Clinical Profile of Lipid Transfer Protein Syndrome in a Mediterranean Area

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Nonspecific lipid transfer proteins (LTPs) are present in several plant foods. LTPs are highly stable during thermal processing and digestion [1,2]. Reactivity of IgE to LTPs is often associated with severe systemic symptoms [3].

LTPs are the most important family of plant food allergens in Spain [4]. Pru p 3 is the predominant LTP in terms of recognition of IgE by a patient [5]. Owing to structural homology, LTPs from various allergen sources are generally cross-reactive to various types of IgE. However, sensitization profiles vary widely between allergic patients [6].

The aims of this study were to describe the clinical and sensitization profile of patients with LTP syndrome and to determine a clinical pattern of severity.

The study sample comprised consecutive patients referred to the Allergy Unit of Hospital Universitari Germans Trias i Pujol, Badalona, Spain during 2016 (a total of 560 patients with food allergy were screened). Selection was based on a clear history of plant food allergy and IgE-mediated sensitization to Pru p 3 in a skin prick test. A control group was selected based on IgE-mediated sensitization to Pru p 3 without associated food allergy. Patients—or their representatives in the case of children—provided their informed consent, and the study was approved by the local ethics committee (PI-17-074).

The clinical evaluation comprised an exhaustive medical history, skin prick tests with a common panel of aeroallergens, plant food allergens, and purified and enriched peach LTP components (Bial-Aristegui). Specific IgE to Pru p 3 and total IgE were determined using ImmunoCAP (Thermo Fisher), and IgE to the allergen components were determined using the microarray-based IgE detection chip ImmunoCAP ISAC (Thermo Fisher). ImmunoCAP and ISAC results higher than 0.35 kU/L and 0.3 ISU/E, respectively, were considered positive.

The χ^2 or Fisher exact test was used to compare categorical variables; an analysis of variance or the Kruskal-Wallis test was used to compare quantitative variables. Statistical significance was set at $P<.05$.

A total of 84 patients with a mean age of 27.88 years (IQR, 3-62) were included in the study. Of these, 54 were women (64.3%) and 40 (47.6%) had respiratory allergy.

The patients were divided into 3 groups according to the manifestations observed after plant food ingestion based on their clinical history (tolerance test not performed), as follows: anaphylactic reactions (37 [44%]), restricted reactions in skin and/or oropharyngeal tract (36 [42.9%]), and asymptomatic sensitization to LTPs (11 [13.1%]).

The 3 groups had a similar gender distribution, although the asymptomatic patients were younger than the patients with food allergy ($P<.05$). The time since diagnosis and the mean age at onset of symptoms were similar in both clinical groups. A lower mean value of Pru p 3 was observed among asymptomatic patients ($P<.05$).

The food responsible for the first reaction was Rosaceae in 41 patients (48.8%), tree nuts in 24 (28.6%), and other vegetables in 6 (7.1%), with no statistically significant differences between groups, although other vegetables were more frequent in the group of systemic reactions (2.8% vs 13.5%). The presence of cofactors associated with the allergic reaction (alcohol, nonsteroidal anti-inflammatory drugs, and exercise) was observed in 30/73 patients, and these were more frequent in the group of patients with anaphylaxis ($P<.05$).

Sensitization to plane tree and mugwort was much more frequent among patients with food allergy, regardless of severity. There were no differences in sensitization to plant food.

The frequency of recognition of the food LTP was as follows: Pru p 3, 94%; Jug r 3, 82.14%; Ara h 9, 76.19%; Cor a 8, 55.95%; and Tri a 14, 16.6%. There were no differences between the groups. The LTP profile is summarized in the Table. Mean LTP recognition was 3.90 in the asymptomatic group, 5.42 in the group with urticaria/angioedema/oral allergy syndrome, and 5.18 in the anaphylaxis group. More LTPs were recognized in the food-allergic patients than in the asymptomatic ones ($P<.05$). Pla a 3 and Art v 3 were the LTPs in the ISAC platform, which most commonly recognized patients with clinical food allergy. No differences were observed between restricted and generalized reactions.

Our study comprised only patients with a positive skin prick test result to a purified LTP extract from peach (adult and pediatric patients). The study could also be limited by the lack of a control group of patients with plant food allergy not sensitized to LTP and the fact that the group of asymptomatic patients was smaller than the 2 clinical groups (no more sensitized asymptomatic patients were found, even though Pru p 3 was regularly tested). Including a comparison with patients not sensitized to LTP and a larger group of sensitized patients would make interpretation of the data much more straightforward.

We observed differential characteristics between sensitized asymptomatic patients and patients with plant food allergy. The asymptomatic patients were slightly younger and presented a lower mean value of Pru p 3 than symptomatic patients. Plane tree and mugwort are much more frequent among patients with food allergy, regardless of the severity. IgE testing with Pla a 3 and Art v 3 may serve as a marker to identify allergic patients at risk of LTP-mediated food reactions, as found in recent surveys on LTPs in patients from the Mediterranean area [7,8].

The most frequently involved food in both clinical groups was peach, consistent with findings from a multicenter study [9]. Furthermore, vegetables were more frequently involved in the group of patients with anaphylaxis. Palacin et al [10] observed that patients did not develop allergy easily against green beans or lettuce during the first stage of polysensitization. Therefore, in patients in whom the food allergy first manifested with a reaction to a vegetable, the patients were likely previously polysensitized without clinical symptoms.

The presence of cofactors enhancing food allergy was greater in the group of patients with anaphylaxis and was the only statistically different variable between the clinical groups. We observed high recognition of Pru p 3 (94%), which was the best marker of sensitization to LTPs in the population we studied. The number of LTPs recognized in food-allergic patients was greater than in asymptomatic patients, although the molecular spread did not affect the severity of food allergy symptoms.

Our observations suggest the existence of a natural history of sensitization to LTPs that tends not only towards polysensitization, but also towards a higher degree of sensitization. However, the severity of food allergy would depend on specific individual factors.

To conclude, as the only variable associated with severity is the presence of cofactors, we recommend the prescription of adrenaline autoinjectors to patients sensitized to LTPs with cofactor-enhanced food allergy, regardless of the severity of the allergic symptoms.

Table. Lipid Transfer Protein Profile

	Asymptomatic	Restricted Reactions	Generalized Reactions	*P* Value	Total
Cor a 8	4 (36.36%)	22 (61.1)	22 (59.45%)	>.05	48 (57.1%)
Jug r 3	8 (72.72%)	30 (83.3%)	31 (83.78%)	>.05	69 (82.14%)
Ara h 9	8 (72.72%)	29 (80.55%)	27 (72.97%)	>.05	64 (76.10%)
Tri a 14	1 (9.1%)	7 (19.44%)	6 (16.21%)	>.05	14 (16.66%)
Pru p 3	10 (90.9%)	35 (97.22%)	34 (91.89%)	>.05	79 (94%)
Pla a 3	6 (54.54%)	29 (80.6%)	34 (91.89%)	<.05	69 (82.14%)
Art v 3	4 (36.36%)	27 (75%)	23 (62.2%)	<.05	54 (64.28%)
Par j 2	1 (9.1%)	6 (16.7%)	7 (18.9%)	>.05	14 (16.66%)
Ole e 7	1 (9.1%)	10 (27.77%)	8 (21.62%)	>.05	19 (22.61%)

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

1. Scheurer S, Lauer I, Foetisch K, San Miguel Moncin M, Retzek M, et al. Strong allergenicity of Pru av 3, the lipid transfer protein from cherry, is related to high stability against thermal processing and digestion. J Allergy Clin Immunol. 2004 Oct;114(4):900-7.
2. Asero R, Mistrello G, Roncarolo D, Vriesc S, Gautierd MF, Ciuranae C, et al. Lipid Transfer Protein: A Pan-Allergen in Plant-Derived Foods That Is Highly Resistant to Pepsin Digestion. Int Arch Allergy Immunol. 2000;122:20-32.
3. Pastorello EA, Robino AM. Clinical role of lipid transfer proteins in food allergy. Mol Nutr Food Res. 2004;48:356-62.
4. Fernández Rivas M. Food Allergy in Alergológica-2005. J Investig Allergol Clin Immunol. 2009;19:S2:37-44.
5. Fernández-Rivas M, González-Mancebo E, Rodríguez-Pérez R, Benito C, Sánchez-Monge R, Salcedo G, et al. Clinically relevant peach allergy is related to peach lipid transfer protein, Pru p 3, in the Spanish population. J Allergy Clin Immunol. 2003;112:789-95
6. Egger M, Hauser M, Mari A, Ferreira F, Gadermaier G. The role of lipid transfer proteins in allergic diseases. Curr Allergy Asthma Rep. 2010 Sep;10(5):326-35.
7. Wangorsch A. Molecular cloning of plane pollen allergen Pla a 3 and its utility as diagnostic marker for peach associated plane pollen allergy. Clin Exp Allergy. 2016;46(5):764-74.
8. Pascal M, Muñoz-Cano R, Reina Z, Palacín A, Vilella R, Picado C, et al. Lipid transfer protein syndrome: clinical pattern, cofactor effect and profile of molecular sensitization to plant-foods and pollens. Clin Exp Allergy. 2012:42;1529-39.
9. Goikoetxea MJ, Berroa F, Cabrera-Freitag P, Ferrer M, Núñez-Córdoba JM, Sanz ML, et al. Do Skin Prick Test and In Vitro Techniques Diagnose Sensitization to Peach Lipid Transfer Protein and Profilin Equally Well in Allergy to Plant Food and Pollen? J Investig Allergol Clin Immunol. 2015;25(4):283-7.
10. Palacín A, Gómez-Casado C, Rivas LA, Aguirre J, Tordesillas L, Bartra J, et al. Graph based study of allergen cross-reactivity of plant lipid transfer proteins (LTPs) using microarray in a multicenter study. PLoS One. 2012;7(12);e50799.

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