

# Natural Tolerance Development to Peach in a Child with Lipid Transfer Protein Allergy

## Aquisição Natural de Tolerância ao Pêssego numa Criança Alérgica a Proteínas de Transferência de Lípidos



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### ABSTRACT

Non-specific lipid transfer proteins (LTPs), present in multiple plant foods and pollens, are the predominant allergen in peach allergy in the Mediterranean region and may induce life-threatening allergic reactions. Although reasonably studied in adults, LTP allergy has been rarely described in children, and to the best of the author's knowledge, natural tolerance development during childhood to this allergen has not been reported to date. The authors reported the case of a 21 month-old boy who presented urticaria and facial edema 15 minutes after eating a peach. Sensitization to peach LTP was confirmed by skin prick tests and specific IgE. At the age of 32 months, skin prick tests and specific IgE to peach LTP were negative, so a food challenge was performed. The child tolerated one medium-sized peach. Peach and peach-related fruits were reintroduced in the child's diet. The authors discuss the relevance of regular allergy workup and dietary recommendations in children with LTP allergy.

**Keywords:** Carrier Proteins/immunology; Child; Food Hypersensitivity; Fruit Proteins/immunology; Immune Tolerance; Prunus Persica

### RESUMO

As proteínas de transferência de lípidos [lipid transfer proteins (LTP)] são proteínas presentes em alimentos vegetais e pólenes, e constituem os principais alérgenos na alergia a pêssego na região mediterrânica, podendo induzir anafilaxia. A alergia a estas proteínas tem sido predominantemente reportada em adultos e casos de aquisição natural de tolerância não foram descritos. Os autores descrevem o caso de uma criança de 21 meses que apresentou urticaria e angioedema da face 15 minutos após a ingestão de um pêssego. A sensibilização a LTP foi confirmada por testes cutâneos por picada e IgE específica positivos para a LTP do pêssego. Onze meses depois, estes testes para a LTP do pêssego foram negativos, tendo sido realizada prova de provocação em que a criança tolerou um pêssego médio. A reintrodução na dieta de pêssego e frutos relacionados foi bem tolerada. Os autores discutem a necessidade da reavaliação regular e orientação da dieta de evicção nas crianças com alergia a LTPs.

**Palavras-chave:** Criança; Hipersensibilidade Alimentar; Proteínas da Fruta/imunologia; Proteínas de Transporte/imunologia; Prunus Persica; Tolerância Imunológica

### INTRODUCTION

Non-specific lipid transfer proteins (LTPs) are ubiquitous plant allergens, described as the main cause of primary food allergy in adults from Southern Europe.<sup>1,2</sup> LTPs are the major allergens in *Rosaceae* fruits (e.g. peach, apple, cherry), but they can be present in other plant-derived foods as well as in pollens.<sup>1,4</sup>

In LTP-allergic patients, the wide range of reaction-eliciting foods may be explained by their molecular similarity, resulting in cross-reactivity between LTPs present in botanically related and unrelated foods.<sup>1,3,5</sup>

Since LTPs are stable to heat, gastric digestion, and food preservation methods, they may induce symptoms with ingestion of fresh and/or processed food, and clinical manifestations may range from mild symptoms to anaphylaxis.<sup>1,2,4</sup>

Allergy to LTPs has been reasonably described in adults but rarely in children. Moreover, the development of natural tolerance in an LTP allergic child has not been previously reported.

### CASE REPORT

The authors report the case of a 21 month-old boy who presented with facial and abdominal urticaria, as well as

with edema of the lips and eyelids 15 minutes after eating an unpeeled peach. No other foods were ingested at that time. He was treated with oral corticosteroids and antihistamines in the emergency department and discharged symptom-free two hours later. Peach was previously tolerated but the child stopped eating peach, apricot and nectarine after this reaction. Peeled apple, pomegranate, peanut and walnut ingestion was continued, without symptoms. Skin prick tests (SPTs) to *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Lepidoglyphus destructor*, cat, dog, birch, olive, grass pollen mix, *Parietaria*, *Alternaria* (Roxall-Aristegui®, Bilbao, Spain) were negative (positive if wheal diameter  $\geq$  3.0 mm; histamine 10 mg/mL, 3.0 mm; negative control, 0 mm). As seen in Table 1, SPTs with food extracts were positive to peach LTP, peach, walnut, almond and cherry, and negative to apple and peanut. Specific IgE (sIgE) to rPru p 3 (peach LTP;  $\geq$  0.35 UK<sub>A</sub>/L, positive) was 0.62 UK<sub>A</sub>/L and 0.43 UK<sub>A</sub>/L for rJug r 3 (walnut LTP;  $\geq$  0.35 UK<sub>A</sub>/L, positive), as seen in Table 1. At this point, parents were advised to maintain peach, apricot and nectarine avoidance. Despite positive SPTs, tree nut ingestion was continued since it did not induce any symptoms.<sup>6</sup> Emergency medication, a written action plan and LTP allergy

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Table 1 – Summary of workup

| Tests   | Age, months                        |                 |       |        |      |
|---|------------------------------------|-----------------|-------|--------|------|
|   | 7                                  | 21              | 32    | 55     |      |
| SPTs, mean wheal diameter measure in millimetres †, ‡ | Cow's milk                         | 3.0             | 4.5   | 3.0    | NP   |
|   | α-lactoalbumin                     | 7.0             | 5.0   | 7.0    | NP   |
|   | β-lactoglobulin                    | 5.0             | 3.0   | 5.0    | NP   |
|   | Casein                             | 3.5             | 7.5   | 3.5    | NP   |
|   | Peach LTP                          | NP              | 6.5   | 0.0    | NP   |
|   | Peach                              | NP              | 4.0   | 0.0    | NP   |
|   | Walnut                             | NP              | 5.0   | 0.0    | NP   |
|   | Hazelnut                           | NP              | 7.5   | 0.0    | NP   |
|   | Almond                             | NP              | 4.0   | 0.0    | NP   |
|   | Cherry                             | NP              | 3.0   | 0.0    | NP   |
|   | Histamine 10 mg/mL                 | 6.0             | 3.0   | 4.0    | NP   |
|   | Negative control                   | 0.0             | 0.0   | 0.0    | NP   |
|   | SPECIFIC IgE, kU <sub>A</sub> /L § | Total IgE, KU/L | 39.60 | 123.00 | NP   |
| Cow's milk  |                                    | 14.40           | 27.10 | NP     | 7.05 |
| nBos d 4 (α-lactoalbumin)                             |                                    | 10.90           | 6.10  | NP     | 1.54 |
| nBos d 5 (β-lactoglobulin)                            |                                    | 2.68            | 2.66  | NP     | 0.30 |
| nBos d 8 (casein)                                     |                                    | 7.15            | 23.80 | NP     | 6.72 |
| rPru p 3 (peach LTP)                                  |                                    | NP              | 0.52  | 0.04   | NP   |
| rJug r 3 (walnut LTP)                                 |                                    | NP              | 0.43  | 0.03   | NP   |

†: Skin Prick tests (SPTs) were considered positive if wheal diameter  $\geq 3.0$  mm (Roxall-Aristegui, Bilbao, Spain); ‡: SPTs were negative to apple and peanut at 21 and 32 months-old; §: ImmunoCap, Thermo-Fisher. NP: not performed.

information were provided to the parents. No accidental ingestions were reported.

As relevant medical history, the child presented at the age of seven months perioral urticaria and lip swelling five minutes after eating milk-containing baby food. At 18 months old, during a visit to his uncle's house, he presented generalized urticaria and conjunctivitis after eating a ham sandwich (the ham was stored in contact with cheese). There were no more accidental exposures. SPT and sIgE to milk and components performed at 7, 21, 32 and 55 months are all described in Table 1. At 12 months, an oral food challenge (OFC) with milk was suggested but the parents refused. Considering the probability of milk allergy resolution in childhood, SPT and sIgE to milk and peach LTP were repeated at 32 months.<sup>7</sup> After this reaction, sIgE nBos d 8 (casein) increased from 7.15 UK<sub>A</sub>/L to 23.80 UK<sub>A</sub>/L and the authors decided to postpone the OFC with milk. At the 55 months reassessment, no accidental reactions were reported and sIgE to nBos d 4, nBos d 5 and nBos d 8 decreased, but the parents did not consent to an OFC with milk.

While monitoring milk allergy at 32 months old, evaluation of peach LTP sensitization was contemplated, and previously positives SPTs to peach LTP, peach, walnut, almond and cherry, as well as the sIgE to rPru p 3 and rJug r 3, turned negative. Skin prick-to-prick tests (SPPTs) to peach peel and pulp were negative (histamine 10 mg/mL, 4 mm; negative control, 0 mm). Considering the negative SPT and SPPT to peach, and the negative SPT and sIgE to peach

LTP, an OFC with unpeeled peach was performed after parental written informed consent at four years old, after being postponed twice for viral infections and later because of the COVID-19 pandemic. OFC started with lip challenge, followed by four doses of peach administered 30 minutes apart, with semi-logarithmic increases, reaching a cumulative dose of 154.23 g (a full medium peach).<sup>8</sup> The period of observation after the last dose was two hours, and no symptoms occurred during this period. Peach, apricot and nectarine were reintroduced in the child's diet at home and no reactions were reported upon re-exposure.

## DISCUSSION

Natural tolerance is well described in children with milk and egg allergies, with most patients outgrowing milk and/or egg allergy throughout childhood. Other prevalent food allergies, such as peanut and fish allergy, have a less favourable prognosis.<sup>9</sup> Allergy to LTPs in children is a scarcely reported but emerging subject.

The authors reported the first case of natural tolerance to peach in a LTP allergic child. The diagnosis was suspected based on the clinical symptoms elicited by peach ingestion and supported by the positive SPT to peach LTP, peach, almond and walnut extracts, and positive sIgE to rPru p 3 and rJug r 3.<sup>10</sup> Tolerance to peach was confirmed by a negative oral food challenge (performed after negative SPTs to peach LTP, peach, almond and walnut extracts, negative sIgE to rPru p 3 and rJug r 3, and negative SPPT to peach)

and successful reintroduction of peach and peach-related fruits in the child's diet.

Some methodological limitations need to be mentioned, as the lack of an OFC to confirm the diagnosis of LTP allergy. This diagnosis was based on a suggestive history, and positive SPT and sIgE, supporting an LTP sensitization pattern. The child's age, risk of severe reaction upon re-exposure, and parental concerns were all taken into account in the decision of not performing an OFC with peach.

To the authors' knowledge, this is the first report of natural tolerance development in an LTP allergic child. The present case reinforces the importance of regularly testing sensitized young children as routinely done in egg and milk allergies; this is a particularly relevant since management of LTP allergy involves challenging preventive strategies, given the widespread diffusion of the protein and its variable degree of cross-reactivity.

Dietary avoidance of important nutritious foods, such as fruits and vegetables, may affect the child's health, growth, and not only the child's quality of life but also their parents' and caretakers'. For these reasons, dietary avoidance measures should be based on clinical reactivity and not merely on sensitization.<sup>6</sup>

As such, the child was advised to avoid only the food, which triggered symptoms (peach and similar fruits) and to preserve the regular ingestion of other LTP-containing foods that elicited no symptoms upon ingestion, including those with positive SPT (almond and walnut). The partial homology between LTP from different foods, the fact that sensitization does not indicate allergy, allows LTP-allergic

subjects to ingest all tolerated foods until evident symptoms arise.<sup>6</sup> This approach may avert unnecessary and deleterious restrictive diets and potentially contribute to natural tolerance development as a physiological form of immunotherapy.<sup>6,11</sup>

#### AUTHORS CONTRIBUTION

All authors had an equal contribution to the literature research; draft and distribution of the questionnaire; analysis of the results; draft of the paper.

#### PROTECTION OF HUMANS AND ANIMALS

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association.

#### DATA CONFIDENTIALITY

The authors declare having followed the institutional protocols regarding publication data.

#### PATIENT'S CONSENT

Obtained.

#### COMPETING INTERESTS

The authors have no competing interests to declare concerning this work.

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