

Hypothesis & Experience
Case Report



Treatment with lipid transfer protein sublingual immunotherapy: slowing down new sensitizations

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ABSTRACT

Food allergy (FA) is a potentially life-threatening condition, food allergen immunotherapy, targeting the underlying mechanisms, is a potentially curative strategy in FA. A 46-year-old woman had an episode of facial angioedema and urticaria after mandarin ingestion and other episode of urticaria, abdominal pain, and facial angioedema after eating hazelnuts and almonds 4 years ago and contact urticaria (CU) with the manipulation of the peach skin. Three years ago, she suffered a facial and glottis angioedema, generalized urticaria, vomiting, and abdominal pain 10–15 minutes after eating green beans. She was treated with intravenous corticosteroids and antihistamines and intramuscular epinephrine, with complete resolution within a few hours. She no longer consumed nuts, and she avoided vegetables or fruits that caused her symptoms. Prick-prick test were performed, being positive with lettuce, eggplant, and cabbage and negative for cauliflower and broccoli. Total IgE (UniCAP method, kU/L) was 39.3, specific IgE Prup3 lipid transfer protein (LTP), 3.9; specific IgE to peanut, peach, pear, lemon, almond, avocado, walnut, cherry, and green bean were also positive. We decided to try to stop the march of the LTP sensitizations. Sublingual immunotherapy with a peach extract quantified in 12 µg/mL of peach allergen Prup3 was then initiated without any adverse event, and she has good adherence to the treatment. After 1 year, single-blind oral challenge test with peach, mandarin, and aubergine, were performed up to a portion dose (approximately 100 g) with all good tolerances.

Keywords: Food allergy; Lipid transfer protein; Immunotherapy; Desensitization; Allergen challenge test

INTRODUCTION

Food allergy (FA) is a potentially life-threatening condition, often impairing quality of life. The current approach in FA management is based on avoidance of trigger food and the use of rescue treatment if needed. FA immunotherapy is a potentially curative treatment as is based on targeting the underlying hypersensitivity mechanisms.

Conflict of Interest

The authors received technical assistance from ALK-Abelló Laboratories for the in vitro allergy study. Lucia Jimeno Nogales is currently an employee at ALK-Abelló Laboratories.

CASE REPORT

A 46-year-old woman, with previous clinical record of rhinoconjunctivitis with sensitization to grass pollen and plane tree pollen, was referred to our Allergy Unit. Four years ago, she suffered a facial angioedema and urticaria after mandarin ingestion and another episode of urticaria, abdominal pain, and facial angioedema after eating hazelnuts and almonds. She had also developed in the last 4 years, oropharyngeal itchiness and erythema with beans, aubergine, cabbage, cherries, chard, spinach, lettuce, peach, as well as contact urticaria (CU) when handling peach.

Three years ago, she suffered a facial and glottis angioedema, generalized urticaria, vomiting, and abdominal pain 10–15 minutes after eating green beans. She was treated with corticosteroids, antihistamines, and epinephrine, with complete resolution within a few hours.

Since then, she has not consumed any more fruits, vegetables, or nuts that would cause her symptoms.

Skin prick tests with a panel of commercial extract were performed (ALK-Abelló, Madrid, Spain), being positive for plane tree pollen, green bean, peanut, hazelnut, walnut, lettuce, peach, apple, and kiwi and lipid transfer protein (LTP) extract. Prick-by-prick test were performed, being positive with lettuce, eggplant, and cabbage and negative for cauliflower and broccoli. Total IgE (UniCAP method, kU/L) was 39.3, specific IgE Prup3 LTP, 3.9; specific IgE to peanut, peach, pear, lemon, almond, avocado, walnut, cherry, and green bean were also positive.

Over the last few years, she had experienced more and more reactions with a growing number of foods that brought her to a restrictive diet, with a decrease in her quality of life. For this reason, we decided to try to stop the LTP march. Sublingual immunotherapy (SLIT) (ALK-Abelló) with a peach extract quantified in 12 µg/mL of peach allergen Prup3 was then initiated. After informed consent was signed, she started the treatment in our Immunotherapy Unit. The protocol was a rush schedule in a single day with increasing sublingual doses of (0.05, 0.2, 0.4, and 0.8 mL, each 30 minutes) of a 50 µg/mL vial of Prup3, to continue with the maintenance dose of 0.2 mL per day (**Table 1**), without any adverse event and good adherence to the treatment. After 1 year receiving SLIT daily, we decided to perform a single-blind oral challenge test (SBOCT) with peach, in order to know the efficiency of the immunotherapy.

The SBOCT with peach was performed up to a dose of 150 g (approximately 1–1.2 mg of Prup3) without any reaction. Up to 7 doses (starting dose: approximately 3 µg of Prup3) were administered with a 30-minute interval, and after the last dose, the patient remained under observation for at least 1 hour (**Table 2**).

Table 1. Sublingual immunotherapy protocol

Day	Drop	Time
1st day	1 drop (0.05 mL)	30 Minutes (symptom monitoring)
Vial 4 (hospital treatment)	4 Drops	30 Minutes
	8 Drops	30 Minutes
	16 Drops	30 Minutes
2nd day onwards	4 Drops per day	-
Vial 4 (home treatment)		

Table 2. Single-blind oral challenge test with peach

Peach dose (g)	Estimated dose of prup3 (μ g)	Symptom monitoring time (min)	Approximate cumulative dose (μ g)
0.5-1	3-6	30	4
2.2	15	30	19
4.5	31	30	50
9	62	30	112
18	124	30	236
36	248	30	484
80	551	60	1,035

Table 3. Variations in the allergological study

Variable	Before SLIT	2 Years after SLIT
Total IgE (kU/L)	39.3	59.2
IgE Pru p 3 (kU/L)	2.24	2.14
IgG 4 (peach LTP) (mgA/L)	-	0.26
Skin prick test (peach) (mm)	5×9	5×5

SLIT, sublingual immunotherapy; LTP, lipid transfer protein.

Six months later, a SBOCT with mandarin and aubergine, was performed up to a portion dose (approximately 100 g) both were well tolerated.

At this point, after 2 years with SLIT, we decided to repeat the allergological study to observe the immunological effects (**Table 3**). Prick test with LTP extract decreased, but with no significance difference. A significant IgG4 (0.26) to Prup3 was observed. Total IgE was 59.2 KU/L, and LTP IgE decreased to 2.14 kU/L.

The patient tolerated peach, mandarin, and aubergine despite specific positive skin tests and IgE. This improved patient's quality of life and no more new symptoms with other food have appeared until now. However, she is not interested in SBOCT with green beans or nuts, and she will continue with immunotherapy for one more year.

DISCUSSION

The LTP family is widely found in fruits, vegetables, and nuts, and has been suggested to be responsible for immunological cross-reactivity between them and pollens [1, 2]. One of the most important aspects in LTP hypersensitivity syndrome is the extreme variability of its clinical expression. Many patients remain asymptomatic despite strong LTP sensitization [3]. Our patient suffered a severe anaphylaxis once after eating green beans, and also developed CU with peach. It is well known that LTP is probably the main cause of food-induced CU in Spain, and peach is the reference of LTP-related FA in our country [4]. CU may remain the only sign of LTP hypersensitivity syndrome in more than 60% of the patients [3].

Most patients suffer the "LTP march," by acquiring new sensitizations along the years decreasing their quality of life. Allergic reactions to other plant-derived foods (cereals, onion, celery, onion, broccoli...) are much rare and occur generally in those with high Prup3 IgE levels [4, 5].

SLIT with peach has proved to be safe, as no serious adverse events have been observed [6, 7].

In a review of the literature, Gómez et al. [1] reported 48 peach allergic patients (with moderate and severe systemic reactions) being assessed for 1 year. The immunological effect induced by the Prup3 SLIT decreased the Prup3-specific IgE levels. This has also been observed in other immunological studies after SLIT treatment [8]. In addition, they also proved that clinical and immunological changes happen not only to peach but also for other LTP foods that induce severe reactions. In other works published, data suggested that SLIT could induce desensitization [9].

We report a patient in whom, after 2 years of Prup3 SLIT, immunological changes and clinical tolerance have been achieved, not only for peach but also for other relevant LTP food allergens [1, 6]. As it is based on studies published in the literature, we consider that the maintenance of treatment for 3 years may be appropriate, although more patients and long-term studies of tolerance once treatment is complete would be needed. Nevertheless, we proposed to the patient to continue eating different fruits and vegetables with LTP in order to maintain tolerance. In our patient, the immunotherapy has stopped the “LTP march,” preventing from new sensitizations, and allowing her to tolerate food she was allergic to, with a positive impact in her quality of life.

REFERENCES

1. Gómez F, Bogas G, González M, Campo P, Mayorga C. The clinical and immunological effects of Pru p 3 sublingual immunotherapy on peach and peanut allergy in patients with systemic reactions. *Clin Exp Allergy* 2017;47:339-50.
[PUBMED](#) | [CROSSREF](#)
2. Enrique E, Utz M, De Mateo JA, Castelló JV, Malek T, Pineda F. Allergy to lipid transfer proteins: cross-reactivity among pomegranate, hazelnut, and peanut. *Ann Allergy Asthma Immunol* 2006;96:122-3.
[PUBMED](#) | [CROSSREF](#)
3. Cuesta-Herranz J, Lázaro M, de las Heras M, Lluch M, Figueredo E, Umpierrez A, Hernandez J, Cuesta C. Peach allergy pattern: experience in 70 patients. *Allergy* 1998;53:78-82.
[PUBMED](#) | [CROSSREF](#)
4. Asero R, Piantanida M, Pinter E, Pravettoni V. The clinical relevance of lipid transfer protein. *Clin Exp Allergy* 2018;48:6-12.
[PUBMED](#) | [CROSSREF](#)
5. Pastorello EA, Pravettoni V, Farioli L, Primavesi L, Scibilia J, Piantanida M, Mascheri A, Conti A. Green bean (*Phaseolus vulgaris*): a new source of IgE-binding lipid transfer protein. *J Agric Food Chem* 2010;58:4513-6.
[PUBMED](#) | [CROSSREF](#)
6. De Luque Piñana V, Lopez Ruiz C, Gonzalez Montaña MD, de la Calle Toral A, Guardia Martinez P. Tolerance of administration of sublingual extract peach immunotherapy, compared with conventional regimen. *Allergy* 2015;70:527-613.
7. Fernández-Rivas M, Garrido Fernández S, Nadal JA, Díaz de Durana MD, García BE, González-Mancebo E, Martín S, Barber D, Rico P, Tabar AI. Randomized double-blind, placebo-controlled trial of sublingual immunotherapy with a Pru p 3 quantified peach extract. *Allergy* 2009;64:876-83.
[PUBMED](#) | [CROSSREF](#)
8. García BE, González-Mancebo E, Barber D, Martín S, Tabar AI, Díaz de Durana AM, Garrido-Fernández S, Salcedo G, Rico P, Fernández-Rivas M. Sublingual immunotherapy in peach allergy: monitoring molecular sensitizations and reactivity to apple fruit and Platanus pollen. *J Investig Allergol Clin Immunol* 2010;20:514-20.
[PUBMED](#)
9. Canonica GW, Cox L, Pawankar R, Baena-Cagnani CE, Blaiss M, Bonini S, Bousquet J, Calderón M, Compalati E, Durham SR, van Wijk RG, Larenas-Linnemann D, Nelson H, Passalacqua G, Pfaar O, Rosário N, Ryan D, Rosenwasser L, Schmid-Grendelmeier P, Senna G, Valovirta E, Van Bever H, Vichyanond P, Wahn U, Yusuf O. Sublingual immunotherapy: World Allergy Organization position paper 2013 update. *World Allergy Organ J* 2014;7:6.
[PUBMED](#) | [CROSSREF](#)