

A Curious Case of Exercise-Induced Wheat Allergy in Adulthood

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Food-dependent exercise-induced anaphylaxis (FDEIA) is a rare, life-threatening syndrome characterized by anaphylactic symptoms triggered by the combination of exercise and the ingestion of a specific sensitizing food [1,2]. Concomitant medications and alcohol intake can act as additional facilitating factors. As opposed to what happens in exercise-induced anaphylaxis, exercise on its own is well tolerated in FDEIA, as is ingestion of the sensitizing food if not associated with exercise. We report a case of wheat-dependent exercise-induced anaphylaxis in adulthood.

A 59-year-old man was referred to our department for recurrent episodes of anaphylaxis. He had had 2 similar episodes consisting of the sudden development of rhinoconjunctivitis, generalized urticaria, facial and upper airway angioedema, dyspnea, and loss of consciousness that required medical assistance in the emergency room. These episodes occurred while he was out walking following a home-made dinner that consisted of vegetable soup and wheat-based bread. There were no symptoms when he performed exercise after ingestion of food other than cereals. The patient would take his prescription medication, namely furosemide, atorvastatin, and acetylsalicylic acid (ASA), at dinner time. It is noteworthy that he denied the occurrence of symptoms with the ingestion of wheat and ASA in the absence of exercise. There were no other co-factors such as alcohol consumption or stress.

The patient had no previous history of atopy, allergy, or intolerance to food or drugs. The anaphylactic episodes started

when the patient was 55 years old, following coronary heart surgery and the prescription of furosemide, atorvastatin, and ASA. This also coincided with changes in the patient's lifestyle, with light dinners consisting of soup and bread and regular exercise, mainly walks after dinner.

On admission to our department, 2 months after the second episode of anaphylaxis, the physical examination was unremarkable. Laboratory studies including complete blood count, sedimentation rate, serum electrolytes, liver and renal function tests, complement and serum tryptase levels, and skin biopsy were all normal. The patient had a high level of total IgE (443 IU/mL). Skin prick tests using commercial extracts of common aeroallergens and cereals (ALK, Abelló) as previously described [3] were negative. Prick-to-prick tests with wheat, rye, corn, oat, and rice flours provided by the bakery where the patient had bought the bread on the days of the episodes were performed. Prick-to-prick tests carried out in a control group of 5 healthy individuals were all negative. Specific IgE was measured using the ImmunoCAP FEIA system (Phadia) following the manufacturer's recommendations. Levels above 0.35 kU/L were considered positive. The results of the prick-to-prick tests and specific IgE determinations are shown in the Table. Oral challenges with wheat and exercise were not performed due to the patient's coronary heart disease.

The patient was advised to avoid eating wheat and rye 3 hours before and 1 hour after exercise. Patient education included detailed information on foods that may contain hidden cereals. A written emergency plan including self-injectable adrenaline, cetirizine, and prednisolone was delivered. ASA (100 mg/d) was replaced by clopidogrel (75 mg/d), after consulting the patient's cardiologist. The patient was advised to avoid other nonsteroidal anti-inflammatory drugs (NSAIDs). He continued to eat corn, barley, oats, and rice. With the avoidance measures taken, no more allergic symptoms or anaphylactic episodes occurred. Total IgE declined to 173 IU/mL and specific IgE to wheat, rye, and recombinant omega-5 gliadin decreased to 0.38, 0.63, and 4.14 kU/L, respectively.

The diagnosis of FDEIA triggered by wheat ingestion was strongly supported by our results. The presence of specific IgE to recombinant ω -5-gliadin (r ω -5-gliadin) was demonstrated. This is the major causative allergen in wheat-dependent exercise-induced anaphylaxis (WDEIA), and has

Table. Skin Prick Tests and Specific IgE Results

| Allergen Source | Prick Test (Wheal Diameter) | Prick-to-Prick Test (Wheal Diameter) | Specific IgE, kU/L | |
|---------------------------------|-----------------------------|--------------------------------------|--------------------|----------------|
| Histamine | Positive (5 mm) | | | |
| Flours | Wheat | Negative | Positive (8 mm) | 0.9 (class 2) |
| | Rye | Negative | Positive (10 mm) | 4.2 (class 3) |
| | Barley | Negative | Positive (4 mm) | 0.06 (class 0) |
| | Corn | Negative | Positive (4 mm) | 0.05 (class 0) |
| | Oats | Negative | Negative | 0.04 (class 0) |
| | Rice | Negative | Negative | 0.04 (class 0) |
| ω -5-gliadin (rTri a 19) | | | 9.7 (class 3) | |

been reported to cause reactions in approximately 80% of all patients with this condition [4]. In our patient, the level of specific IgE to wheat and rye was particularly low compared with that to ω -5-gliadin. This finding is in accordance with previous reports [4,5], indicating a higher capacity of the recombinant allergen molecule to detect allergen-specific IgE. Matsuo et al [5] demonstrated that the sensitivity of the in vitro test measuring specific IgE to ω -5-gliadin is highest in the identification of patients with WDEIA, with lower sensitivities seen for wheat, gluten, and the high-molecular-weight glutenin subunit. Furthermore, the authors estimated that the cutoff value for specific IgE to ω -5-gliadin giving maximal efficiency in the diagnosis of WDEIA was 0.89 kU_A/L [5]. Because of the high level of specific IgE to ω -5-gliadin (9.7 kU/L) in our patient, we did not consider it essential to perform an oral challenge to confirm the clinical diagnosis. Besides, we considered that oral challenge with wheat and exercise was contraindicated because of the patient's heart condition.

This case is unusual because of the late age of onset and the combination of different triggering factors. The patient had increased the ingestion of wheat, particularly in the evenings when he used to take ASA, just before exercising. The pathophysiology of FDEIA is not fully understood [2]. Possible explanations involve physiological changes that occur during exercise, such as enhanced plasma osmolality, decreased pH, blood flow redistribution, and increased sensitivity of basophils and mast cells to degranulation [1,6]. Moreover, as both food and exercise are independently tolerated, several factors need to occur synergistically to produce symptoms. One critical factor is the increased intestinal permeability to allergens that occurs with exercise and that is dependent of enhanced tissue enzyme activity, which facilitates additional epitope recognition [2]. It is well described that the intake of ASA and other NSAIDs can enhance the induction of type I allergic symptoms when combined with food and exercise in patients with FDEIA [2,6,7]. These drugs might increase gastrointestinal permeability to allergens and allergic histamine release from human leukocytes [6-8]. It has also been recognized that exercise and ASA intake, even at low doses, act synergistically to produce severe symptoms [7,10]. In the particular case of WDEIA patients, Matsuo et al [9] demonstrated that exercise and ASA increase levels of circulating gliadin. Furthermore, they observed that blood gliadin levels were correlated with clinical symptoms, strongly supporting the hypothesis that exercise and ASA facilitate allergen absorption from the gut.

In our opinion the low baseline absorption of ω -5-gliadin was probably significantly enhanced by the additional effects of exercise and ASA intake, and the synergistic effect of these co-factors was sufficient to amplify the symptoms and trigger anaphylaxis.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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