

Profilins and Food Dependent Exercise-Induced Anaphylaxis

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The term "anaphylaxis" defines an acute, life-threatening, generalized reaction with various clinical presentations that concern the skin, respiratory, gastrointestinal, and cardiovascular systems [1-3]. The occurrence of anaphylaxis after physical activity defines the type of exercise-induced anaphylaxis (EIA). In about a third of cases, cofactors like food intake, temperature, and drugs (especially nonsteroidal anti-inflammatory drugs) can be identified [4]. When the associated cofactor is food ingestion, the correct diagnosis is food-dependent EIA (FDEIA) [1].

Lipid transfer proteins (LTPs) and profilins are panallergens found in many plant foods; while the LTPs are a common cause of food-induced anaphylaxis (FIA) in the Mediterranean area and they have also been proposed as a main cause of FDEIA [5]; Nevertheless, profilin is hardly ever involved in the triggering of FIA, and even strangely in FDEIA. That is the reason why we describe two cases:

Patient 1, A 12 years-old boy with personal history of rhino-conjunctivitis and bronchial asthma due to allergy to grass pollens (GP). He experienced multiple episodes of FDEIA (urticaria, dyspnea, rhinoconjunctivitis and abdominal pain), during intense exercise, about 30-90 minutes after eating several fruits and / or vegetables (peach, pumpkin, carrot and tomato)(Table 1). The patient tolerates all fruits and vegetables unless he practices physical exercise and he tolerates physical exercise if he does not eat fruits and vegetables in the previous 4 hours,

Allergy study (AS):

Skin prick test (SPT) with commercial extracts (peach, pumpkin, tomato, wheat, carrot) and prick-prick with the fruits and vegetables involved (peach, pumpkin, tomato, carrot, wheat and pumpkin): All positive (mean wheal > 3,3 mm)

SPT with commercial extracts: pollens (grass and olive) and purified palm tree profilin: All positive, LTP, and other pollens and aeroallergens: Negative, Ig E total (kU/L) (360), Specific IgE (kU / L): rPhl p 1+rPhl p 5b (Phleum) (75), rOle e1 (olive) (0,6), ImmunoCAP (ISAC) (ISU-E-standardized units-), profilins: Bet v 2 (2,6), rHev b 8 (5,1) and rMer a 1 (3,8), Remaining of determinations of the ISAC were negative, Tryptase: 3,4mcg/L

There was no recurrence of symptoms of the anaphylaxis in the last five years avoiding the intake of fruits and vegetables 4 hours before exercise,

Patient 2, A 28 years-old boy with personal history of rhinoconjunctivitis and bronchial asthma due to allergy to grass and olive pollens, He experienced a single episode of FDEIA (urticaria, dyspnea, dizziness, hypotension and tachycardia, during intense exercise, about 60 minutes after eating fruit (peach), While the ingestion, immediately, he had oropharyngeal itching, hydrorinorrhea and sneezing about 5 minutes (Table 1), The patient tolerates physical exercise if he does not eat peach neither other vegetables in the previous 4 hours and tolerates peach, other fruits and vegetables if he does not exercise,

AS:

SPT with commercial extracts (peach, tomato, wheat, carrot) and prick-prick with peach: All positive (mean wheal > 3,3 mm), SPT with pollens extracts (grass and olive pollen and purified palm tree profilin): All positive, LTP, other pollens and aeroallergens: Negative,

Total Ig E: 1180 kU / L, Specific IgE (kU / L): rPhl p 1+rPhl p 5b (Phleum) (75), rOle e1 (olive) (0,6), ImmunoCAP (ISAC) (ISU-E-standardized units-), profilins: Bet v 2 (20), rHev b 8 (39) and rMer a 1 (27), The remaining of determinations of the ISAC were negative, Tryptase: 2,6 mcg/L,

There was no recurrence of symptoms of the anaphylaxis in the last years avoiding the intake of vegetables 4 hours before exercise,

The first report dates back to 1979[1,4], when a patient experienced anaphylaxis after eating shellfish and performing exercise, EIA is relatively rare[6,7], a largest epidemiological study detected a prevalence of 0,048%, In Europe, about 30% of cases of EIA are associated with cofactors [1,4],

When EIA is associated with exercise, it is called FDEIA, whose incidence is increasing [6], but the mechanisms involved of FDEIA development are unclear, It has been suggested that exercise lowers the threshold of food allergy [8],

Our patients had EIA, However, later, they tolerated the exercise, Therefore, we suspect that exercise could be an associated cofactor[1,4]

A detailed history allowed us to rule out the involvement of drugs and alcohol intake, but in both patients, there was a history of fruits and/or vegetables intake in at least 4 hours before the onset of symptoms, Bearing it in mind, the cofactor in both cases could be a vegetable food, since the most important cofactor is food ingestion[1], For this reason and besides the history of pollinosis in both patients, we carried out the allergy study with plant foods[6] to detect if the patients were sensitized to ingested vegetables,

Gliadin and LTPs are the main allergens involved in the FDEIA [9], Living in the Mediterranean area, we thought of LTP as a possible cofactor [5] but the allergy study showed us that both patients were not sensitized to LTP but profilin was positive, This vegetable protein is generally related to mild reactions, such as

oral allergy syndrome, even though we have found a case published 25 years ago of FDEIA by lychee with sensitization to profilins, In recent years, serious allergic reactions caused by profilins have been known especially in areas of high exposure to GP, because allergic asthmatic patients are frequently sensitized to profilin[1,10],

Due to the food intake, the symptoms, and the results of the allergy study, both patients were diagnosed with FDEIA by profilin [10]

FDEIA is a rare but serious condition that can have a significant impact on patients' lives [7], Moreover, early diagnosis and identification of the associated cofactor is essential, because if it is a vegetable panallergen (like in our patients), it's very important to guide an early treatment with epinephrine (autoinjector) and the prevention of further episodes with adequate [1] information on cross-reactivity between vegetables, It should be advised to avoid exercise at least 4 hours after eating causal foods,

Overall, in severe reactions such as FDEIA, the profilin should be considered as a trigger allergen, especially if the patient lives in an area of high exposure to GP,

References:

1. Pravettoni V, Incorvaia C, Diagnosis of exercise-induced anaphylaxis: current insights, *Journal of Asthma and Allergy*, 2016;9:191-8,
2. Simons FE, Ebisawa M, Sanchez-Borges M, Thong BI, Worm M, Tanna LK, et al, Update of the evidence base: World Allergy Organization anaphylaxis guidelines, *World Allergy Organ J*, 2015;8:32,
3. Gómez-Soler R, Caballero ML, Incidence of Anaphylaxis Recorded During 1 Year by the Municipal Emergency Service of Madrid (SAMUR-PC), *J Investig Allergol Clin Immunol*, 2018;28(6):438-40,
4. Medrala W, Cieřlik K, Barg W, Skotny A, Siwak E, Wolanczyk-Medrala A, Naproxen Increases the Severity of Food-Dependent Exercise-Induced Anaphylaxis: A Case Report, *J Investig Allergol Clin Immunol*, 2014;24(6):439-62,
5. Mota I, Gaspar A, Benito-Garcia F, Correia M, Arêde C, Piedade S, et al, Anaphylaxis Caused by Lipid Transfer Proteins: An Unpredictable Clinical Syndrome, *Allergol Immunopathol (Madr)*, 2018;46 (6):565-70,
6. Benito-Garcia F, Ansotegui IJ, Morais-Almeida M, Diagnosis and prevention of food-dependent exercise-induced anaphylaxis, *Expert Rev Clin Immunol*, 2019;15(8):849-56,
7. Foong RX, Giovannini M, du Toit G, Food-dependent exercise-induced anaphylaxis, *Curr Opin Allergy Clin Immunol*, 2019;19(3):224-8,
8. Asaumi T, Ebisawa M, How to manage food dependent exercise induced anaphylaxis (FDEIA), *Curr Opin Allergy Clin Immunol*, 2018;18(3):243-7,
9. Bartra J, Araujo G, Muñoz-Cano R, Interaction between foods and nonsteroidal anti-inflammatory drugs and exercise in the induction of anaphylaxis, *Curr Opin Allergy Clin Immunol*, 2018;18(4):310-16,
10. Rodríguez Del Río P, Díaz-Perales A, Sánchez-García S, Escudero C, Ibáñez MD, Méndez-Brea P, et al, Profilin, a Change in the Paradigm, *J Investig Allergol Clin Immunol*, 2018;28(1):1-12,

Table 1. Demographic, clinical, and allergological characteristics of the patients (1 and 2)

	Patient 1	Patient 2
Age	12	28
Sex	Male	Male
Countrywherethepatientslive	Spain (Centre)	Spain (Centre)
Comorbidities	Rhinoconjunctivitis Asthma	Rhinoconjunctivitis Asthma
Symptoms	Cutaneous Respiratory Gastrointestinal	Oral allergysyndrome Cutaneous Respiratory Gastrointestinal Hypotension
Episodes of food dependent - exercise induced anaphylaxis and food involved	Multiple Peach, pumpkin, carrot, wheat and tomato	Single Peach
AllergyStudy Cutaneoustests (positive)	Grasspollen Peach, pumpkin, carrot, wheat and tomato	Gras and olive pollens Peach
Serologicalallergystudy (Profilins)(kU/L)	r Bet v 2: 2.6 rHev b 8: 5.1 rMer a 1: 3.8	r Bet v 2: 20 rHev b 8: 39 rMer a 1: 27