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Onset of oral allergic syndrome during birch sublingual immunotherapy

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KEY WORDS

Sublingual immunotherapy, oral allergic syndrome, birch allergy, food allergy

SUMMARY

Pollen allergy may be frequently associated with oral allergy to fruits and/or vegetables (the so called oral allergic syndrome). Some studies reported a possible positive effect exerted by allergen-specific immunotherapy on OAS course, while others did not. A case of OAS case onset after starting sublingual immunotherapy is reported.

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Oral allergic syndrome (OAS) is a common allergic disorder sustained by a pollen-fruit cross reaction. OAS is defined by the occurrence of itchy mouth from eating some fruits and vegetables. The most frequent OAS is that appearing in patients who are allergic to birch pollen and report symptoms in the mucosa of the oropharyngeal area when eating fruits from the Rosaceae family (1,2). The reported prevalence of OAS among patients with allergy to birch pollen has varied from 25% to 90% (3-5), although it is generally agreed that more than 70% of birch pollen-allergic patients suffer from OAS (1). It is of note that pollen symptoms are typically seasonal, following pollen allergen exposure, whereas OAS symptoms can persist throughout the year. Several studies investigated whether allergen-specific immunotherapy may also cure OAS in pollen allergic patients (6-16). However, the outcomes were conflicting. For this reason, a randomized study on patients with birch-apple syndrome to evaluate the

outcome of subcutaneous immunotherapy (SCIT) or sublingual immunotherapy (SLIT) on OAS course has been recently performed (17). Twenty patients were treated by SCIT and 20 by SLIT. After 1 year treatment, 2 of 8 SCIT and 1 of 7 SLIT-treated patients developed complete tolerance to apple as provided by oral apple challenge. However, changes in allergen specific IgE did not relate to clinical improvement (17). On the other hand, it was previously reported that birch immunotherapy might induce OAS occurrence (18).

Here, a case of OAS appearing after the first SLIT course in a female patient (M.S. 40 years old) is reported. The patient had been suffering from seasonal spring allergic rhinoconjunctivitis for 10 years. Skin prick test was positive for birch pollen; serum specific IgE levels were 20.6 kU/L to Bet v1, and negative to Bet v2 and Bet v4 (ImmunoCap System, Phadia, Milan, Italy). No IgE specific for other airbor-

ne allergens, including house-dust mites (*D. farinae* and *D. pteronyssinus*), cat, dog, grasses mix, Compositae mix, *P. judaica*, olive trees, *Alternaria tenuis*, *Cladosporium*, and *Aspergilli* mix were detected. Thus, she was an ideal candidate to a successful immunotherapy. In addition, as antihistamines were scarcely effective, SLIT with birch pollen extract was started during the late fall. The woman was fruit-tolerant before the start of SLIT course. Few weeks after starting SLIT (i.e. during the winter), the patient reported OAS after eating fresh apple, that is still persisting in the fall season. Subsequently, OAS to peach, cherry, and carrot occurred as well. Altogether, the clinical response to SLIT was weak as symptom severity and drug use were similar to the previous pollen season. As the patients refused to take another blood sample that could be useful to measure the serum Bet v 1 IgE levels and also to rule out the Pru p 3/Mal d 3 hypersensitivity, a prick-prick test was performed using the fresh offending foods and scored positive for all.

This is the first case of OAS occurring during the first immunotherapy course in author's personal clinical experience (lasting more 30 years). Two main relevant limitations of this case report have to be considered: first, the patients had high Bet v 1 specific IgE levels, and some studies show that a high level of birch pollen or Bet v 1-specific IgE may be frequently associated with OAS (19,20); second, Pru p 3/Mal d 3 hypersensitivity was not ruled out; hence, it is possible that OAS was not induced by the SLIT. Moreover, although several studies investigating the effects of SLIT/SCIT on OAS reported positive effects, the fact that immunotherapy might also theoretically cause or favor the onset of OAS should be considered and pointed out to patients when immunotherapy is proposed. Finally, it has been very recently reported that the gradually increasing consumption of apple might induce tolerance, but the observation of a relapse after discounting of apple consumption and absence of immunologic changes suggest that induced tolerance is only transient (21). This report underlines the complex network beneath the link between birch allergy and OAS. In conclusion, the possibility that immunotherapy, including SLIT, might induce the onset of OAS which could occur even in absence of specific IgE against Bet v 1 and Bet v2 should be considered.

References

- Bohle B. The impact of pollen-related food allergens on pollen allergy. *Allergy* 2007; 62: 3-10
- Eriksson NE, Formgren H, Svenonius E. Food hypersensitivity in patients with pollen allergy. *Allergy* 1982; 37: 437-43
- Katellaris CH. Food allergy and oral allergy or pollen-food syndrome. *Curr Opin Allergy Clin Immunol* 2010; 10: 246-51
- Vieths S, Scheurer S, Ballmer-Weber B. Current understanding of cross-reactivity of food allergens and pollens. *Ann N Y Acad Sci* 2002; 964: 47-68
- Westman M, Stjærne P, Asarnoi A, et al. Natural course and comorbidities of allergic and nonallergic rhinitis in children. *J Allergy Clin Immunol* 2011 (in press)
- Asero R. How long does the effect of birch pollen injection SIT on apple allergy last? *Allergy* 2003; 58: 435-8
- Kinaciyan T, Jahn-Schmid B, Radakovic A, et al. Successful sublingual immunotherapy with birch pollen has limited effects on concomitant food allergy to apple and the immune response to the Bet v 1 homolog Mal d 1. *J Allergy Clin Immunol* 2007; 119: 937-43
- Bolhaar ST, Tiemessen MM, Zuidmeer L, et al. Efficacy of birch-pollen immunotherapy on cross-reactive food allergy confirmed by skin tests and double-blind food challenges. *Clin Exp Allergy*. 2004; 34: 761-9.
- Asero R. Effects of birch pollen-specific immunotherapy on apple allergy in birch pollen-hypersensitive patients. *Clin Exp Allergy*. 1998; 28: 1368-73.
- Hansen KS, Khinchi MS, Skov PS, Bindslev-Jensen C, Poulsen LK, Malling HJ. Food allergy to apple and specific immunotherapy with birch pollen. *Mol Nutr Food Res*. 2004; 48: 441-8.
- Kelso JM, Jones RT, Tellez R, Yunginger JW. Oral allergy syndrome successfully treated with pollen immunotherapy. *Ann Allergy Asthma Immunol*. 1995; 74: 391-6.
- Asero R. Fennel, cucumber, and melon allergy successfully treated with pollen-specific injection immunotherapy. *Ann Allergy Asthma Immunol*. 2000; 84: 460-2.
- Bucher X, Pichler WJ, Dahinden CA, Helbling A. Effect of tree pollen specific, subcutaneous immunotherapy on the oral allergy syndrome to apple and hazelnut. *Allergy*. 2004; 59: 1272-6.
- Herrmann D, Henzgen M, Frank E, Rudeschko O, Jäger L. Effect of hyposensitization for tree pollinosis on associated apple allergy. *J Investig Allergol Clin Immunol*. 1995; 5: 259-67.
- Valenta R, Niederberger V. Recombinant allergens for immunotherapy. *J Allergy Clin Immunol*. 2007; 119: 826-30
- Möller C. Effect of pollen immunotherapy on food hypersensitivity in children with birch pollinosis. *Ann Allergy*. 1989; 62: 343-5.
- Mauro M, Russello M, Incorvaia C, et al. Birch-apple syndrome treated with birch pollen immunotherapy. *Int Arch Allergy Immunol*. 2011; 156: 416-22.
- Modrzyński M, Zawisza E. Possible induction of oral allergy syndrome during specific immunotherapy in patients sensitive to tree pollen. *Med Sci Monit*. 2005; 11: CR351-5.
- Geroldinger-Simic M, Zelniker T, Aberer W, et al. Birch pollen-related food allergy: clinical aspects and the role of allergen-specific IgE and IgG4 antibodies. *J Allergy Clin Immunol*. 2011; 127: 616-22.e1.
- Asero R, Massironi F, Velati C. Detection of prognostic factors for oral allergy syndrome in patients with birch pollen hypersensitivity. *J Allergy Clin Immunol*. 1996; 97: 611-6.
- Kopac P, Rudin M, Gentinetta T, et al. Continuous apple consumption induces oral tolerance in birch-pollen-associated apple allergy. *Allergy* 2011 (in press).