

Anaphylaxis with Apple. LTP Syndrome

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Abstract

In recent years, allergic reactions to food have suffered a significant increase, especially in the pediatric population.

The new techniques of molecular diagnosis allow us to understand the reason of certain allergies and especially the cross reactions that exist between allergies to pollens and allergies to fruit due to the presence of proteins called panallergens, groups of proteins very similar to each other from the point of conformational view but with different epitopes that trigger different allergic reactions.

One of these proteins are the Lipid Transfer Protein (LTP), present in many fruits, especially the Rosaceae group and whose main example would be the Prup3 of the peach, but also others present in apples, strawberries, etc. These proteins are responsible for clinical conditions that can range from pruritus in the mouth to anaphylaxis.

We present a case of anaphylactic reaction when eating apples and whose diagnosis can be understood through molecular diagnostic techniques. We must also take into account the presence of cofactors or factors that trigger anaphylactic reactions, the most important being sports and non-steroidal anti-inflammatory drugs, which may favor the appearance of anaphylaxis in patients who have previously tolerated food without allergic reactions.

Keywords: *Cofactors; Food Allergy; Fruit; LTP Syndrome; Oral Allergy Syndrome; Profilins*

Introduction

Anaphylactic shock is a true medical emergency that can compromise the patient's life. Many may be the triggering causes, in our case it was a patient with a fruit allergy. Food allergy is a growing pathology in recent years, with an estimated prevalence of 6 - 8% in children under four years of age and 1 - 3% in adults [1]. In children older than 5 years, the most frequently involved allergen is fruit and among the fruits, the family of rosaceae (peach, apple, pear, cherry, apricot, plum, nectarine, strawberry) is responsible for the majority of reactions in older children and adults. We must bear in mind that in some people the presence of certain cofactors is necessary and in the case of our patient it is revealed years later, when exposed to a cofactor as is the physical exercise after the apple intake, this fact being to take into account when treating patients with allergies to fruits.

Clinical Case

A 12-year-old male patient who attended paediatric emergencies due to clinical symptoms of initially facial itching with erythema and lesions with wheals that progressively extended to the trunk and extremities after a football game. As background refers the intake of an apple minutes before starting the sport.

The picture yields after administration of oral antihistamine and oral corticoid that are maintained for a few days.

Two weeks later he suffers from a generalized urticarial with labial angioedema and after the tongue, which is followed by a persistent cough, coinciding again with the practice of a football match and which cedes after 10 minutes. After being referred to the emergency room of the health centre is diagnosed with hives and dyspnoea and after administration of antihistamines is referred to your home requesting review in External Consultations of Allergological Pediatrics.

After questioning the patient about the second episode of anaphylaxis, this refers to the intake of a natural fruit juice 60 minutes before performing physical exercise.

Questioned about reactions with fruits or vegetables, the patient reports that for about a year or so he has noticed itching in his mouth when eating certain fruits such as peach, watermelon, melon, plum, strawberries and apple. Questioned about the intake of nuts refers that he does not take them because he has never liked them.

Family background

Father: Allergic asthma with sensitization to olive pollen, *Phleum*, *Lolium* and *Cynodon*.

Mother: Allergic rhinitis with sensitization to *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* and allergic to prawns.

Personal history: At 5 years he was diagnosed with moderate intermittent allergic rhinitis and mild allergic conjunctivitis with sensitization to olive and grass pollen. He received specific immunotherapy for 4 years with clinical remission of nasoconjunctival symptoms and discharge at 10 years of age. From infancy he reports repeated outbreaks of atopic dermatitis.

Supplementary tests

Prick test with food (cm): Peach: 7 x 5, Strawberry: 3 x 3, Apple: 6 x 6, LTP: 5 x 5, Profilin: 6 x 5

Prick-prick with food (cm): Peach: 5 x 5, Strawberry: 4 x 4, Apple: 4 x 4, Plum: 4 x 4

IgE specifics: Peach: 25.3 IU/ml. Strawberry: 11.4 IU/ml, Apple: 19.9 IU/ml, Plum: 15.4 IU/ml, Almond: 8.9 IU/ml.

Molecular diagnosis: Pru p 3 (peach): 12.7 IU/ml, Mal d 3 (apple): 10.9 IU/ml, Pru 3 (apricot): 5.4 IU/ml, Pru av 3 (cherry): 3, 1 IU/ml, Pru d 3 (plum): 3.5 IU/ml, Cor a 8 (hazelnut): 4.8 IU/ml, Jug r 3 (walnut): 1.8 IU/ml, Art v 3 (artemisia): 27.9 IU/ml.

With this data he was finally diagnosed as anaphylactic shock by apple, LTP syndrome.

Discussion

Food anaphylaxis is defined as an immunological reaction of hypersensitivity caused by a food and mediated by IgE antibodies. Food allergy is a growing pathology in recent years, with an estimated prevalence of 6 - 8% in children under four years of age and 1 - 3% in adults [1]. In children under 14, food allergy is the third reason for consultation in Pediatric Allergology, with the fruit being the allergen most frequently involved in children over 5 years of age. Among the fruits, the family of Rosacea (peach, apple, pear, cherry, apricot, plum, nectarine, strawberry) is responsible for the majority of reactions in older children and adults. Apple allergy is much more prevalent in Central and Northern Europe than in Southern Europe.

Two major groups of entities have been described according to the sensitization patterns: oral allergy syndrome (OAS) and generalized symptoms (OS), which include anaphylaxis and urticaria [2]. In the North and Central Europe the apple allergy is associated with allergy to pollens, especially that of birch. Symptoms after apple intake are mild, like OAS. In Southern Europe, on the other hand, apple allergic patients present more frequently severe symptoms that are not associated with allergy to birch pollen and are cross-reactive with other fruits such as peaches, as is the case with our patient. In this group the LTP (Pru p 3) is the main responsible for these sensitizations.

Foods contain different proteins and each of these can act as an allergen. Some proteins are specific to each food and others are shared by other foods of the same species or family, or even from distant species. Four different allergens have been identified in the apple: Mal d 1, a protein related to pathogenesis (Protein Related-10); Mal d 2, a thaumatin (Lipid Transfer Protein); Mal d 3 (LTP) and Mal d 4 (profilin).

Each food is composed of multiple components, of which only some behave as allergens. The allergenic components can be classified as belonging to different families of proteins according to their function and structure. A current concept is that of panallergens [3]. They are antigenic families identified by molecular biology that share a highly conserved protein sequence throughout phylogenetic evolution and have important functions (defence, storage) in the corresponding animal or plant species. These allergens explain many of the cross-reactions between foods of different species and families of the animal and vegetable kingdoms. The most studied at present are: profilins, LTP (lipid transfer protein) and PR-10 (proteins related to pathogenesis).

Profilins are very similar proteins in their primary sequence with a homology higher than 70%, present in all pollens and plants and also in all eukaryotic cells, which contribute to cross reactions between species without botanical relationship. They are rarely associated with clinical symptoms, but can cause demonstrable or even severe reactions in a small minority of patients.

The LTP are stable to heat and digestion, causing reactions also against cooked food. They often present with systemic and more serious reactions, added to the OAS and with allergic reactions to fruits and vegetables in southern Europe. PR-10 or proteins related to pathogenesis are thermolabile. They are homologues of the major birch allergen (Bet v 1) and are often associated with local symptoms such as OAS and allergic reactions to foods in northern Europe (fruits Rosacea, hazelnut, carrot and celery).

Advanced Disease Beyond TME

In food allergy, we must bear in mind that in some people the presence of certain cofactors [4,5] (physical exercise, nonsteroidal anti-inflammatory drugs or NSAID, stress, alcohol) is necessary for an allergic reaction to occur. It is suspected that the responsible mechanism consists of accelerating the absorption of food in the intestine and thus modulate the severity of symptoms. That is why when LTP are involved, if the cofactors are not detected and prevented, they can represent a serious risk for the development of severe or fatal anaphylaxis episodes.

In patients with apple allergy, sensitization to pollens seems to make it less likely that severe symptoms occur, although this is not true in our patient [6]. Pastorello, *et al.* stated that patients allergic to peach and positive for LTP (Pru p 3), were less likely to show severe symptoms if they presented sensitization to profilin (Pru p 4 or Mal d 4) or PR-10 (Pru p 1 or Mal d 1).

Atopic patients in southern Europe, with allergies to peaches and apples, may have OAS and, in this situation, profilin is a very important sensitizer.

The treatment of food allergy consists in the avoidance of the responsible food and take the adrenaline auto-injectors with them, if there have been anaphylaxis [7].

Conclusion

In summary, we present the case of a patient sensitized to LTP and profilin. Due to its sensitization to profilin, from infancy it had several concomitant allergies against grasses and other pollens, as well as fruits of the Rosacea family and other fruits that manifested as OAS. The sensitization to LTP is usually related to serious reactions, which in the case of our patient is revealed years later, when exposed to a cofactor as is the physical exercise after the intake of apple. In the context of the study to be carried out in Paediatric Allergology, it is

recommended to include profilin and LTP in the routine diagnosis of apple allergic patients. Regarding the action in primary care, the community doctor should consider the presence of all possible cofactors (drugs, physical exercise, etc.) that increase the risk of anaphylaxis to alert food allergic patients and reduce the incidence of same.

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