

Cross-reactivity syndromes: presentation of two cases and review of the literature

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SUMMARY: Işık S, Arıkan-Ayyıldız Z, Çağlayan-Sözmen Ş, Fırınıcı F, Tuncel T, Karaman Ö, Uzuner N. Cross-reactivity syndromes: presentation of two cases and review of the literature. Turk J Pediatr 2014; 56: 291-294.

Cross-reactivity has important consequences in some immune disorders, including allergic and autoimmune diseases, which can affect both diagnostic and therapeutic approaches. One of the most common cross-reactivity syndromes is pollen-food syndrome (PFS). The patient is sensitized with pollen by the airways and exhibits an allergic reaction to food antigen with a structural similarity to the pollen. PFS usually presents with pruritus and swelling of the mouth and throat during or just after ingestion of fresh, uncooked fruits and vegetables. Latex fruit syndrome is another cross-reactivity syndrome. It is the association of latex allergy and allergy to plant foods, which affects up to 50% of latex-allergic patients. Here, we present two cases with cross-reactivity syndrome.

Key words: cross-reactivity, latex-fruit syndrome, pollen-food syndrome.

Cross-reactivity (CR) occurs when an adaptive immune response to a particular antigen causes reactivity to other antigens that are structurally related to each other¹. CR has important consequences in some immune disorders, including allergic and autoimmune diseases, which can affect both diagnostic and therapeutic approaches.

The role of CR in food allergy was described as early as 1942 with recognition that individuals sensitized to pollen allergens were more likely to exhibit allergic symptoms upon eating certain fruits. The symptoms of the reactions they described were limited to the oral cavity, so it was called "oral allergy syndrome"². It became clear later that the symptoms of some patients progress to involve the other organ systems, so the term "pollen food syndrome" and "class 2 food allergy" began to be used. Other associations have been described, which are thought to have the same type of underlying molecular mechanisms, in which the initial sensitizer is not pollen. One of them is latex-fruit syndrome. Natural rubber latex is a product of the rubber tree *Hevea brasiliensis*³. Latex fruit syndrome is the association of latex

allergy and allergy to plant foods, which affects up to 50% of latex-allergic patients⁴.

Here we present two cases with CR syndrome.

Case Reports

Case 1

A 12-year-old girl presented with a three-year history of seasonal hay fever and food allergy. The detailed history revealed that she developed itching of the lips, mouth, throat, and then swelling of the lips soon after oral contact with some kinds of foods including apple, peach, kiwi, carrot, and tree nut. The general physical examination was normal except for allergic shiner (Fig. 1). Complete blood count and total eosinophil count were within normal limits. Total immunoglobulin (Ig)E was found to be high (913 IU/ml; normal value: 10-80 IU/ml). Skin prick tests (SPTs) were found positive for inhalant allergens: grass pollen mix (*Holcus lanatus*, *Dactylis glomerata*, *Lolium perenne*, *Phleum pratense*, *Poa pratensis*, *Festuca pratensis*): 6 mm, tree pollen mix (*Alnus glutinosa*, *Corylus avellana*, *Populus alba*, *Ulmus scabra*, *Salix caprea*): 4 mm, *Dermatophagoides farinae*: 6 mm, and *Dermatophagoides pteronyssinus*:

6 mm. The following results were obtained in prick to prick testing: apple: 5 mm, carrot: 6 mm, kiwi: 4 mm, peach: 5 mm, and tree nut: 5 mm. Immunotherapy was proposed for this case, but her family declined the treatment.

Case 2

A 14-year-old boy presented with itching and hyperemia on his eyes and rhinorrhea after skin contact with chestnut; however, there was no reaction after chestnut ingestion. He had a three-year history of asthma and had undergone multiple operations because of spina bifida, anal atresia, pes equinovarus deformity, and left ureteropelvic junction stenosis. He was performing clean intermittent urinary catheterization for his neurogenic bladder. He had no reactions with kiwi, banana, potato, or tomato. He experienced hyperemia in his eyes and sneezing when he had contact with a balloon. There was no history of severe reactions to balloon and chestnut. His general physical examination and laboratory findings were normal (total eosinophil count, IgE level, etc.). Latex-specific IgE level was 17.4 IU/ml (normal value: <0.35 IU/ml). SPT was positive for Robinia: 3 mm, *Dermatophagoides farinae*: 3 mm, *Dermatophagoides pteronyssinus*: 4 mm, and latex: 6 mm, and prick to prick test was negative with chestnut, kiwi, banana, and avocado. Specific IgE for chestnut was found negative. Avoidance to latex was recommended for this patient. An adrenalin autoinjector was prescribed.

Discussion

Food allergy is an important public health problem that affects children and adults worldwide. It can be divided into class 1 and class 2. Class 1 food allergy is considered as the traditional food allergy and occurs in the

gastrointestinal tract. Class 2 food allergy is caused by allergic sensitization to inhalant allergens that cross-react with food allergens because of structural similarity⁵.

Cross-reactivity (CR) syndromes have been described between phylogenetically close and also distant species. In distant species, the responsible allergens are usually homologous proteins belonging to specific families of molecules. Thus, both the taxonomic classification of the organism and the molecular classification of the allergens should be known in the case of CR syndromes⁶.

The mainstay of treatment of all types of food allergy is avoidance. In many studies, it has been demonstrated that SPT and *in vitro* evidence of IgE antibodies to foods do not always correlate with the presence of clinical symptoms^{7,8}. In a previous study, patients known to have a food allergy were tested for cross-reactive foods by SPT and immunoCAP, and less than 15% of positive results were found to be clinically relevant⁸. Thus, advising patients to avoid all foods known to induce CR very likely leads to unnecessary dietary restriction. Patients who had CR syndromes to some foods should be assessed separately with each of the other foods. Our second patient had chestnut allergy, but there were no reactions with other suspected fruits in latex-fruit syndrome like kiwi, banana and avocado.

Similar allergen structures have been reported between ragweed and the gourd family (watermelon, cucumbers, zucchini, cantaloupe) and bananas, and birch pollen shares allergen epitopes with apples, carrots, celery, hazelnut, potatoes, kiwi, and parsnips⁹. In a group of 72 children (6-16 years) with severe rhinoconjunctivitis and allergy to birch pollen

Table I. Patterns of Pollen-Fruit and Vegetable Cross-Reactivity

Pollen	Food cross-reactivity
Birch	Fruits: apple, peaches, plumbs, nectarine, cherry, pears Nuts: almond, hazelnut Vegetables: carrot, celery, raw potato
Ragweed	Fruits: melons, banana Vegetables: tomato, cucumber
Mugwort	Vegetables: carrot, celery Spices: caraway seeds, parsley, coriander, anise seeds, fennel seeds
Grasses	Fruits: melons, kiwi, peaches Vegetables: tomato

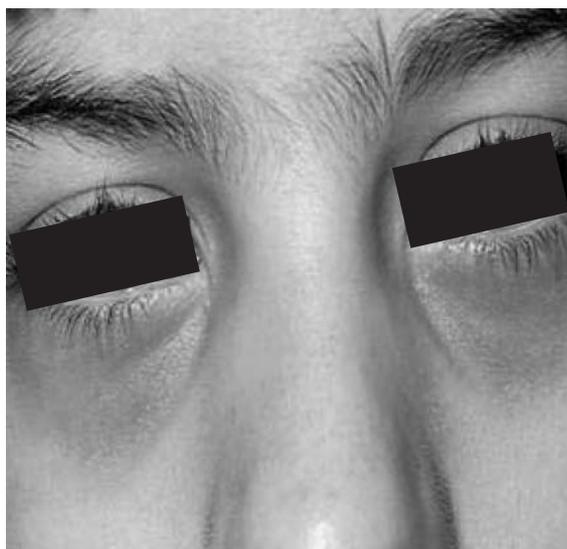


Fig. 1. Allergic shiner of Case 1.

participating in a clinical trial of birch pollen immunotherapy, 93% reported symptoms upon ingestion of fruits and/or vegetables¹⁰. Tree and grass pollen share allergens with apples, tree nut, peaches, oranges, carrots, tomatoes, and cherries⁹ (Table I). Our first case had allergic rhinitis and food allergy. After investigation, her SPT was found positive to grass pollen and apple, tree nut, peach, carrot, and tomato. We thought tree and grass pollens were the responsible allergens for the CR in this case.

Chestnut (*Castanea sativa*) is a member of the Fagaceae family. Most cases of IgE-mediated hypersensitivity to chestnuts have been attributed to the so-called latex-fruit syndrome, in which ingestion of fruits such as avocado, kiwi, banana, and more rarely, chestnut leads to urticaria and anaphylaxis in latex-sensitized individuals. Health care providers and patients with urological problems requiring catheterization are known to have an increased risk for latex allergy. Sensitization is present in 40% of patients with spina bifida¹¹. About 50-60% of latex allergy patients may present with adverse reactions after ingestion of cross-reacting vegetable foods¹². The most important molecular basis of the latex-fruit syndrome is the homology between the hevein (Hev b 6.02) of the latex with the hevein like N-terminal domain of the class 1 chitinases of plants¹³, although some determinants of the catalytic portion of these chitinases

may also contribute to CR with latex¹⁴. The other allergens that have homologs in plant foods and are potential causes of CR are Hev b1, Hev b2, Hev b4, Hev b5, Hev b6, Hev b6.03, Hev b7, Hev b9, Hev b10, Hev b12, and hevamine. The most frequently involved foods are banana (28%), avocado (28%), chestnut (24%), and kiwi (20%). With these foods, clinical symptoms are often severe⁶. In our second patient, he experienced allergic symptoms after contact with chestnut and balloon. After obtaining the history of spina bifida and multiple operations, latex-fruit syndrome was suspected. His latex-specific IgE and SPT with latex were positive. His SPT and specific IgE with chestnut were found negative. Our patient had allergic symptoms upon contact with chestnut, but not after its ingestion. Development of contact urticaria progressing to anaphylaxis after topical application of a chestnut-containing facial peeling mask has been reported in the literature in only one patient¹⁵. Therefore, to the best of our knowledge, this is the first case of chestnut-induced allergic contact conjunctivitis linked to the latex-fruit syndrome.

Although the current therapy for food allergy is mainly dependent on avoidance, there are studies regarding the use of immunotherapy in food allergy¹⁶. There continues to be mixed evidence with regard to the effect of immunotherapy with pollen allergens on the related food allergy¹⁷. In some studies, it is suggested that specific pollen immunotherapy would improve symptoms resulting from associated food in some pollen-food syndromes¹⁸. Thus, it can be concluded that patients with pollen-food syndromes should be evaluated for pollen immunotherapy.

In conclusion, considering the cross-reaction between latex and many food items, we believe that all patients who present to the clinic with a complaint of allergy to chestnut or tropical fruits should be carefully investigated for the presence of latex allergy. It should be noted that there might be contact allergy to chestnut. On the other hand, patients with allergic rhinitis and asthma should be evaluated for pollen-food syndromes. Patients with pollen-food syndrome should be considered for pollen immunotherapy.

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