

LETTER TO THE EDITOR

Hydrolyzed wheat protein-containing facial soap-induced wheat-dependent exercise-induced anaphylaxis in a patient without filaggrin mutations

Dear Editor,

Wheat-dependent exercise-induced anaphylaxis (WDEIA) is a type of immediate hypersensitivity in which anaphylaxis develops when exercise is performed within several hours of ingestion of wheat products. Recently, an increasing number of patients with WDEIA who developed the condition during or after using continuously hydrolyzed wheat protein (HWP)-containing soap have been reported in Japan;¹ however, not all users of HWP (Glupearl 19S)-containing soap suffer from WDEIA. Therefore, its predisposing factor should be pursued.

Filaggrin (*FLG*) is an epidermal protein that optimizes and maintains skin barrier functions. A deficiency in *FLG* is a major predisposing factor to the development of atopic dermatitis, contact hypersensitivity to nickel, and other allergic diseases, such as peanut allergy.² This raises the notion that a skin barrier defect plays an important role in WDEIA associated with HWP. Herein, we report a patient with WDEIA sensitized to HWP that was used in facial soap without filaggrin mutations.

A 51-year-old woman had been using HWP-containing facial soap frequently and vigorously every day since 2004. Three months after she started to use HWP-containing soap, she suddenly developed angioedema on the eyelids and an urticarial rash on the face. She experienced similar episodes many times between 2004 and 2009 when eating food containing wheat was followed by mild exercise, but she kept using HWP-containing facial soap continuously. Her symptoms were limited to her face. In July 2009, she developed anaphylactic shock after ingesting normal wheat products. Based on the anaphylactic shock episode, we suspected that she had WDEIA. She had no history of atopic dermatitis or gastrointestinal food hypersensitivities. In addition, she did not exhibit dry skin.

After a skin prick test with Glupearl 19S diluted 1:10 000, she developed eyelid angioedema, dyspnea and a generalized urticarial rash on her entire upper extremity (Fig. 1). A serum allergen-specific immunoglobulin (Ig)E test (Immuno CAP; Phadia, Uppsala, Sweden) for wheat was 0.36 UA/mL and gluten-specific IgE was 0.40 UA/mL. Serum omega-5 gliadin-specific IgE antibody titers were within normal limits. Most patients with a common type of WDEIA reacted to omega-5 gliadin, but patients with HWP-WDEIA did not have specific IgE for omega-5 gliadin.

It is highly likely that the continual use of HWP-containing soap may have sensitized individuals when HWP penetrated the skin. The sensitivities to HWP may cross-react with natural wheat antigen.¹ Mutations in human *FLG* are associated with atopic dermatitis and are presumed to provoke a barrier deficiency.² We examined also whether this patient carried an *FLG* mutation reported in the Japanese population by direct genome sequencing (R501X, 3321delA, S1695X, Q1701X, S2554X, S2889X, S3296X, K4022X), which revealed that she had no *FLG* mutation.³

Kitagaki *et al.* demonstrated that repeated application of contact sensitizing to the same skin site results in a shift in the time course of antigen-specific hypersensitivity responses from a typical delayed-type hypersensitivity to immediate-type hypersensitivity in mice. This seems to apply in this case.⁴

The widespread use of HWP in food (such as preserved food and ham) and non-food products may multiply the risk of sensitization.⁵ The aggregation of peptide-bearing unmodified wheat proteins and others created by hydrolysis are possible factors in the allergenicity of HWP.⁵ It has recently been regarded that food allergy is due to skin barrier defects, especially because of an *FLG* mutation. However, our case suggests that even in patients without apparent skin barrier defects, the entrance of large molecules of antigens may occur by continuously using facial soap, resulting in increased percutaneous sensitization. The cause of the destruction of skin bar-

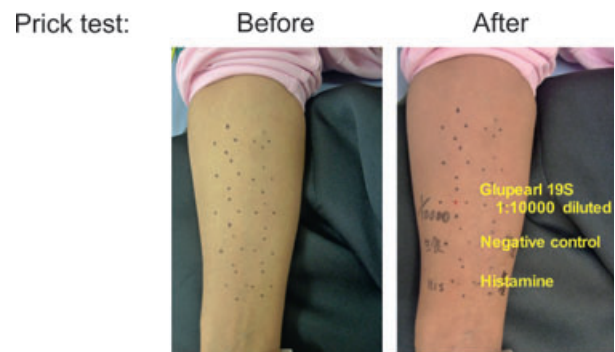


Figure 1. Skin prick test with Glupearl 19S diluted 1:10 000 induced severe generalized urticarial rash on the entire upper extremity.

riers other than *FLG* mutations could exist. Soap contains surfactants that may cause destruction of skin barriers. Excessive face washing may cause skin barrier disruption by surfactants. Intriguingly it has also been reported that WDEIA sensitized to HWP was induced by not only skin sensitization but also rhinoconjunctival sensitization.¹ Therefore, this observation raises the possibility that epicutaneous/rhinoconjunctival sensitization may be related not only with genetic factors but also with environmental/external factors.

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