Rosaceae-associated exercise-induced anaphylaxis with positive SPT and negative IgE reactivity to Pru p 3

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Summary

Background: Food-dependent-exercise-induced anaphylaxis (FDEIA) is characterized by anaphylactic symptoms after exercise following ingestion of food. We present a case of FDEIA induced by Rosaceae fruits showing some diagnostic problems. Material and methods: A 12 years-old boy with seasonal allergy to olive and cypressus pollens, experienced two distinct episodes of FDEIA, grade 4 and 3 of the Sampson Scale respectively, during intense exercise, about 30 minutes after eating a peach with peel or some cherries. SPT with commercial peach extract and fresh Rosaceae fruits scored positive while SPT with a date palm profilin-enriched extract was negative. On in vitro tests total IgE were 44 kU/l and IgE for peach, cherry, Pru p 3, Pru p 1, Bet v 1, Bet v 2, Bet v 4 were negative. SPT with Pru p 3 UniCAP device (cellulose polymer in a plastic reserve highly binding allergen protein) was negative. An oral food challenge, performed at rest using a commercial peach juice, scored negative. An immunoblot analysis performed with peach extract was negative.

Discussion: The main peculiarity of this case of FDEIA is the discrepancy between positive SPT and negative in-vitro findings. The positive SPT with the commercial peach extract suggested hypersensitivity to lipid transfer protein; however, no IgE reactivity to rPru p 3 was found in-vitro. The negative immunoblot analysis, possibly caused by the low levels of specific IgE, did not allow us to investigate the nature of the relevant allergen protein further. It is possible that this patient reacted to a different peach allergen or, alternatively, that he recognized an isoform of LTP that is different from that in Uni-CAP. Conclusion: This case emphasizes once more the diagnostic relevance of SPT with extracts and fresh material to be performed before investigating IgE reactivity to single allergen components in-vitro.

Introduction

Food-dependent exercise-induced anaphylaxis (FDEIA) is a clinical condition characterized by anaphylactic episodes associated with both exercise and ingestion of food, which are independently tolerated. In previous studies of FDEIA the syndrome has been associated with wheat, seafood, peanut, egg, milk, vegetables and fruits (1, 2).

We report a case of FDEIA induced by Rosaceae fruits. There are two major clinical patterns of allergy to this fruit family: one is oral allergy syndrome (OAS) caused by sensitization to Bet v 1 homologous proteins in patients with birch pollens allergy and/or by sensitization to profilin (3-5); another is associated with sensitization to lipid transfer proteins (LTP), heat- and pepsin-stable proteins, and may cause both OAS and systemic reactions more;
the latter is often observed in patients living in the Mediterranean area (3, 6, 7). The absence of detectable sensitization to all these proteins in our patient suggests the possible association with a novel allergen.

**Case report**

A 12 year-old boy with a history of seasonal allergic rhinoconjunctivitis caused by both olive and cypress pollens but not suffering from asthma, experienced two distinct episodes of food-dependent exercise-induced anaphylaxis (FDEIA), grade 4 and 3 of the Sampson Scale (2006) (8) respectively, during intense exercise after eating Rosaceae fruits. The first time, while swimming in the sea 30 minutes after eating a peach with peel, he experienced throat itching followed by generalized urticaria, angioedema, throat constriction and dispnoea. He was brought immediately to the ER and treated with corticosteroid im. Respiratory and cutaneous symptoms disappeared after 10 minutes and 2 hours, respectively. One year later, he had sudden abdominal cramps, itchiness of his hands and feet, generalized urticaria, angioedema, sneezing and slight throat constriction while playing football. Thirty minutes before the episode he had eaten some cherries. He was brought to the Emergency Department and treated with oral anti-histamines and corticosteroid im. The boy had regularly played football and swum in swimming pool and also tolerated peaches and cherries without any problem before.

**Methods and results**

**Skin tests**

The skin prick tests (SPT), performed with a commercial peach extract (containing LTP 30 µg/ml) (9) and with a date palm profilin-enriched extract (Pho d 2 50 mcg/ml) (10) (both by ALK-Abelló, Madrid, Spain) and the prick-prick tests performed with fresh Rosaceae fruits, showed a wheal average diameter as follows: peach extract, cherry, plum, apricot = 4 mm, peach pulp = 6 mm, peach peel = 2 mm, pear = 5 mm, apple = 2 mm, profilin = 0 mm, histamine (1%) = 5 mm, negative control = 0 mm.

**On in-vitro test**

On in-vitro tests using ImmunoCAP (Phadia, Upsala, Sweden) total IgE were 44 kU/l and IgE, for whole peach and cherry extracts, Pru p 3, Pru p 1, Bet v 1, Bet v 2, and Bet v 4 scored negative; Ole e 1 and Cup a 1 were positive (0,74 and 16,3 kU/l respectively).

**Skin tests with rPru p 3**

A SPT using the Pru p 3 UniCAP device was carried out. To this end, the little sponge with the binding allergen was pulled out of its plastic receptacle and applied for three or five minutes on the patient’s skin that had been previously scarified; the reaction was evaluated after 15 minutes. Further a prick-prick test with the same sponge was performed. All these tests scored negative in our patients but were positive in 3 control patients showing IgE reactivity to Pru p 3 both in vivo (SPT by ALK-Abelló) and in vitro (UniCAP) (Fig. 1).

**Exercise challenge test**

Patient’s pulmonary function tests were normal. An exercise challenge test was negative.

**Food challenge test**

A specific food-exercise challenge was not performed due to the risk of anaphylaxis. An open food challenge, performed while resting using a commercial peach juice containing 90% fruit and at least 10% peel that had produced a 5 mm wheal on SPT, scored negative. After this challenge, as an attempt to give an oral immunotherapy (OIT), the boy continued taking 125 ml of the same commercial peach juice on alternate days avoiding exercise both prior and after drinking the juice. However, two
months later, after fasting for about 8 hours and at rest, he experienced a new episode with generalized urticaria and abdominal pain soon after drinking the same juice.

**Discussion**

This case of FDEIA was characterized by a discrepancy between positive clinical history and SPT and negative in-vitro findings. One previous study (11) reported two cases of peach-induced anaphylaxis scoring negative on ImmunoCAP with rPru p 3, rPru p 1 and rPru p 4 occurring in adults. On immunoblot analysis the IgE of the two patients were bound to peach proteins showing a molecular weight of about 10 kDa, maybe an isoform of Pru p 3. As far as we know, this is the first case reported in a pediatric patient. The negative result of the immunoblot analysis, that was possibly caused by low levels of specific IgE, did not allow us to investigate the nature of the relevant allergen protein further. The positive SPT with the commercial peach extract suggests hypersensitivity to a peach protein other than the Bet v 1-like allergen, Pru p 1, and profilin, Pru p 4, that are normally missing in that extract. Surprisingly, no IgE reactivity to rPru p 3 was found in-vitro and in vivo, although virtually the totality of those who react to that peach extract recognize the peach lipid transfer protein. It is therefore possible that this patient reacted to a different peach allergen or, alternatively, that he recognized a LTP isoform different from that in UniCAP. This case emphasizes once more the importance of carrying out the diagnostic workup first by SPT using both extracts and fresh material before investigating IgE reactivity to single allergen components in-vitro. Interestingly, the patient eventually reacted also to peach juice that was ingested after fasting and in the absence of exercise. Fasting has recently been described as a risk factor for systemic reaction to food (12) likewise exercise (13), drugs (14), or both (15). It is possible that the proteins are absorbed more rapidly in an empty gastrointestinal tract or, alternatively, that a more efficient digestion of the matrix by pepsin may lead to an increased concentration of purified allergen that comes in contact with the gut mucosa (12).

**Immunoblot analysis**

An immunoblot analysis was performed as well using whole peach extract as substrate. However, possibly due to the low concentration of specific IgE or of the relevant allergen protein, it scored negative.

**References**