



# A Pediatric Case of Wheat-Dependent, Exercise-Induced Anaphylaxis Solely Associated with High-Molecular-Weight Glutenin

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Received: 6 April 2022 / Accepted: 23 June 2022 / Published online: 16 July 2022  
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*To the Editor:* In wheat-dependent, exercise-induced anaphylaxis (WDEIA) patients, the positive rate of specific IgE of wheat, gluten, omega-5 gliadin, and high-molecular-weight (HMW) glutenin was reported to be 41.0%, 43.5%, 82.0%, and 12.8%, respectively [1]. On stratification by age, the positive rate of omega-5 gliadin was shown to be 92.8% in WDEIA patients  $\geq 20$  y old but 46.1% in patients  $< 20$  y old. Omega-5 gliadin may not be a major allergen for pediatric WDEIA patients.

An 11-y-old boy presented with a history of 4 episodes of anaphylaxis. Based on his clinical history, we suspected that he had WDEIA. Although specific IgE tests conducted by ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden) were negative for wheat, gluten, and omega-5 gliadin, exercise for 2 h after meals and wheat intake before exercise were prohibited. Since then, he had been free from symptoms. A definite diagnosis of WDEIA was made at the age of 14 y based on the positive result of the exercise provocation test of wheat. Specific IgE tests examined by enzyme-linked immunoassay were positive for HMW glutenin (3.51 kUE/L), but neither alpha/beta gliadin nor gamma gliadin.

In diagnosing WDEIA in children, the usefulness of HMW glutenin has been suggested; the positive rate of HMW glutenin (38.9%) was higher than that of omega-5 gliadin (27.8%) [2]. HMW glutenin-positive cases were also reported to be positive for wheat, omega-5 gliadin, and alpha/beta/gamma gliadin [3]. Three WDEIA patients  $< 20$  y old, who

were positive only for HMW glutenin were reported, but their alpha/beta/gamma gliadin levels were not examined [4]. Therefore, to the best of our knowledge, this is the first pediatric WDEIA patient, who was sensitized solely to HMW glutenin, not to wheat, gluten, omega-5 gliadin, and alpha/beta/gamma gliadin.

In conclusion, diagnosing WDEIA in children is challenging, and wheat allergen components including HMW glutenin should be examined. This approach may be substituted for a provocation test.

## Declarations

**Conflict of Interest** None.

## References

1. Morita E, Matsuo H, Chinuki Y, Takahashi H, Dahlström J, Tanaka A. Food-dependent exercise-induced anaphylaxis—importance of omega-5 gliadin and HMW-glutenin as causative antigens for wheat-dependent exercise-induced anaphylaxis. *Allergol Int.* 2009;58:493–8.
2. Fukuda H, Yoshihara S. Usefulness of allergen components in diagnosis of food-dependent exercise-induced anaphylaxis. *J Pediatr Allergy Clin Immunol.* 2017;31:53–7.
3. Hofmann SC, Fischer J, Eriksson C, Bengtsson Gref O, Biedermann T, Jakob T. IgE detection to  $\alpha/\beta/\gamma$ -gliadin and its clinical relevance in wheat-dependent exercise-induced anaphylaxis. *Allergy.* 2012;67:1457–60.
4. Kohno K, Matsuo H, Takahashi H, et al. Serum gliadin monitoring extracts patients with false negative results in challenge tests for the diagnosis of wheat-dependent exercise-induced anaphylaxis. *Allergol Int.* 2013;62:229–38.

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