

EDITORIAL

Pollen–food allergy syndrome

As far back as 1948, an astute allergist noted that ‘patients sensitive to catkin-bearing trees had inconveniences after eating hazelnuts, such as itching and burning in mouth and throat and similar symptoms after eating raw apples and other kinds of fruits’ [1]. Subsequent reports confirmed the association between birch pollenosis and allergic reactions to a wide variety of fruits and vegetables [2,3], and demonstrated other specific associations, for example between ragweed and melons [4]. Reactions to the foods are often confined to oral itching, but may involve more severe systemic reactions [3,5].

Some controversy has existed regarding the name of this phenomenon. Some authors have used the term ‘oral allergy syndrome’ to describe the association between allergic rhinitis to pollens and allergic reactions to cross-reacting substances in fruits and vegetables [5], while other authors use the term to describe oral symptoms caused by any food allergen, unrelated to pollen allergy [6]. As with the term atopy, different authors will continue to have different definitions of oral allergy syndrome, and readers will need to determine how the term is being used in a particular paper [7]. The term ‘pollen–food allergy syndrome’ seems less ambiguous in describing allergy owing to IgE antibody directed at cross-reacting allergens found in pollens and foods [8], especially since the reactions may involve more than oral symptoms [3,5].

Celery allergy has been of particular interest in this pollen–food allergy syndrome because of its strong relationship to two different pollens (birch and mugwort) [9–14] and because of its propensity to cause anaphylaxis [2,5,9,15,16]. In this issue, Drs Scheurer and colleagues report on the characterization and cloning of an important allergen, celery profilin, Api g 4, which shares IgE-binding epitopes with Bet v 2, birch pollen profilin [17].

Celery (*Apium graveolens*) is botanically related to anise, caraway, carrot, celeriac, coriander, dill, fennel, parsley and parsnip [18]. Patient’s making IgE antibody to allergens in celery often also demonstrate IgE antibody to these related foods, presumably due to similar allergens in the botanical relatives [19]. Although anaphylactic reactions to spices such as coriander can occur [20], most patients with this immunological cross-reactivity do not demonstrate clinical cross-reactivity, i.e. they do not react when they ingest the spices [21]. This same phenomenon has been demonstrated with other food families, e.g. the vast majority of peanut-allergic patients with positive skin tests to other legumes are able to consume these other foods uneventfully [22].

More often in the pollen–food allergy syndrome, the pollens and foods are not botanically-related but nonetheless contain ‘conserved’ homologous proteins [23–25]. Celery allergy has been described in association with both birch and mugwort pollenosis [9–14]. These cross-reactivities are due to Bet v 1 and homologues in the birch/celery-allergic patients, and to Bet v 2 (profilin) and other homologues in both birch/celery and mugwort/celery-allergic patients [13,14]. These differences may relate to the geographical distribution of birch and mugwort [26]. Immunological cross-reactivity extends in some cases to T cells as well. One of the most common birch pollen-associated food allergies involves apple. Cross-reacting T cell epitopes have been identified between Bet v 1 and the major apple allergen Mal d 1 [27].

Another interesting question about pollen–food allergy syndrome is, which came first? Do patients react to food allergens after first being sensitized to the cross-reacting pollen allergens or vice versa? Evidence suggests that the former is more likely or more common. Allergy to fresh fruits and vegetables is much more common among patients with pollenosis than among those without pollen allergy [2,3]. The geographical distribution of pollen allergens and associated celery allergens mentioned above again suggests that pollen sensitization is primary [26]. Furthermore, a patient with pre-existing pollenosis has been reported to have had an anaphylactic reaction to his very first ingestion of a particular fruit [28]. Experimental evidence in animals also supports the notion that pollen allergy is the primary event [29].

Since pollen–food allergy syndrome is due to cross-reacting allergens, one would predict that pollen allergen immunotherapy could lead to a resolution not only of the allergic rhinitis but perhaps resolution of the associated food allergy. This was examined in a trial of immunotherapy in children with allergic rhinitis to birch pollen and allergic reactions to fruits and nuts [30]. Injection immunotherapy with birch or mixed tree pollen was compared to oral immunotherapy with birch pollen and oral placebo. Forty-six per cent (18/39) of children in the injection immunotherapy groups reported an improvement in food allergy compared to 21% (3/14) in the oral birch immunotherapy group and 14% (2/14) in the oral placebo group. Another report describes a patient with severe pollen–food allergy syndrome who underwent standard pollen immunotherapy [31]. Clinically he reported a complete resolution not only of his hayfever symptoms but also of his food reactions. He had a reduction in the size

of not only his pollen skin tests and IgE antibody tests, but also of his food skin tests and IgE antibody tests. Western blots demonstrated several bands of similar molecular weights in the pollen and food extracts, which all decreased in intensity with pollen immunotherapy. A third study reported that 84% of patients with birch pollenosis and oral symptoms after eating fresh apples reported a significant reduction in, or total disappearance of their food allergy symptoms on pollen immunotherapy, whereas no patient in a control group not receiving immunotherapy reported such improvement [32]. Thus it would appear that many patients with pollen–food allergy syndrome could expect standard pollen immunotherapy to alleviate both their pollen and food induced symptoms. A more detailed characterization of these cross-reacting allergens, as with celery profilin [17], should allow a more precise explanation, and treatment for this fascinating syndrome.

References

- Juhlin-Dannfelt C. About the occurrence of various forms of pollen allergy in Sweden. *Acta Med Scand*, 1948; 130: 563–77.
- Hannuksela M, Lahti A. Immediate reactions to fruits and vegetables. *Contact Dermatitis*, 1977; 3:79–84.
- Eriksson NE, Formgren H, Svenonius E. Food hypersensitivity in patients with pollen allergy. *Allergy*, 1982; 37:437–43.
- Anderson LB, Dreyfuss EM, Logan J, Johnstone DE, Glaser J. Melon and banana sensitivity coincident with ragweed pollinosis. *J Allergy*, 1970; 45:310–9.
- Ortolani C, Ispano M, Pastorello E, Bigi A, Ansaloni R. The oral allergy syndrome. *Ann Allergy*, 1988; 61:47–52.
- Amlot PL, Kemeny DM, Zachary C, Parkes P, Lessof MH. Oral allergy syndrome (OAS): symptoms of IgE-mediated hypersensitivity to foods. *Clin Allergy*, 1987; 17:33–42.
- Kelso JM. Oral allergy syndrome? *J Allergy Clin Immunol*, 1995; 96:275.
- Lessof MH, Kelso JM. Pollen–food allergy syndrome. *J Allergy Clin Immunol*, 1996; 98:239–40.
- Pauli G, Bessot JC, Dietemann-Molard A, Braun PA, Thierry R. Celery sensitivity: clinical and immunological correlations with pollen allergy. *Clin Allergy*, 1985; 15:273–9.
- Pauli G, Bessot JC, Braun PA, Dietemann-Molard A, Kopferschmitt-Kubler MC, Thierry R. Celery allergy: clinical and biological study of 20 cases. *Ann Allergy*, 1988; 60: 243–6.
- Vallier P, Dechamp C, Vial O, Deviller P. A study of allergens in celery with cross-sensitivity to mugwort and birch pollens. *Clin Allergy*, 1988; 18:491–500.
- Wuthrich B, Stager J, Johansson SG. Celery allergy associated with birch and mugwort pollinosis. *Allergy*, 1990; 45: 566–71.
- Vieths S, Jankiewicz A, Wuthrich B, Baltes W. Immunoblot study of IgE binding allergens in celery roots. *Ann Allergy Asthma Immunol*, 1995; 75:48–55.
- Bauer L, Ebner C, Hirschwehr R, Wuthrich B, Pichler C, Fritsch R, Scheiner O, Kraft D. IgE cross-reactivity between birch pollen, mugwort pollen and celery is due to at least three distinct cross-reacting allergens: immunoblot investigation of the birch–mugwort–celery syndrome. *Clin Exp Allergy*, 1996; 26:1161–70.
- Kauppinen K, Kousa M, Reunala T. Aromatic plants – a cause of severe attacks of angio-edema and urticaria. *Contact Dermatitis*, 1980; 6:251–4.
- Forsbeck M, Ros AM. Anaphylactoid reaction to celery. *Contact Dermatitis*, 1979; 5:191.
- Scheurer S, Wangorsch A, Haustein D, Vieths S. Cloning of the minor allergen Api g 4, profilin from celery (*Apium graveolens*) and its cross-reactivity with birch pollen profilin Bet v 2. *Clin Exp Allergy*, 2000; 30:962–971.
- National Institute of Allergy and Infectious Diseases. Adverse reactions to foods. NIH Publication no. 84–2442 July. 1984.
- Stager J, Wuthrich B, Johansson SG. Spice allergy in celery-sensitive patients. *Allergy* 1991; 146:475–8.
- Bock SA. Anaphylaxis to coriander: a sleuthing story. *J Allergy Clin Immunol*, 1993; 91:1232–3.
- Niinimäki A, Hannuksela M, Mäkinen-Kiljunen S. Skin prick tests and in vitro immunoassays with native spices and spice extracts. *Ann Allergy Asthma Immunol*, 1995; 75:280–6.
- Bernhisel-Broadbent J, Sampson HA. Cross-allergenicity in the legume botanical family in children with food hypersensitivity. *J Allergy Clin Immunol*, 1989; 83:435–40.
- Enberg RN, Leickly FE, McCullough J, Bailey J, Ownby DR. Watermelon and ragweed share allergens. *J Allergy Clin Immunol*, 1987; 79:867–75.
- Valenta R, Duchene M, Ebner C, Valent P, Sillaber C, Deviller P, Ferreira F, Tejkl M, Edelman H, Kraft Det al. Profilins constitute a novel family of functional plant pan-allergens. *J Exp Med*, 1992; 175:377–85.
- Ebner C, Hirschwehr R, Bauer L, Breiteneder H, Valenta R, Ebner H, Kraft D, Scheiner O. Identification of allergens in fruits and vegetables: IgE cross-reactivities with the important birch pollen allergens Bet v 1 and Bet v 2 (birch profilin). *J Allergy Clin Immunol*, 1995; 95:962–9.
- Hoffmann-Sommergruber K, Demoly P, Crameri R, Breiteneder H, Ebner C, Laimer Da Camara Machado M, Blaser K, Ismail C, Scheiner O, Bousquet J, Menz G. IgE reactivity to Api g 1, a major celery allergen, in a Central European population is based on primary sensitization by Bet v 1. *J Allergy Clin Immunol*, 1999; 104:478–84.
- Fritsch R, Bohle B, Vollmann U, Wiedermann U, Jahn-Schmid B, Krebitz M, Breiteneder H, Kraft D, Ebner C. Bet v 1, the major birch pollen allergen, and Mal d 1, the major apple allergen, cross-react at the level of allergen-specific T helper cells. *J Allergy Clin Immunol*, 1998; 102:679–86.
- Kelso JM, Jones RT, Yunginger JW. Anaphylaxis after initial ingestion of rambutan, a tropical fruit. *J Allergy Clin Immunol*, 1998; 102:145–6.
- Valenta R, Kraft D. Type 1 allergic reactions to plant-derived food: a consequence of primary sensitization to pollen allergens. *J Allergy Clin Immunol*, 1996; 97:893–5.
- Moller C. Effect of pollen immunotherapy on food

- hypersensitivity in children with birch pollinosis. *Ann Allergy*, 1989; 62:343–5.
- 31 Kelso JM, Jones RT, Tellez R, Yunginger JW. Oral allergy syndrome successfully treated with pollen immunotherapy. *Ann Allergy Asthma Immunol*, 1995; 74:391–6.
- 32 Asero R. Effects of birch pollen-specific immunotherapy on apple allergy in birch pollen-hypersensitive patients. *Clin Exp Allergy*, 1998; 28:1368–73.

J. M. KELSO
Allergy Division
Naval Medical Center
San Diego
CA 92134–5000
USA