

## Report

# Eighteen cases of wheat allergy and wheat-dependent exercise-induced urticaria/anaphylaxis sensitized by hydrolyzed wheat protein in soap

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**Abstract**

**Background** Glupearl 19S, an acid-hydrolyzed wheat protein (HWP), is used widely in Japan as a moisturizing ingredient in facial soaps. Since 2010, there has been an increasing number of reports of contact urticaria and wheat allergy resulting from the use of products containing this substance.

**Case reports** Sixty-one patients who had used HWP-containing facial soap visited our hospital. Thirty-five of these experienced urticaria or anaphylaxis after consuming wheat-containing food.

**Results** Eighteen of the 35 patients tested positive to 0.01% Glupearl 19S solution. Wheat-specific IgE and serum gluten-specific IgE were higher in the patients with HWP allergy than in non-HWP allergy patients. Among the patients who tested positive to Glupearl 19S on the skin prick test, nine experienced HWP–wheat-dependent exercise-induced anaphylaxis, and four experienced food-dependent anaphylaxis. Moreover, four of these patients not only experienced food-dependent anaphylaxis but also a worsening of the symptoms during exercise.

**Discussion** The clinical symptomatology was so variable that the patients were classified into six groups. We found that patients with HWP allergy tended to manifest symptoms of both HWP–wheat-dependent exercise-induced anaphylaxis and contact urticaria. The etiology of hydrolyzed wheat protein allergy is unknown. Patients with a history of these symptoms need to be informed about the risk of consuming wheat-containing foods and the importance of excluding such items from their diet.

**Introduction**

Hydrolyzed wheat protein (HWP), manufactured by using high temperatures and a strong acid to break down wheat gluten into its constituent amino acids (deamidation), is a common ingredient in both food and non-food items such as cosmetics, shampoos, and hair conditioners, where it is used as a moisturizing ingredient under the product name Glupearl 19S. Its widespread use has resulted in increasing reports of hypersensitivity resulting from ingestion of the substance or contact with the skin. Previous reports found that HWP triggered immediate contact urticaria in some individuals following the use of cosmetics containing this ingredient.<sup>1</sup> Since 2010, reported cases of contact urticaria and wheat allergy following the use of facial soap (Cha-no-Shizuku®; Yuuka Co. Ltd., Fukuoka, Japan) containing acid-HWP have risen steeply. According to the Japanese Allergy Association and the Japanese

Ministry of Health and Welfare, more than 400 patients to date have reportedly experienced an allergic reaction following the use of HWP-containing facial soap.

The publicity surrounding these cases has led numerous patients to visit our hospital for consultations, with the result that many were diagnosed with wheat allergy. The symptoms, serum specific IgE levels, and skin prick test results of 18 patients who were diagnosed with anaphylaxis induced by HWP-containing soap are discussed below.

**Case reports**

Sixty-one patients visited Tokyo Medical University Hospital between December 2010 and May 2012. All had used the same HWP-containing facial soap. Thirty-five patients reported that they had experienced urticaria or anaphylaxis after consuming wheat-containing food,

with symptoms in some cases apparently occurring when the patients exercised within 15 minutes of ingesting the food. For example, case 7, a 57-year-old woman, had been using soap containing HWP (Glupearl 19S) for 24 months. The patient reported developing a rash on the eyelids and buccal region whenever she consumed bread within 15 minutes of using soap containing Glupearl 19S. Case 5, a 47-year-old woman, had been using soap containing Glupearl 19S for 36 months. She eventually developed contact urticaria as a result and experienced anaphylaxis during light exercise (walking) following ingestion of pasta (Table 1). The skin prick test was carried out on 35 patients using wheat (commercial wheat flour extract [1 : 20 wt/vol; Torii Pharmaceutical Co., Tokyo, Japan]), 0.01% Glupearl 19S solution (kindly donated by Dr. Fukutomi, Sagamihara National Hospital, Sagamihara, Japan), positive histamine controls (10 mg/mL), and a negative saline solution control. The reactions were measured after 15 minutes in accordance with the method employed by the European Academy of Allergy and Clinical Immunology.<sup>2</sup> Eighteen of the 35 patients tested positive to 0.01% Glupearl 19S solution and were diagnosed with HWP allergy.

## Results

The average age of the patients with HWP allergy who tested positive to Glupearl 19S on the skin prick test was

$45.6 \pm 3.6$ . The ratio of female/male was 17 : 1. The average duration of the anaphylaxis associated with use of HWP-containing soap was  $34.7 \pm 8.6$  months (Table 1). The average serum level of wheat-specific IgE was higher in patients who tested positive to Glupearl 19S on the prick test than in patients who tested negative. However, the total IgE levels, gluten-specific IgE levels, and  $\omega$ -5 gliadin-specific IgE levels did not vary significantly between these two groups (Fig. 1). With regard to the occurrence of clinical symptoms following the use of soap among the Glupearl 19S skin prick test-positive patients, 10 of the patients with HWP allergy experienced contact urticaria and six patients experienced both contact urticaria, and food-dependent anaphylaxis. Fourteen patients had HWP–wheat-dependent exercise-induced anaphylaxis (HWP-WDEIA). Furthermore, four patients presented not only food-dependent anaphylaxis and contact urticaria but also experienced worsening symptoms with physical activity such as walking. One case (case 1) reported a worsening of anaphylaxis following both exercise and ingestion of aspirin (Table 1).

## Discussion

Hydrolyzed wheat protein has begun to be used widely in shampoos, soaps, and other cosmetics. In 2010, there were a number of reports of individuals in Japan who developed contact urticaria and allergy to wheat-based

**Table 1** Clinical features of patients with hydrolyzed wheat protein-sensitized urticaria or anaphylaxis

| Patient/case no. | Age (years) | Gender | Atopy | Length of use (months) | Anaphylaxis-inducing food             | Contact urticaria | Food-dependent urticaria/anaphylaxis | Wheat-dependent, exercise-induced urticaria/anaphylaxis |
|------------------|-------------|--------|-------|------------------------|---------------------------------------|-------------------|--------------------------------------|---------------------------------------------------------|
| 1                | 55          | F      |       | 15                     | Bread                                 | ND                | —                                    | + Aspirin-induced                                       |
| 2                | 54          | F      |       | 31                     | Bread                                 | —                 | +                                    | —                                                       |
| 3                | 44          | F      |       | 48                     | Flour noodles, pasta                  | —                 | +                                    | —                                                       |
| 4                | 21          | F      | AR    | 12                     | Bread, flour noodles, deep-fried food | +                 | —                                    | +                                                       |
| 5                | 47          | F      |       | 36                     | Bread, pasta, quiche                  | +                 | +                                    | +                                                       |
| 6                | 68          | F      |       | 48                     | Bread                                 | —                 | —                                    | +                                                       |
| 7                | 57          | F      | AR    | 24                     | Bread                                 | +                 | +                                    | —                                                       |
| 8                | 24          | F      |       | 15                     | Bread                                 | +                 | +                                    | +                                                       |
| 9                | 49          | F      |       | 48                     | Flour noodles                         | +                 | +                                    | —                                                       |
| 10               | 39          | F      |       | 18                     | Tempura, pasta                        | +                 | +                                    | +                                                       |
| 11               | 29          | F      | AR    | ND                     | Pasta                                 | —                 | —                                    | +                                                       |
| 12               | 34          | F      | AD    | 72                     | Bread                                 | +                 | —                                    | +                                                       |
|                  |             |        | AR    |                        |                                       |                   |                                      |                                                         |
| 13               | 39          | F      |       | 19                     | Bread                                 | —                 | —                                    | +                                                       |
| 14               | 35          | F      | AR    | 60                     | Bread                                 | ND                | —                                    | +                                                       |
| 15               | 65          | F      | AR    | 24                     | Chinese noodles                       | +                 | —                                    | +                                                       |
| 16               | 29          | F      | AR    | 12                     | Bread, pasta, pizza                   | +                 | —                                    | +                                                       |
| 17               | 59          | F      |       | ND                     | Pasta                                 | +                 | +                                    | +                                                       |
| 18               | 73          | M      |       | 60                     | Bread, Chinese noodles                | —                 | —                                    | +                                                       |

AD, atopic dermatitis; AR, allergic rhinitis; BA, bronchial asthma; ND, no data.

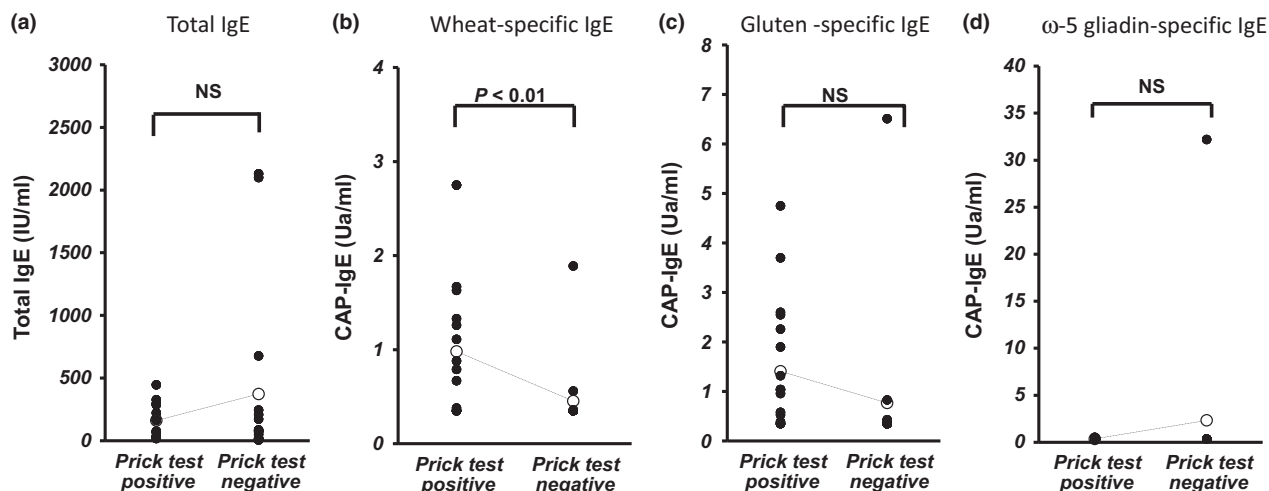


**Figure 1** Comparison of serum IgE levels between hydrolyzed wheat protein prick test-positive and -negative patients. (a) Total IgE, (b) wheat-specific IgE, (c) gluten-specific IgE, and (d) ω-5 gliadin-specific-IgE with CAP system. Closed circles show each IgE level in the patients. Open circles show the average IgE levels. Analysis by Students *t*-test

food after using HWP-containing facial soap. The wide publicity surrounding these cases caused anxiety in many consumers, prompting visits to the hospital for consultations regarding possible wheat allergy. Of the 61 patients who were seen at our hospital for suspected wheat allergy, 18 were diagnosed with wheat allergy sensitized by HWP-containing facial soap.

To clarify the differences in clinical symptomatology, the patients were divided into six groups (Table 1): group I consisted only of cases of contact urticaria; group II only of food-dependent urticaria/anaphylaxis; group III only of wheat-dependent, exercise-induced urticaria/anaphylaxis; group IV of contact urticaria and food-dependent urticaria/anaphylaxis; group V of contact urticaria and wheat-dependent, exercise-induced urticaria/anaphylaxis; and group VI of contact urticaria and

both food-dependent urticaria/anaphylaxis and wheat-dependent, exercise-induced urticaria/anaphylaxis (Table 2). None of the patients in our study fell into group I. However, six of the 18 patients fell into group III and four fell into group V. These data suggest that HWP allergy tends to produce symptoms of wheat-dependent, exercise-induced urticaria/anaphylaxis rather than food-dependent urticaria/anaphylaxis. Interestingly, ω-5 gliadin-specific IgE was not detected in patients with wheat-dependent, exercise-induced urticaria/anaphylaxis sensitized by HWP, whereas serum wheat- and gluten-specific IgE were detected strongly in many of these patients. Generally, classical cases of wheat-dependent, exercise-induced urticaria/anaphylaxis react to ω-5 gliadin-specific IgE, but there have been exceptions among previously reported HWP-sensitized cases.<sup>3–5</sup> Among our patients, four of the HWP-

**Table 2** The clinical categories of hydrolyzed wheat protein allergy in 18 Glupearl 19S prick test-positive patients

| Group no. | Symptoms          |                                      |                                                         | No. of clinical cases          |
|-----------|-------------------|--------------------------------------|---------------------------------------------------------|--------------------------------|
|           | Contact urticaria | Food-dependent urticaria/anaphylaxis | Wheat-dependent, exercise-induced urticaria/anaphylaxis |                                |
| Group I   | +                 |                                      |                                                         | 0                              |
| Group II  |                   | +                                    |                                                         | 2                              |
| Group III |                   |                                      | +                                                       | 6 (1 case was aspirin induced) |
| Group IV  | +                 | +                                    |                                                         | 2                              |
| Group V   | +                 |                                      | +                                                       | 4                              |
| Group VI  | +                 | +                                    | +                                                       | 4                              |
|           |                   |                                      | Total                                                   | 18                             |

dependent, exercise-induced urticaria/anaphylaxis cases experienced contact urticaria, while another four presented contact urticaria and food-dependent anaphylaxis. While the etiology of contact urticaria and food-dependent anaphylaxis mediated by skin or nasal mucosal sensitization is clear, the pathogenesis of HWP-WDEIA has yet to be explained. We suggest that an allergen in HWP-WDEIA cross-reacts with a wheat allergen to produce the symptoms. There is one clinical report of the remission of HWP-WDEIA symptoms after the patient discontinued use of HWP-containing soap for six months.<sup>5</sup> Unfortunately, none of the cases in this study showed a remission of anaphylaxis by this method. This fact underscores the need for patients with a history of these symptoms to be informed about the risk of consuming wheat-containing foods and the importance of excluding such items from their diet. Much further research and long-term observation are needed to clarify anaphylaxis induced by wheat.

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