

Food-dependent exercise-induced anaphylaxis (FDEIA) suspected triggered by lipid transfer protein in a Chinese child: A case report

Nannan Jiang^{1,2,3,†}, Kai Guan^{4,5,6,†}, and Li Xiang^{1,2,3,*}

ABSTRACT

Lipid transfer protein (LTP) has been documented as the dominant protein involved in food-induced anaphylaxis and food-dependent exercise-induced anaphylaxis (FDEIA) patients from Mediterranean European countries. To date, there is no report of FDEIA triggering by LTP in China. A 12-year-old Chinese boy experienced recurrent anaphylaxis during intense exercise for 3 months. Specific immunoglobulin E was performed using ImmunoCAP (Thermo Fisher Scientific, Sweden) and Euroline (EUROIMMUN, Germany). He was sensitized to several pollens, mainly mugwort (62 KUA/L), and was found to have detectable immunoglobulin E in multiple foods: cereal (wheat, barley, oat maize, rice, buckwheat, and common millet), fruits (peach, apple, grape, cherry, and orange), vegetables (lettuce, cabbage, broccoli, cauliflower, tomato, and celery), and legumes and nuts (soybean, peanut, and walnut). He also showed sensitization to LTP components from mugwort Art v3 (79.7 KUA/L) and wheat Tri a14 (12.4 KUA/L), but negative to gluten, gliadin, and omega-5 gliadin. We advised our patient to carry an epinephrine auto-injector, not to exercise alone, and to avoid wheat and fruit/vegetable ingestion for at least 4 hours before exercise or when taking non-steroidal anti-inflammatory drugs. After a 6-month follow-up, the patient has experienced no episode of anaphylaxis. We reported the first documented FDEIA case suspected triggered by LTP in a Chinese child. Clinicians should be aware of LTP sensitization when anaphylaxis occurs during exercise in individuals with multiple pollen and food sensitization.

Keywords: Anaphylaxis; food-dependent exercise-induced anaphylaxis; lipid transfer protein

1. Introduction

Food-dependent exercise-induced anaphylaxis (FDEIA) is a rare and severe form of immunoglobulin E (IgE)-mediated

¹Department of Allergy, Beijing Children's Hospital, Capital Medical University, National Center for Children's Health, Beijing, China, ²Key Laboratory of Major Diseases in Children, Ministry of Education, Beijing, China, ³China National Clinical Research Center for Respiratory Diseases, Beijing, China, ⁴Department of Allergy, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China, ⁵Beijing Key Laboratory of Precision Medicine for Diagnosis and Treatment of Allergic Disease, Beijing, China, ⁶National Clinical Research Center for Dermatologic and Immunologic Diseases, Beijing, China

*Correspondence to Li Xiang

Department of Allergy, Beijing Children's Hospital, Capital Medical University, National Center for Children's Health, No.56 Nanlishi Road, Xicheng District, 100045, Beijing, China.

Tel: +86-105-961-6934

Fax: +86-105-961-6934

Email: dr_xiangli2022@126.com

†Nannan Jiang and Kai Guan contributed equally to this article as co-first authors.

The data and materials are available from the corresponding authors based on reasonable requirements.

The authors obtained informed consent for publication from the patient. The patient understands his personal information will not be published.

The case was reviewed and approved by the Ethical Committee of Beijing Children's Hospital.

Copyright © 2024. Asia Pacific Association of Allergy, Asthma and Clinical Immunology. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Received: 2 December 2023; Accepted: 2 July 2024

Published online 7 August 2024

<http://dx.doi.org/10.5415/apallergy.0000000000000154>

food allergy where ingestion of a specific food associated with physical exercise within 4 hours triggers anaphylaxis. Various types of food can be responsible for FDEIA, the food triggers are influenced by geographical location and local diet [1]. The most commonly reported food trigger for FDEIA is wheat, and omega-5-gliadin (Tri a 19) as a major wheat allergen has been identified as a major allergen in Chinese wheat-dependent exercise-induced anaphylaxis (WDEIA) [2]. Tri a 14 is seldom described as responsible for Chinese WDEIA patients, in contrast, the wheat allergen Tri a 14 has been demonstrated as major wheat allergen involvement in a few European WDEIA cases [3]. Tri a 14 belongs to lipid transfer proteins (LTP). LTP represents the dominant protein that causes allergic reactions to fruits, vegetables, and nuts in adults and children from Mediterranean European countries [4]. LTP is also responsible for food-induced anaphylaxis as well as FDEIA [5], and recently, data have demonstrated that LTP is also the main elicitor of food-dependent non-steroidal anti-inflammatory drug (NSAID)-induced hypersensitivity (FDNIH) in Mediterranean countries [6]. LTP-triggered FDEIA is rarely reported in patients from other geographical regions, here we report a Chinese child with poly-sensitization to pollen and food who experienced anaphylaxis suspected triggered by LTP.

2. Case report

A 12-year-old Chinese boy was referred to the department of allergy for recurrent anaphylaxis during exercise for 3 months. The first episode occurred during intense exercise for 30 min (playing football) after the ingestion of beef noodles. He was referred to our hospital emergency department (ED) for flushing, hives, and dyspnea, and the patient developed loss of consciousness and vomiting during transport to ED. On admission

Table 1.
Specific IgE of aeroallergen and food allergen

Aeroallergen and food allergen and allergen component	IgE, KU _A /L	Aeroallergen and food allergen and allergen component	IgE, KU _A /L
T-IgE	636 KU/L	Fruits	
Aeroallergens		Peach (f95)	26.25 KU/L
Alternaria alternata (m6)	1.82 KU _A /L	Apple (f49)	13.43 KU/L
Birch (t3)	2.84 KU _A /L	Grape (f50)	0.54 KU/L
Ragweed (w1)	10 KU _A /L	Cherry (f97)	16.74 KU/L
Goosefoot (w10)	5.94 KU _A /L	Orange (f33)	53.67 KU/L
Mugwort (w6)	62 KU _A /L	Legumes and nuts	
Cereals		Soybean	1.68 KU _A /L
Barley (f6)	3.03 KU _A /L	Peanut	23.4 KU _A /L
Oat (f7)	16.7 KU _A /L	Walnut (f256)	30.63 KU/L
Maize (f8)	16.2 KU _A /L	Sweet chestnut (f361)	0.70 KU/L
Rice (f9)	5.13 KU _A /L	Shellfish	
Buckwheat (f11)	1.65 KU _A /L	Shrimp (f24)	2.73 KU/L
Common millet (f55)	17.3 KU _A /L	Spices	
Foxtail millet (f56)	13.0 KU _A /L	Anise (f271)	1.60 KU/L
Gluten (f79)	0.24 KU _A /L	Allergen components and CCD	
Gliadin (f98)	0.01 KU _A /L	CCD	0 KU/L
Wheat (f4)	0.60 KU _A /L	rTri a19 (f416)	0 KU _A /L
Vegetables		rTri a14 (f433)	12.4 KU _A /L
Lettuce (f215)	6.75 KU/L	nArt v1 (w231)	1.22 KU _A /L
Cabbage (f216)	26.2 KU/L	nArt v3 (w233)	79.7 KU _A /L
Broccoli (f260)	23.3 KU/L		
Cauliflower (f291)	14.7 KU/L		
Tomato (f25)	0.70 KU/L		
Celery (f85)	37.63 KU/L		

CCDs, cross-reactive carbohydrate determinants.

to ED, he was hypotensive (BP: 80/50 mm Hg) and had tachycardia (HR: 136 beats per min). Treatment with epinephrine, corticosteroids, bronchodilation, and fluid therapy led to fully recovery within 24 hours. Four weeks after the first episode, he experienced with immediate generalized urticaria and shortness of breath after wheat bread ingestion after exercise, and he took an oral antihistamine at home and recovered within 2 hours. The third episode occurred during exercise (also playing football), 30 min after ingestion of hamburger (wheat bread, beef, and lettuce) and orange juice, he experienced facial edema, hives, and developed hypotension during transport to ED. He was treated with epinephrine and fully recovered within 2 hours. His medical history included allergic asthma and allergic rhinitis from 9 years of age, and he had sometimes experienced urticaria after eating peanuts. Specific IgE was performed using ImmunoCAP (Thermo Fisher Scientific, Sweden) and Euroline (EUROIMMUN, Germany). He was sensitized to several pollens mainly mugwort (62 KUA/L) and was found to have detectable IgE to multiple foods: cereal (wheat, barley, oat maize, rice, buckwheat, and common millet), fruits (peach, apple, grape, cherry, and orange), vegetables (lettuce, cabbage, broccoli, cauliflower, tomato, and celery), and legumes and nuts (soybean, peanut, and walnut) (Table 1). The patient's total serum IgE level was 636 KU/L. The patient showed sensitization to LTP components from mugwort Art v3 (79.7 KUA/L) and wheat Tri a 14 (12.4 KUA/L), but negative to gluten, gliadin, and omega-5 gliadin. The patient was advised to avoid foods containing wheat and fruit/vegetables before exercise. After a six-month follow-up, the patient has experienced no episode of anaphylaxis since these recommendations were implemented.

3. Discussion

We report the first documented FDEIA case suspected of being triggered by LTP in a Chinese child. Several foods are involved in FDEIA, wheat is the most commonly reported [1]. Our

previous study has identified omega-5-gliadin (Tri a 19), as the main allergen involved in Chinese WDEIA [2]. Tri a 14 has been identified as a relevant allergen associated with baker's asthma [7], but Tri a 14 is seldom described as responsible for WDEIA and wheat-induced anaphylaxis. In our patient, wheat triggered 2 episodes, with exercise (episode 1) and without exercise (episode 2), interestingly, the patient showed negative to gluten, gliadin, and omega-5 gliadin but positive to Tri a 14, which suggested that the sensitization to wheat may be mediated by LTP (Tri 14), not by gluten and gliadin, thus Tri a 14 seems to be responsible for the anaphylactic events. Further investigation should be advisable, to identify the real importance and incidence of Tri a 14 in WDEIA in pediatric patients.

Our patient showed multiple food hypersensitivity, which is also reported in a large percentage of individuals with FDEIA, who also have a high rate of sensitization to LTP [8]. The patient had a clinical history consistent with IgE-mediated allergic reactions after the ingestion of multiple LTP-containing foods including, wheat, lettuce, and orange juice (episode 3). ImmunoCAP testing demonstrated elevated serum IgE to cereals, fruits, and vegetables, nuts, all of which contain LTPs that can contribute to clinical allergic reactivity. LTP is by far responsible for the largest number of FDEIA and FDNH in Mediterranean European countries [6, 8]. The clinical and laboratory findings in this case lead to the conclusion that LTP is the culprit food trigger of FDEIA. LTP sensitization is rare but increasingly reported in the Chinese population [9]. A study recently published data demonstrated that LTPs (Pru p 3, Ara h 9 and Cor a8) have been suggested as major food allergens for mugwort pollen-related food allergies in China and may contribute to systemic reactions.

This case also highlights the potential challenge of maintaining a balance between avoiding multiple cross-reactive foods and containing a nutritious diet, especially in children with sensitization to multiple LTPs. However, the clinical expression of LTP hypersensitivity is extremely variable, with many patients

that tolerate foods they are strongly sensitized to [10]. Severe reactions only in the presence of co-factors such as exercise, NSAIDs, or alcoholic beverages, and subjects experience severe allergic reactions despite low specific IgE levels. In fact, whether patients should be advised to avoid all foods to which they are sensitized but may be tolerant, or be recommended to continue their ingestion, is still undefined.

Avoidance is a key treatment of FDEIA management. We advised our patient to carry an epinephrine auto-injector, not to exercise alone, and to avoid wheat and fruit/vegetable ingestion for at least 4 hours before exercise or when taking NSAIDs. The role of important wheat allergens, such as LTP, is still unknown in wheat. Clinicians should be aware of LTP sensitization when anaphylaxis occurs during exercise in individuals with multiple pollen and food sensitization.

Acknowledgements

We appreciate the patients and investigators (Xudong Zhang and Hui Guan) who participated in this case report.

Funding

This study was supported by the Project for Development of Beijing Municipal Research Ward (BCRW202101) and the Respiratory Research Project of the National Clinical Research Center for Respiratory Diseases (code. HXZX-20210203, HXZX-20210204, HXZX-202107). Beijing Collaborative Research Project of Integrated Traditional Chinese and Western Medicine on Major and Refractory Diseases (Children Pulmonary Allergic Diseases—Collaborative Research Demonstration Project of Integrated Traditional Chinese and Western Medicine); No. 2023BJSZDYNJBXTGG-005.

Conflicts of interest

The authors have no financial conflicts of interest.

Author contributions

Jiang and Guan made substantial contributions to acquisition of the cases, interpreted the data, and drafted the article. Xiang made substantial contributions to conception and design,

revised the manuscript and gave final approval of the version to be published.

References

1. Wong GK, Krishna MT. Food-dependent exercise-induced anaphylaxis: is wheat unique? *Curr Allergy Asthma Rep* 2013;13:639-644.
2. Jiang NN, Wen LP, Li H, Yin J. A new diagnostic criteria of wheat-dependent, exercise-induced anaphylaxis in China. *Chin Med J (Engl)* 2018;131:2049-2054.
3. Capra ME, Paulis NGD, Montagni M, et al. An unusual case of wheat dependent exercise induced anaphylaxis (WDEIA) triggered by Tri a 14 in a pediatric patient: a case report. *Eur Ann Allergy Clin Immunol* 2018;50:187-189.
4. Mastroianni C, Tripodi S, Caffarelli C, Perna S, Di Rienzo-Busino A, Sfika I, Asero R, Dondi A, Bianchi A, Povesi Dascola C, Ricci G, Cipriani F, Maiello N, Miraglia Del Giudice M, Frediani T, Frediani S, Macri F, Pistoletti C, Dello Iacono I, Patria MF, Varin E, Peroni D, Comberati P, Chini L, Moschese V, Lucarelli S, Bernardini R, Pingitore G, Pelosi U, Olcese R, Moretti M, Cirisano A, Faggian D, Travaglini A, Plebani M, Verga MC, Calvani M, Giordani P, Matricardi PM; Italian Pediatric Allergy Network (I-PAN). Endotypes of pollen-food syndrome in children with seasonal allergic rhinoconjunctivitis: a molecular classification. *Allergy* 2016;71:1181-1191.
5. Asero R. In patients with LTP syndrome food-specific IgE show a predictable hierarchical order. *Eur Ann Allergy Clin Immunol* 2014;46:142-146.
6. Sánchez-López J, Araujo G, Cardona V, García-Moral A, Casas-Saucedo R, Guilarte M, Torres MJ, Doña I, Picado C, Pascal M, Muñoz-Cano R, Bartra J. Food-dependent NSAID-induced hypersensitivity (FDNIH) reactions: unraveling the clinical features and risk factors. *Allergy* 2021;76:1480-1492.
7. Palacin A, Varela J, Quirce S, del Pozo V, Tordesillas L, Barranco P, Fernandez-Nieto M, Sastre J, Diaz-Perales A, Salcedo G. Recombinant lipid transfer protein Tri a 14: a novel heat and proteolytic resistant tool for the diagnosis of baker's asthma. *Clin Exp Allergy* 2009;39:1267-1276.
8. Romano A, Scala E, Rumi G, Gaeta F, Caruso C, Alonzi C, Maggioletti M, Ferrara R, Palazzo P, Palmieri V, Zeppilli P, Mari A. Lipid transfer proteins: the most frequent sensitizer in Italian subjects with food-dependent exercise-induced anaphylaxis. *Clin Exp Allergy* 2012;42:1643-1653.
9. Deng S, Yin J. Mugwort pollen-related food allergy: lipid transfer protein sensitization and correlation with the severity of allergic reactions in a Chinese population. *Allergy Asthma Immunol Res* 2019;11:116-128.
10. Pascal M, Vazquez-Ortiz M, Folque MM, Jimenez-Feijoo R, Lozano J, Dominguez O, Piquer-Gibert M, Giner MT, Alvaro M, Dias da Costa M, García-Paba B, Machinena A, Alsina L, Yagüe J, Plaza-Martin AM. Asymptomatic LTP sensitisation is common in plant-food allergic children from the Northeast of Spain. *Allergol Immunopathol (Madr)* 2016;44:351-358.