Allergologia et immunopathologia
Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica
www.all-imm.com

CASE REPORT OPEN ACCESS

Component-resolved diagnostics in pediatric wheat-dependent exercise-induced anaphylaxis: A case report

Manabu Miyamoto[a]*, Nobuyuki Maruyama[b], Shigemi Yoshihara[a,c]

[a]*Department of Pediatrics, Dokkyo Medical University, Tochigi, Japan*
[b]*Laboratory of Food Quality Design and Development, Graduate School of Agriculture, Kyoto University, Kitashirakawa Oiwake-cho, Sakyo-ku, Kyoto, Japan*
[c]*Allergy Center, Dokkyo Medical University, Tochigi, Japan*

Received 1 January 2025; Accepted 7 March 2025
Available online 1 July 2025

KEYWORDS
allergens;
exercise-induced allergies;
omega-5 gliadin;
triticum aestivum;
wheat hypersensitivity

Abstract
Wheat-dependent exercise-induced anaphylaxis (WDEIA) is a subtype of immunoglobulin E (IgE)-mediated wheat allergy characterized by symptoms from wheat intake followed by physical exercise. Although omega-5 gliadin-specific IgE (sIgE) is widely used for diagnosing WDEIA, its sensitivity is lower in children than in adults. This report describes a 13-year-old male with suspected wheat allergy who experienced anaphylaxis following wheat ingestion and exercise. ImmunoCAP results revealed positive sIgE for wheat and gluten but negative results for omega-5 gliadin. An open-label oral food challenge combined with exercise confirmed the diagnosis of WDEIA. Notably, alpha/beta gliadin sIgE was detected using an enzyme-linked immunosorbent assay with the patient's serum, suggesting that alpha/beta gliadin can serve as an alternative marker in pediatric cases where omega-5 gliadin sIgE is undetectable. This suggests that omega-5 gliadin sIgE alone may not be appropriate for diagnosing WDEIA in children. Instead, utilizing a combination of other wheat protein components may enhance both sensitivity and specificity in diagnosis.

Introduction

Wheat-dependent exercised-induced anaphylaxis (WDEIA) is a subtype of immunoglobulin E (IgE)-mediated wheat allergy.[1] The omega-5 gliadin-specific IgE (sIgE) detection method has been widely used in diagnosing WDEIA, demonstrating a high sensitivity of 89.3% and specificity of 88.9% in affected patients[2]; however, in children, the positive rate of omega-5 gliadin sIgE is lower than that in adults (46.1% in children, 92.8% in adults).[3] The use of sIgE testing for Tri a 14, a nonspecific lipid transfer protein found in wheat as well as for high-molecular-weight (HMW) glutenin,

***Corresponding author**: Manabu Miyamoto, Department of Pediatrics, Dokkyo Medical University, 880 Kitakobayashi, Mibu, Shimotsuga, Tochigi, Japan. Email address: manabu-m@dokkyomed.ac.jp

https://doi.org/10.15586/aei.v53i4.1316

low-molecular-weight glutenin, and alpha/beta gliadin (Tri a 21), has been shown in patients who are negative for omega-5 gliadin.[1,4-6] Recently, novel WDEIA diagnostic markers have been developed; however, their effectiveness in children remains unclear.[7] In this report, we address the limitations of omega-5 gliadin IgE in diagnosing children with WDEIA and explore the potential of alpha/beta gliadin as an alternative biomarker.

Case Report

A 13-year-old male visited Dokkyo Medical University Hospital for the diagnosis of wheat allergy. He had not eliminated wheat from his diet prior to consultation. After consuming lunch containing wheat and subsequently exercising, he developed urticaria, dyspnea, coughing, and nausea, ultimately leading to anaphylaxis. The ImmunoCAP test (Thermo Fisher Scientific, Uppsala, Sweden) results indicated sIgE levels of 3.50 UA/mL for wheat, 4.95 UA/mL for gluten, and < 0.10 UA/mL for omega-5 gliadin. When he was 14 years old, an open-label oral food challenge (OFC) was conducted for diagnosis. After eating 300 g of wheat noodles (equivalent to 7.8 g of wheat protein), which was the maximum amount he could consume, he underwent exercise without taking aspirin. Ten minutes after commencing the exercise, he experienced pruritus, urticaria on his trunk, and dyspnea, leading to a diagnosis of WDEIA. Pre-exercise examination revealed a plasma tryptase concentration of 1.5 μg/L and a histamine concentration of 1.08 ng/mL; however, the levels immediately post-exercise increased to 1.9 μg/L and 1.74 ng/mL, respectively. Using the patient's serum, enzyme-linked immunosorbent assay using recombinant proteins demonstrated a positive result for alpha/beta gliadin (Tri a 21) (Table 1). We performed this assay in the same method as previously reported.[8] Subsequently, the patient avoided allergic reactions by refraining from exercise after wheat intake.

Written informed consent from the parents of the patient was obtained for the publication of this report.

Discussion

We reported a pediatric patient with WDEIA who was negative for omega-5 gliadin sIgE. Morita et al. indicated that the power of detection in the omega-5 gliadin sIgE was insufficient in pediatric patients with WDEIA (< 20 years).[3] Previous case reports have highlighted cases where children exhibited only HMW glutenin sIgE.[5,6] Aoki et al. reported that in five patients with WDEIA without sensitization to omega-5 gliadin, sIgE to alpha/beta gliadin MM1, which has < 70% protein sequence homology with alpha/beta gliadin (Tri a 21), and low molecular weight (LMW)-m glutenin subunit 8 was detected in all cases.[7] Notably, three of these five patients were children aged between 9 and 17 years. Our suggestion is that omega-5 gliadin sIgE alone is inadequate as a biomarker for the diagnosis of WDEIA in children, highlighting the necessity to test for multiple allergen component sIgE. However, a significant challenge remains: the components used in these studies are not standardized and cannot be used in general clinical practice. Further comprehensive studies are needed to determine whether sensitization to the allergen components already identified should be assessed individually or in combination to enhance diagnostic accuracy and clinical management of WDEIA in pediatric populations.

Table 1 Result of specific IgE levels using enzyme-linked immunosorbent assay.

Allergen	Specific IgE level (kU_E/L)
Nonspecific lipid transfer protein 1	0.01
Gamma gliadin	0.26
Alpha/beta gliadin	1.74
High-molecular-weight glutenin	0.16
Tetrameric alpha-amylase inhibitor CM1/CM2	0.36
Alpha purothionin	0.08

Conclusion

Omega-5 gliadin sIgE alone may not be an adequate diagnostic marker for WDEIA in children. Its use in conjunction with other wheat protein components may enhance both sensitivity and specificity in the diagnostic process.

Acknowledgments

We thank all the staff members who assisted with the oral food challenge test.

Author Contributions

All authors contributed equally to this article.

Conflicts of Interest

The authors declare no potential conflicts of interest with respect to research, authorship, or publication of this article.

Funding

None.

References

1. Preda M, Popescu FD, Vassilopoulou E, Smolinska S. Allergenic biomarkers in the molecular diagnosis of IgE-mediated wheat allergy. Int J Mol Sci. 2024;25(15):8210. https://doi.org/10.3390/ijms25158210
2. Chen H, Huang N, Li Wj, Dong X, Qi SS, Wang YN, et al. Clinical and laboratory features, and quality of life assessment in wheat dependent exercise-induced anaphylaxis patients

from central China. J Huazhong Univ Sci Technolog Med Sci. 2016;36:410–5. https://doi.org/10.1007/s11596-016-1601-z
3. 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(4):493–8. https://doi.org/10.2332/allergolint.09-RAI-0125
4. Faihs V, Kugler C, Schmalhofer V, Scherf KA, Lexhaller B, Mortz CG, et al. Wheat-dependent exercise-induced anaphylaxis: Subtypes, diagnosis, and management. J Dtsch Dermatol Ges. 2023;21(10):1131–5. https://doi.org/10.1111/ddg.15162
5. Watanabe C, Ando Y, Kumagai H, Miyamoto M, Fujita Y, Kato M, et al. A pediatric case of wheat-dependent, exercise-induced anaphylaxis solely associated with high-molecular-weight glutenin. Indian J Pediatr. 2022;89(9):937. https://doi.org/10.1007/s12098-022-04319-5
6. Kohno K, Matsuo H, Takahashi H, Niihara H, Chinuki Y, Kaneko S, 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(2):229–38. https://doi.org/10.2332/allergolint.12-OA-0495
7. Aoki Y, Yagami A, Sakai T, Ohno S, Sato N, Nakamura M, et al. Alpha/beta gliadin MM1 is a novel antigen for wheat-dependent exercise-induced anaphylaxis. Int Arch Allergy Immunol. 2023;184(10):1022–35. https://doi.org/10.1159/000531056
8. Maruyama N, Nakagawa T, Ito K, Cabanos C, Borres MP, Movérare R, et al. Measurement of specific IgE antibodies to Ses i 1 improves the diagnosis of sesame allergy. Clin Exp Allergy. 2016;46(1):163–71. https://doi.org/10.1111/cea.12626