

## Case Report

# Diagnosis and long-term management of hydrolyzed wheat protein wheat-dependent exercise-induced anaphylaxis

Jun-ichi Hirata, Munehiko Ohya, and Keiji Kumon

Department of Emergency and Critical Care Medicine, Kinki University Faculty of Medicine, Nara Hospital, Nara, Japan

**Case:** A 37-year-old woman was admitted to the emergency room with bilateral periorbital edema, hypotension, and expiratory stridor that developed 30 min after starting to hang out washing following consumption of a jam bun. Despite no food allergies or similar episodes, she had recently developed facial wheals after bathing.

**Outcome:** She was immediately and repeatedly administered adrenalin and succinic acid hydrocortisone sodium for wheat-dependent exercise-induced anaphylaxis. On the third hospital day, radioallergosorbent testing reactions to wheat, gluten, and omega-5 gliadin were mildly positive; skin-prick tests for hydrolyzed wheat protein and a face-wash challenge were positive. Therefore, we diagnosed hydrolyzed wheat protein wheat-dependent exercise-induced anaphylaxis. Despite advising her about hyposensitization, the episode recurred and an adrenalin auto-injector was prescribed.

**Conclusion:** Differentiating hydrolyzed wheat protein wheat-dependent exercise-induced anaphylaxis from conventional wheat-dependent exercise-induced anaphylaxis is important owing to their severity and similarities. Each requires long-term management of patients' etiological conditions by advising them about hyposensitization and prescribing adrenalin auto-injectors.

**Key words:** Face-wash challenge test, hydrolyzed wheat protein, radioallergosorbent test, skin-prick tests, wheat-dependent exercise-induced anaphylaxis

## INTRODUCTION

**H**YDROLYZED WHEAT PROTEIN wheat-dependent exercise-induced anaphylaxis (HWP-WDEIA) is a rare but recurrent condition with potentially life-threatening clinical features, including hypotension and shock.<sup>1,2</sup> The diagnosis may be difficult because the combination of wheat ingestion and exercise is necessary to precipitate symptoms,<sup>1,2</sup> which may not be apparent. Therefore, the emergency room management of WDEIA not only involves the management of symptoms, but also patient education to prevent recurrence.

Hydrolyzed wheat protein WDEIA is similar to conventional wheat-dependent exercise-induced anaphylaxis (CO-WDEIA) in that they both cause exercise-induced anaphylaxis that is not dependent on the intensity of the exercise. However, immunological studies have differentiated

HWP-WDEIA from CO-WDEIA, and an increasing number of HWP-WDEIA case reports have been published since 2009.<sup>1,2</sup> It is important to differentiate these forms of anaphylaxis for the long-term management of patients, which includes hyposensitization of patients once the etiology has been determined. Explaining hyposensitization to patients effectively, providing patient education about anaphylaxis, and improving patient acceptance of adrenalin auto-injectors are important issues. Here, we report a case of HWP-WDEIA that was diagnosed based on the results of hydrolyzed wheat protein (Glupearl 19S) skin-prick test<sup>3</sup> and a face-wash challenge test. An adrenalin auto-injector was prescribed after the patient experienced two similar episodes.

## CASE

**A** 37-YEAR-OLD WOMAN WAS admitted to the emergency room in a confused but conscious state following the sudden onset of breathing difficulties, itchy eyes, nasal discharge, lips and tongue irritation, bilateral periorbital edema (Fig. 1), and lower extremities flare and edema (Fig. 2), 30 min after starting to hang out washing. The fact

**Corresponding:** Jun-ichi Hirata, MD, PhD, Department of Emergency and Critical Care Medicine, Kinki University Faculty of Medicine, Nara Hospital, 1-1248, Otsuda, Ikoma, Nara 630-0293, Japan. E-mail: qq-hira@i.softbank.jp; qq-hira@hyo-med.ac.jp. Received 1 Dec, 2014; accepted 5 Jan, 2015; online publication 27 April, 2015



**Fig. 1.** Bilateral periorbital edema, tongue flare, and edema in a 37-year-old woman who developed symptoms 30 min after starting to hang out washing following consumption of a jam bun. She had also recently developed facial wheals after bathing.



**Fig. 2.** Flare and edema on the lower extremities in a 37-year-old woman admitted to the emergency room with bilateral periorbital edema, hypotension, and expiratory stridor that developed 30 min after starting to hang out washing following consumption of a jam bun. She had also recently developed facial wheals after bathing.

that she experienced these symptoms soon after eating a jam bun for breakfast was unusual. Although she had never experienced a similar episode, she had recently developed facial wheals and nasal discharges after bathing. Her medical

history was unremarkable; she had no food allergies. On emergency room arrival, clinical examination results confirmed hypotension (blood pressure, 90/63 mmHg) and tachycardia (134 b.p.m.); she had a body temperature of 37.1°C. Her breathing was tachypneic (24 breaths/min) with an expiratory stridor, and peripheral oxygen saturation from the air in the room was 82%. She was slightly agitated and emitted hoarse cries, but could not obey instructions. She attempted to open her eyes, but could not because of the presence of massive bilateral periorbital edema. Furthermore, she possibly had bilateral pitting edema on her lower extremities. Findings from thyroid, lymph node, abdominal, and gynecological examinations were normal. Considering a diagnosis of anaphylactic shock, we initiated early treatment, pending a more detailed examination.

The total serum immunoglobulin (Ig) E level was elevated at 302 IU/mL. Radioallergosorbent tests showed mildly positive reactions to class 3 wheat, gluten, and omega-5 gliadin. Skin-prick tests showed positive reactions to wheat and the bathing soap used, which was administered as a 0.1% Glupearl 19S solution in saline.<sup>3</sup>

The woman was placed flat on her back with her legs elevated; she was provided oxygen supply. She was immediately treated with 0.3 mg adrenalin i.m., twice every 30 min, continuously, and 100 mg succinic acid hydrocortisone sodium i.v. three times every 6 h for 2 days. Her breathing spontaneously improved, but the periorbital edema persisted until the next day. The patient was discharged on the third hospital day. No symptoms were observed when aspirin was consumed alone or when she was challenged with wheat alone. However, when she was hospitalized for observation on another occasion, a face-wash challenge test induced facial wheals. On the basis of her medical history and the positive provocation test results, we diagnosed her with WDEIA caused by Glupearl 19S. One month later, she was admitted to the emergency room with similar symptoms caused by exercising after eating noodles. After this episode, she was prescribed an adrenalin auto-injector.

## DISCUSSION

WHEAT IS AMONG the most frequent food allergens in adults. Allergies to wheat are known to develop in adults, one of which is WDEIA.<sup>1</sup> Conventional clinical experiences show periorbital edema, flare, and urticaria on the face to be the main clinical manifestations of wheat allergies, but this is not true in WDEIA, which is characterized by systemic pomphus. Since 2009, such cases were often reported as “atypical” in adult women.<sup>2</sup> Allergies in these atypical wheat allergy cases appeared to manifest as peculiar erethisms associated with the hydrolyzed wheat protein,

Glupearl 19S, present in particular soap types, the use of which can precede reactions caused by the ingestion of food containing wheat.<sup>2</sup> Importantly, we identified this allergen as the cause of the first anaphylaxis in the current case, but special treatment was not necessary and the same treatment used previously was effective.

Differentiation between CO-WDEIA and HWP-WDEIA is important, because both often occur in association with exercise-induced anaphylaxis. The type of soap used should be considered, because the use of some soaps precedes the onset of HWP-WDEIA. In an immunological study, Chinuki *et al.* suggested that the differentiation between CO-WDEIA and HWP-WDEIA might be characterized by changes in omega-5 gliadin-specific serum IgE antibody levels, which are high in CO-WDEIA and low and/or negative in HWP-WDEIA. Gluten-specific IgE antibody levels are higher than omega-5 gliadin-specific serum IgE antibody levels in HWP-WDEIA.<sup>2</sup> Furthermore, 76.6% of HWP-WDEIA patients were positive for the gluten-specific IgE antibody compared with 37% of CO-WDEIA patients.<sup>2</sup> Although the specific antibodies measured in the current case were mildly positive, the most persuasive evidence for diagnosis was the positive results of the skin-prick test for Glupearl 19S and the face-wash challenge test. Given these findings, it may be difficult to diagnose HWP-WDEIA based on gluten-specific IgE antibody levels and omega-5 gliadin-specific serum IgE antibody levels alone.<sup>2</sup>

In August 2014, 2,169 people in Japan were registered as having HWP-WDEIA.<sup>3</sup> Yokooji *et al.* reported differences in the manifestations of HWP-WDEIA in Japanese patients compared to European patients.<sup>4</sup> Many Europeans with HWP-WDEIA demonstrate an immediate allergic reaction only with ingestion of HWP-containing foods but not with normal wheat product ingestion.<sup>4</sup> In contrast, in Japan, the allergic or anaphylactic reaction is typically precipitated by exercise, and it occurs even with natural wheat product ingestion.<sup>4</sup> This seems to occur because of a specific IgE to HWP that cross-reacts with WP in Japanese HWP-WDEIA patients. Yokooji *et al.* identified the primary IgE-binding epitopes using immunoblotting analysis.

The methods used for long-term management of patients are important. They should be based on the etiology of the allergy and the patient's condition, and clinicians often find this challenging. First, the patient should stop using the soap that causes the reaction, refrain from exercise within 4 h of consuming wheat, and should probably prohibit wheat intake

after consuming aspirin, which can trigger WDEIA-like allergic symptoms. Aspirin consumption does not pose a problem when consumed in the absence of wheat intake.<sup>1</sup> Nevertheless, it is difficult to explain these allergic mechanisms to patients. This was illustrated by our patient who experienced two further anaphylactic episodes despite being advised about the lifestyle changes she should make to avoid allergic reactions.

Second, the adrenalin auto-injector should be carried at all times and used when allergic reactions occur to avoid anaphylaxis. However, medication administered by an s.c. or i.m. injection may have a low uptake because of patient anxieties associated with needles and injections. A good alternative to injections, which should be considered, is tablets that dissolve in the mouth.

## CONCLUSION

THE PREVIOUSLY USED treatment for anaphylaxis was effective in HWP-WDEIA. Results of a Glupearl 19S skin-prick test and a face-wash challenge test helped to clearly differentiate CO-WDEIA from HWP-WDEIA. Patient education, including advice about hyposensitization, and methods for delivering adrenalin to increase the use, are important issues.

## CONFLICT OF INTEREST

NONE.

## REFERENCES

- 1 Morita E, Kunie K, Matsuo H. Food-dependent exercise-induced anaphylaxis. *J. Dermatol. Sci.* 2007; 47: 109–17.
- 2 Chinuki Y, Morita E. Wheat-dependent exercise-induced anaphylaxis sensitized with hydrolyzed wheat protein in soap. *Allergol. Int.* 2012; 61: 529–37.
- 3 The Rheumatism and Allergy Information Center. Information concerning wheat allergy. [cited 3 Feb 2012]. Available from: <http://www.allergy.go.jp/allergy/flour/index.html>.
- 4 Yokooji T, Kurihara S, Murakami T *et al.* Characterization of causative allergens for wheat-dependent exercise-induced anaphylaxis sensitized with hydrolyzed wheat proteins in facial soap. *Allergol. Int.* 2013; 62: 435–45.