
Fennel, cucumber, and melon allergy successfully treated with pollen-specific injection immunotherapy

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Background: In subjects with both pollinosis and vegetable food allergy, most allergenic epitopes of fruits and vegetables are present in pollen. A recent study showed a marked reduction or a total disappearance of apple-induced oral allergy syndrome in patients receiving injection immunotherapy with birch pollen extracts.

Objective: To assess whether vegetable food allergy following other kinds of primary pollinosis may be successfully treated with pollen-specific immunotherapy.

Methods: A 34-year-old woman with long-standing pollinosis and typical oral allergy syndrome (OAS) with the ingestion of both fennel and cucumber and whose OAS was associated with immediate laryngeal edema after the ingestion of melon, was treated with two commercial depot aluminum hydroxide-adsorbed extracts of ¹ grass pollen and ² mugwort pollen 50% + ragweed pollen 50%.

Results: After 36 months of injection specific immunotherapy, the patient was able to tolerate both fresh fennel and cucumber without consequence on open oral challenge tests. After 43 months of immunotherapy, the patient tolerated fresh melon as well on open oral challenge. She has re-introduced these vegetables in her normal diet. Skin tests showed no reactivity to fresh fennel and there was a reduction of the wheal induced by fresh cucumber.

Conclusion: Vegetable food allergy following primary sensitization to pollens, other than birch, may also be effectively reduced by pollen-specific injection immunotherapy.

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INTRODUCTION

Oral allergy syndrome from fresh vegetable foods is the most frequent food allergy in adults^{1,2} and generally follows primary pollen sensitization as a consequence of cross-reactivity between pollen and food allergens.³ Previous studies showed that in subjects with both pollinosis and vegetable food allergy, most allergenic epitopes of fruits and vegetables are present in pollen.^{4,5} As a consequence, one could reasonably expect that in these subjects pollen-specific immunotherapy may reduce food hypersensitivity. Few studies tried to address this issue. A case report showed the disappearance

of oral allergy syndrome (OAS) caused by several fruits and vegetables in a patient treated with to specific immunotherapy with two distinct allergen extract mixtures (a mixture of 15 trees, and a mixture of four grasses, five weeds, two molds, and two mites⁶). In contrast, no effect on food allergy was noted in 72 birch pollen-sensitive children treated with injection or oral immunotherapy.⁷ More recently, however, a controlled study showed a marked reduction or a total disappearance of apple-induced OAS in most adult patients receiving injection immunotherapy with birch pollen extracts.⁸ This effect was associated with a marked reduction of skin reactivity to fresh apple, but no change in specific IgE levels occurred.⁸ This study reports another patient whose food allergy was successfully treated with specific immunotherapy (SIT). In this

situation the result was obtained using two pollen extracts other than birch.

CASE REPORT AND METHODS

The study was carried out on a 34-year-old woman with long-standing pollinosis (rhinoconjunctivitis from the end of April to the end of June and rhinoconjunctivitis and asthma from the beginning of August to the end of September). She reported typical oral allergy syndrome (OAS; characterized by severe oral itching and lips angioedema) immediately after the ingestion of both fennel and cucumber. Her OAS was associated with immediate laryngeal edema after the ingestion of melon. The patient was able to tolerate all other foods without any problem. The patient also had mild perennial rhinitis. The patient was first seen in October, 1995 when the following baseline tests were performed: (1) SPT with commercial extracts (Allergopharma, Reinbeck, Germany) of both seasonal (grass, mugwort, ragweed, pellitory, and birch) and perennial (mites, animal danders, molds) airborne allergens present in this geographic area; (2) SPT with commercial extracts (Dome/Hollister-Stier, Spokane, Washington, 1:20 wt/vol) of a large series of vegetable foods (including celery, carrot, pea, bean, soybean, peanut, walnut, potato, tomato, garlic, onion, orange, apple, pear, peach, cherry, plum, and almond); (3) SPT with fresh fruits (golden delicious apple, fennel, cucumber, and hazelnut) by the prick-prick technique using a 1-mm tip disposable prick lancetter (Bayer).⁹ A SPT with melon was not carried out due to the lack of the fresh fruit in November and because the Dome/Hollister-Stier series did not include a melon extract. All SPT were

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read after 15 minutes and results were graded by comparison with the size of the wheal induced by histamine 10 mg/mL. A wheal size equal or larger than the histamine wheal was scored 3+ and 4+, respectively. Only wheals equivalent or greater than 2+ (ie, 50% of the control wheal) were considered positive.¹⁰

Skin prick test results are summarized in Table 1. The patient showed a very positive SPT with all seasonal airborne allergens extracts (++++ in all cases); the mean diameter of wheals induced by grass, mugwort, ragweed, pellitory, and birch pollens was 30 mm, 30 mm, 20 mm, 10 mm, and 10 mm, respectively (histamine 5 mm). Further, she showed strong skin reactivity to house dust mite (++++). No reactivity was found to molds, cat or dog danders. Skin prick test with commercial food extracts revealed strong reactivity to celery (wheal mean diameter 10 mm), pea, bean, potato, and onion, a moderate reactivity (+++) to garlic, carrot, orange, soybean, and tomato, and a weaker positive tests

(++) to peanut, almond, and walnut. Skin prick tests with Rosaceae (apple, pear, peach, cherry, plum) extracts were negative. Skin prick tests with fresh material were positive for cucumber (++++), fennel (+++), and hazelnut (+++). No reactivity was observed to golden delicious apple.

Pre-SIT IgE specific for airborne allergens were measured by an immunoassay (Kallestad, Austin, Texas). The following levels were found: perennial rye = 16.4 UA/ml (class 3); mugwort 1.1 (2); ragweed 3.7 (3); pellitory 1.7 (2); birch 0.36 (1); house dust mite 3.5 (3). IgE specific for apple, hazelnut, melon, and celery were measured by immunoassay CAP-system (Pharmacia, Uppsala); these tests were all negative but celery (0.97 KU/L; class 2).

On the basis of clinical history, SPT results, and IgE measurements, injection specific immunotherapy with two commercial depot aluminum hydroxide-adsorbed extracts (1) grass pollen mix; (2) mugwort pollen 50% + ragweed pollen 50% (both by Allergop-

harma, Reinbeck, Germany) was started in November 1995. Other allergens positive on SPT, namely birch, pellitory, and house dust mites were not included in the treatment since they did not seem clinically relevant in this patient. Immunotherapy was administered following a perennial schedule: maintenance doses were reduced by half during the pollen's season. Weekly doses were given during the "buildup" (induction) phase in order to reach the planned maintenance dose which was 1.0 mL of vial 3 [corresponding to 5000 T.U. (therapeutic units, the biologic standardization used by Allergopharma)]. The patient could not reach this dose and the highest doses which did not elicit side effects were 0.35 mL of vial III and 0.5 mL of vial III for grass pollen and mugwort + ragweed extracts, respectively. Maintenance doses were given at 3-week intervals.

RESULTS

In November 1998, after 36 months of injection SIT, the patient was re-evaluated. Open oral challenge tests with fresh fennel and cucumber were performed on different days. The patient was asked to chew about 10 g of fresh fennel or fresh cucumber for 1 minute and then to spit it out. Subsequently she was observed for 15 minutes. The patient tolerated both fresh fennel and cucumber without any consequence. She has now re-introduced these vegetables in her normal diet.

Skin prick test with both seasonal airborne allergens and food allergens were carried out. Results are summarized in Table 1. A marked decrease in skin reactivity on SPT with fresh fennel (negative test) and a moderate reduction of the wheal induced by fresh cucumber (+++) were found. Further, skin reactivity against non-offending foods was markedly reduced as well (Table 1). A SPT with a melon extract (kindly prepared by Lofarma, Milan) was weakly positive (++), but no comparison with pre-SIT reactivity was possible since this extract was not available when the patient was first seen. Skin prick tests showed a marked

Table 1. SPT* Results Before and After 3 Years of Injection SIT

	Before SIT†	After SIT
Pollens		
Grass	++++ (30 mm)‡	++++ (10 mm)
Mugwort	++++ (30 mm)	++++ (20 mm)
Ragweed	++++ (20 mm)	++++ (10 mm)
Birch	++++ (10 mm)	+++
Fresh foods		
Fennel	+++	—
Cucumber	++++	+++
Commercial food extracts		
Celery	++++ (1 cm)	++
Carrot	+++	++
Onion	++++	—
Garlic	+++	—
Soybean	+++	++
Pea	++++	+++
Bean	++++	++
Peanut	++	++
Tomato	+++	—
Potato	++++	++
Orange	+++	—
Melon	Not available	++

* SPT = skin prick tests.

† SIT = specific immunotherapy.

‡ Figures in parentheses represent the mean diameter of the wheal.

reduction of skin reactivity against all pollen extracts; interestingly, also birch pollen reactivity was reduced (Table 1).

In July 1999, after 44 months of injection SIT, an open oral challenge with melon was carried out and the fruit was tolerated without any consequence.

DISCUSSION

The SPT profile of this patient, characterized by strong reactivity against several pollens (birch, mugwort, ragweed, grass, and pellitory) as well as against most vegetable foods tested, suggests that profilin was probably a relevant cross-reacting allergen in this subject.^{11,12} The reduction of skin reactivity to birch despite not giving immunotherapy for this pollen represents indirect evidence of profilin cross-reactivity. Profilin is present in many vegetable foods, including Apiaceae, and cucumber^{13–15} as well as cross-reacting allergens in the gourd family and ragweed pollen.¹¹ Profilins are strong sensitizers, but their biologic activity is often poor,¹⁷ a fact which may explain the weak correlation between positive skin tests and clinical allergy in this patient. Since both pollen extracts used for injection SIT in this study contained profilin,¹¹ this patient probably received a double dose of this allergen with immunotherapy. This treatment might have played a role in reducing patient's reactivity against fennel, cucumber, and melon.

These observations suggest that vegetable food allergy following primary sensitization to pollens other than birch may be effectively reduced by pollen-specific injection SIT.

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