

## A case study of apple seed and grape allergy with sensitisation to nonspecific lipid transfer protein

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Lipid transfer proteins can be an important cause of allergy given their stability and high degree of protein sequence homology. We describe the case of a child who developed two separate episodes of anaphylaxis after consuming apple seed and grape, with evidence that nonspecific lipid transfer proteins may have been responsible for these reactions. Lipid transfer protein allergy should be considered when anaphylaxis is inconsistent, such as in patients who can tolerate fruit pulp but react to fresh whole fruit juices.

**Key words:** Seeds; Allergy; Anaphylaxis; Lipid transfer protein

### INTRODUCTION

Allergies to vegetables and fruits develop as a result of secondary sensitisation to foods following primary sensitisation to cross-reactive pollen or latex allergens, or through direct sensitisation to foods through the gastrointestinal tract [1, 2]. In European populations, the vegetables most likely to induce an allergic reaction are carrot, tomato and celeriac, whilst apple, peach and kiwi are the most common causes of allergy to fruit [1].

Allergic reactions may develop following exposure to various components of a particular plant. There are few published case reports describing allergic reactions to citrus or apple seeds without allergy to their pulp or peel [3-5].

Lipid transfer proteins (LTPs) are small, basic proteins found in animals, some fungi and plants. Their stability derives from four conserved disulphide bonds, which confers resistance to heat and proteases, protecting against destruction by gastrointestinal secretions. Plant nonspecific LTPs serve multiple

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functions within the plant, including defence against bacteria and fungi, mediating phospholipid transfer, and the production of protective surface polymers such as cutin. There is a high degree of protein sequence homology between nonspecific LTPs [6].

We describe the case of a child who developed two separate episodes of anaphylaxis after consuming apple seed and grape, with evidence that non-specific LTPs may have been responsible for these reactions.

## CASE REPORT

A 12-year-old female presented to the Emergency Department with generalised urticaria, hypotension and angioedema of the lips and tongue. Her symptoms developed approximately 10 minutes after consuming apple puree, which she prepared by blending whole apples in an electric blender. She had no significant past medical history or allergies, and was not taking any regular medications. Her serum tryptase was elevated to 24.3 µg/L (<11.4). Her baseline serum tryptase was within the normal range (4.8 µg/L) when measured 2 months later. Skin prick testing revealed that she was sensitised to apple seed but not apple pulp (Table 1). She was also sensitised to *Bahia*, *Acacia* sp and *Platanus* sp, but did not have symptoms of allergic rhinitis or oral allergy syndrome.

She presented to the Emergency Department a second time after developing facial angioedema and hypotension 15 minutes after consuming whole, seedless, green grapes. She was walking to school when she developed the allergic reaction. Skin prick testing revealed sensitisation to all components of black grape, including the skin, pulp and seed. Testing also demonstrated sensitisation to green grape skin and pulp. Green grape seed was not tested as only seedless green grapes were available.

Following her reaction to grape, our patient had consumed and tolerated seedless orange, seedless watermelon, rockmelon, pear, tomato (including seeds), papaya, broccoli, potato, carrot, corn, pea, silver beet, peanut, cashew, almond, hazelnut, pistachio, macadamia, cumin, sesame, and poppy seed. She returned for skin prick testing with freshly made extracts of a number of other fruits and seeds (Table 1). Another individual served as a control demonstrating a positive reaction to histamine (5 mm) alone.

The patient went on to have specific IgE testing to 112 individual allergen molecules from 51 different allergens using ImmunoCAP ISAC (Immuno Solid-phase Allergen Chip; Phadia,

Portage, MI, USA). This revealed low to moderate sensitisation to nonspecific LTPs from peanut (Ara h 9), hazelnut (Cor a 8), walnut (Jug r 3), peach (Pru p 3), and mugwort (Art v 3). Other nonspecific LTPs including wall pelitory (Par j 2), wheat (Tri a 14), olive (Ole e 7), and plane tree (Pla a 3) were tested, with negative results. She was not sensitised to any of the storage proteins, PR-10 proteins or profilins included in the ISAC panel.

A diagnosis of allergy to apple seed and grape was made. Given the skin prick and specific IgE results, cross-reactive, nonspecific LTPs were considered to be the likely allergens.

The patient was advised to avoid grape and apple seed as well as seeds of other fruits. She was also advised to avoid pomegranates and cumin as these produced the largest wheal size on skin prick testing. She was prescribed an adrenaline auto-injector and provided with an anaphylaxis action plan.

## DISCUSSION

The patient in this case developed anaphylaxis to apple seed and seedless grape, and was sensitised to a multitude of fruits and/or fruit seeds. However, she was able to tolerate many of the fruits and nuts to which she was sensitised.

We suspect that her allergies and clinically nonsignificant sensitisations may have been due to nonspecific LTPs as the ISAC study only revealed sensitisation to LTPs. Mal d 3 and Vit v 1 are LTPs belonging to apple and grape respectively and may have been the culprit allergens causing her episodes of anaphylaxis. Unfortunately we could not confirm this as these were not part of the ISAC panel.

It is unclear why this patient develops allergies to some nonspecific LTPs but not to others given their strong homology. The mechanism of selective LTP sensitisation may reflect the geography of exposure to different LTPs from common tree and weed sources. Her reactions may have also been dependent on cofactors such as exercise, as she had been walking to school when she developed anaphylaxis to grape. However, the patient had not been exercising when she developed her reaction to apple seed. A possible way of resolving this issue is by organising a future exercise challenge following consumption of a food to which she had clinically nonsignificant sensitisation, such as macadamia nut.

Crushing and cutting seeds likely contributes to increased exposure of LTPs that may have otherwise passed through the

**Table 1.** Skin prick test results

Test	Wheal size <sup>†</sup> (mm)
Histamine	5
Glyserosaline	0
Red apple pulp	0
Green apple pulp	0
Red apple seed	5
Green apple seed	7
Paspalum	5
Plane tree	5
Acacia	5
Birch	0
Red grape pulp	8
Red grape seed	7
Red grape skin	6
Green grape pulp	8
Green grape skin	8
Grape seed oil	5
Lemon seed	5
Lemon pulp	0
Grape fruit seed	5
Grape fruit pulp	4
Orange pulp*	0
Orange seed	0
Mandarin pulp	0
Mandarin seed	0
Pomegranate pulp	10
Pomegranate seed	5
Tomato pulp*	5
Rock melon seed	0
Rock melon pulp*	0
Honey dew melon pulp	0
Honey dew melon seed	0
Water melon pulp*	0
Water melon seed	0
Passion fruit pulp	6
Passion fruit seed	0
Pear pulp*	0
Pear seed	0
Macadamia nut*	7
Almond*	0
Peanut*	5

Test	Wheal size <sup>†</sup> (mm)
Cashew*	0
Pine nut	0
Pecan	5
Walnut	3
Pistachio*	0
Brazil nut	0
Fennel seed	4
Cumin seed*	10
Sesame seed*	5
Caraway seed	0
Poppy seed*	0
Coriander	4
Mustard seed	4
Sunflower seed	3
Tomato seed*	0

\*Foods consumed since episode of anaphylaxis to grape. <sup>†</sup>Average of perpendicular diameters.

gastrointestinal tract undigested. LTPs are typically found in the highest concentration in the skin of fruits. Assuming this patients' apple seed reaction was to an LTP component, it is unclear why she was able to tolerate apple skin. Determining her sensitisation to Mal d 3 using specific IgE testing would help to clarify whether LTPs played a role in her apple seed allergy.

It is interesting to note that skin prick testing to plane tree was positive, although specific IgE testing to plane tree nonspecific LTP (Pla a 3) was negative. A possible explanation for this could be that sensitisation to plane tree was due to reactivity to another non-LTP protein.

Assessing the patient's risk of allergy and advising her on which foods to avoid was challenging, as she was able to tolerate a number of foods to which she was sensitised on skin prick testing. Of note, she was able to tolerate cumin, which produced one of the largest wheals on skin prick testing. This tolerance may have developed as a result of cooking the cumin prior to its consumption, which can denature allergenic epitopes.

Wheal size was not a reliable predictor for developing allergic reactions, as the wheal size for reactive components of grape and apple ranged only from 5–8 mm in diameter, while the wheal size for macadamia nut, which she could tolerate, was a similar size (7 mm). Supervised food challenges would ultimately be required

to clarify which fruits she can safely consume in the future.

In conclusion, this case demonstrates that LTP allergy should be considered, even in low birch pollen environments, when anaphylaxis is inconsistent, such as in patients who can tolerate fruit pulp but react to fresh whole fruit juices.

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