;67:186-8.
9. Salas M, Fernández-Santamaría R, Mayorga C, Barrionuevo E, Ariza A, Posadas T, et al. Use of the Basophil Activation Test May Reduce the Need for Drug Provocation in Amoxicillin-Clavulanic Allergy. *J Allergy Clin Immunol Pract*. 2018;6:1010-8 e2.
10. Galassi N, Fernández Romero DS, Yeyati E, Malbrán A. Diethyltoluamide (DEET) increases CD63 expression in a contact urticaria patient's basophils. *Allergol Immunopathol (Madr)*. 2011;39:55-7.

■ Manuscript received July 20, 2021; accepted for publication October 25, 2021.

Naoki Kajita

Tokyo Metropolitan Children's Medical Center
2-8-29 Musashidai, Fuchu, Tokyo 183-8561
Japan
E-mail: naoki_kajita@tmhp.jp