

Clinical Communications

A novel case discussion of pediatric lipid transfer protein syndrome

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Clinical Implications

- We present a unique case of lipid transfer protein syndrome in a pediatric patient in the United States. Confirmation of the diagnosis required designated ImmunoCAP testing. This case highlights diagnostic and management challenges in this important yet underappreciated allergic condition.

Lipid transfer proteins (LTPs) are allergens widely found in plants and plant-derived foods.^{1,2} Lipid transfer protein syndrome occurs in individuals sensitized to LTPs. Lipid transfer protein syndrome is a significant cause of food-induced anaphylaxis as well as food-dependent exercise-induced anaphylaxis.³ Lipid transfer proteins represent dominant proteins that cause allergic reactions to fruits, nuts, and vegetables in adults and children from the Mediterranean basin; yet, whereas LTP syndrome is common in Mediterranean countries, it is rare in birch endemic areas (ie, northern Europe).⁴ Reports of pediatric LTP syndrome are limited to cases primarily from the Mediterranean region.¹ We report the first documented case of LTP syndrome in a school-age child living in the United States.

The patient was an 8-year-old Black boy with a history of asthma and atopic dermatitis. He had presented with concerns for IgE-mediated reactions to multiple foods. The initial presentation consisted of anaphylaxis at age 4 years after consumption of a lemon cookie. At age 6 years, he developed anaphylaxis after eating a fresh kiwi, and at age 7 years, he had wheezing after drinking kiwi juice. At age 8 years, he also developed immediate generalized hives without anaphylaxis after the separate ingestion of finned fish, macadamia nuts, raspberries, peaches, and grape juice. He was able to tolerate wheat, shellfish, egg, soy, sesame, and dairy. The patient avoided peanuts and tree nuts after the reaction to macadamia, and the family noted that he had had no prior exposure to peanuts or other tree nuts. The timing of each event was not consistent with food-dependent exercise-induced anaphylaxis.

The patient underwent serum-specific IgE testing to foods with reported histories concerning for IgE-mediated reactions, and was found to have detectable IgE to peanut, walnut, and hazelnut (Table I). He was also noted to have elevated reactivity strictly to lipid transfer proteins (LTPs) in nuts by allergen component testing. In addition to the anaphylactic reaction and elevated serum-specific IgE levels to lemon and kiwi, this finding led us to believe that the history of various reactions might have resulted from sensitization to LTPs. Interestingly, the IgE values did not translate into strong skin prick test reactivities (Table I).

The patient had a positive skin prick-to-prick testing response to fresh grape and limited reactivity to fresh lemon and fresh kiwi (Table I). We concluded that the amount of LTP present for prick-to-prick testing to each fresh food item may have been insufficient to achieve significant skin test reactivity. Therefore, we sought additional methods to test for LTP syndrome.

Currently, standardized LTP extracts for various fruits or plants are limited for percutaneous skin testing. A semi-quantitative allergen microarray assay was used to determine the patient's specific IgE sensitization to 112 allergen components, measured using the ImmunoCAP 112 Immuno Solid-phase Allergen Chip (ISAC) platform (Thermo Fisher Scientific, Portage, Mich). Specific IgE values were expressed in ISAC standard units (ISU-E), with values of 0.3 ISU-E or greater considered to be positive. The ISU-E values were grouped into established ranges (<0.3 ISU-E, not detectable; ≥0.3 to <1 ISU-E, low; ≥1 to <15, moderate; and ≥15, very high). The results demonstrated positivity toward all measured LTPs, and the highest level of sensitization was found for the peach LTP Pru p 3. This result is consistent with reports in the literature of the common hierarchical order of sensitizations often found in LTP syndrome patients.³ Additional positive allergen components included species-specific aeroallergens for Bermuda and timothy grass, *Alternaria*, and cockroach. Of specific note, all IgE sensitivities to PR-10 and profilin cross-reactive proteins (eg, Ara h 8, Bet v 2) were undetectable, a phenotype that was previously reported to be consistent with more clinically severe presentations of LTP syndrome.⁵

The patient had a clinical history consistent with IgE-mediated allergic reactions after the ingestion of multiple LTP-containing foods including lemon, kiwi, raspberry, peach, and grape. ImmunoCAP testing demonstrated elevated serum immunoglobulin to lemon, kiwi, and raspberry, all of which contain LTPs that can contribute to clinical allergic reactivity.² ISAC LTP testing confirmed sensitization to all LTP components tested (Table II). Both skin prick testing and prick-to-prick testing showed or suggested sensitization to LTP-containing foods, but many did not elicit wheal responses 3 mm greater than the negative control. This observation may indicate that component testing for LTP-containing foods is more sensitive than skin testing.

ISAC testing showed that the patient was sensitized to a few pollens despite having a negative history of aeroallergen reactivity. The silent sensitization to non-food LTPs might contribute to pan-LTP sensitization and the future development of symptoms to other LTP-containing foods. The clinical and laboratory findings can be compared with those of European children with LTP sensitization, in which sensitization to regional pollens could be associated with broader plant-food LTP sensitization, increased frequency, and greater severity of reactions upon ingestion of LTP-containing foods compared with adults.⁶ Although the clinical history and testing confirm LTP syndrome, co-sensitization with non-LTP allergen families cannot be excluded.

Although LTP syndrome is more common in children living in Mediterranean areas¹ and is rare but increasingly reported in birch-endemic areas of Europe,⁷ to our knowledge, we provide

TABLE I. Serum IgE, skin prick test, and prick-to-prick results

Allergen	IgE, kU/L (negative <0.10)	Skin prick test with extract (wheal/flare)	Prick-to-prick (wheal/flare)
Histamine		6/40 mm	6/40 mm
Saline		0/0 mm	0/0 mm
Peanut	13.8	2/2 mm	
Ara h 1 (F422)	<0.10		
Ara h 2 (F423)	0.13		
Ara h 3 (F424)	<0.10		
Ara h 8 (F352)	<0.10		
Ara h 9 (F427)	34.2		
Brazil nut (F18)	0.21		
Ber e 1 (F354)	<0.10		
Cashew nut (F202)	<0.10		
Codfish (F3)	<0.10		
F020 almond	4.32	3/14 mm	
Grape flesh (tested twice)			3/5 mm 4/4 mm
Grape skin			1/3 mm
Grape juice			2/2 mm
Hazelnut (F17)	17	3/15 mm	
Cor a 1 (F428)	<0.10		
Cor a 8 (F425)	10.4		
Cor a 9 (F440)	<0.10		
Cor a 14 (F439)	<0.10		
Kiwi fruit (F084)	5.48		
Kiwi flesh (tested twice)			2/6 mm 2/3 mm
Kiwi skin			1/2 mm
Lemon (F208)	5.33		
Lemon flesh (tested twice)			2/2 mm 1/2 mm
Lemon skin			0/0 mm
Macadamia nut (rf345)	4.71		
Pecan nut (F201)	1.84		
Pistachio (F203)	2.16		
Raspberry (RF343)	22.3		
Walnut (F256)	28.1	3/11 mm	
Jug r 1 (F441)	0.10		
Jug r 3 (F442)	34.2		

the first report of LTP syndrome in a pediatric patient in the United States. In addition to the unique clinical presentation and laboratory findings related to this patient, this case also highlights the potential difficulties of maintaining a balance between avoiding potentially cross-reactive foods and maintaining a well-balanced, nutritious diet, especially in children with sensitization to multiple LTPs. Sublingual allergen immunotherapy as a disease-modifying treatment has been shown to increase tolerance in some patients with LTP sensitization to Pru p 3 and potentially other food allergens.^{1,8,9} More research is needed to evaluate the use of LTP allergen immunotherapy as a tool to treat these patients, which could positively affect their quality of life, health, and nutrition.

TABLE II. Lipid transfer protein allergy testing

Lipid transfer protein	Component	ISAC standard unit (ISU-E) results
Peanut	Ara h 9	4.5 ISU-E
Hazelnut	Cor a 8	4 ISU-E
Walnut	Jug r 3	9.1 ISU-E
Peach	Pur p 3	13 ISU-E
Mugwort	Art v 3	2.6 ISU-E
Olive pollen	Ole e 7	0.3 ISU-E
Plane tree	Pla a 3	9.5 ISU-E
Wheat	Tri a 14	3.4 ISU-E

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