

# Labile plant food allergens: Really so harmless? Case series and literature review

To the Editor,

Pathogenesis-related proteins group 10 (PR-10) and the plant pan-allergen profilin are the most frequent causes of food allergy in adults living in Italy.<sup>1</sup> These two allergens are thermolabile and pepsin sensitive. Therefore, most food-allergic patients sensitized to PR-10 or profilin experience exclusively oral allergy syndrome (OAS) following the ingestion of unprocessed fruits, nuts, legumes, and vegetables although food sensitization may be asymptomatic. Systemic symptoms have been reported only in association with the soybean PR-10 Gly m4.<sup>2</sup> With this exception, PR-10 and/or profilin hypersensitivities are considered as virtually harmless and no specific preventive measures are recommended. We report some cases of severe systemic reactions following the ingestion of fruits and/or vegetables occurring in PR-10 and profilin-hypersensitive patients which are possibly useful to identify the co-factors that could pose a risk of life-threatening reactions.

## CASE 1

In April 2019, a 57-year-old man with a long history of birch pollen allergy associated with moderate asthma and of oral allergy syndrome (OAS) following the ingestion of fresh apple and hazelnut experienced an anaphylactic reaction characterized by urticaria, severe dyspnea, and hypotension during a business travel. The allergic reaction occurred in the breakfast room of a hotel, immediately after having ginger tea, a brioche, and two glasses of freshly prepared carrot juice. Three doses of 0.3 mg intramuscular adrenalin along with 125 mg of methylprednisolone intravenously were administered in the emergency room to recover the patient. Only PR-10 reactivity was found at the microarray test (Thermo Fisher Scientific, ISAC 112). In September, a second episode of anaphylaxis 10 minutes after eating four raw almonds occurred. At that time, the man had started an antacid treatment with esomeprazole. The allergic reaction resolved gradually after the self-administration of 0.3 mg of adrenalin by autoinjector.

## CASE 2

In July 2014, a 30-year-old woman with grass and house dust mite allergy and a history of melon-induced OAS, known as being hypersensitive to profilin as shown by ISAC test, experienced an

anaphylactic reaction characterized by hypotension and diffuse urticaria with angioedema, followed by respiratory difficulty due to laryngeal obstruction. The adverse reaction occurred during dinner, after the ingestion of six slices of fresh melon with ham and drinking a glass of wine. The patient was brought to the emergency room where she improved after a combination of intramuscular adrenalin and 8 mg intravenous betamethasone. A further ISAC evaluation confirmed the already known exclusive reactivity to grass, house dust mite, and profilins.

## CASE 3

A 20-year-old woman with a history of grass pollen hypersensitivity causing seasonal rhinoconjunctivitis and asthma reported four episodes of OAS followed by generalized urticaria, vomiting, and abdominal pain some minutes after ingesting raw tomato, banana, persimmon, and pesto sauce, respectively, during the last 2 months. The patient tolerated cooked tomato sauce and thermally processed nuts and peanuts. The woman reported a 7 kg weight loss during the last 3 months. In vitro testing showed hypersensitivity to Phl p 1 (8.30 kU/L), Phl p 5 (3.20 kU/L), and Phl p 12 (4.35 kU/L), whereas no reactivity was detected to Bet v 1, Ole e 1, Pru p 3, Ara h 1, Ara h 2, and Ara h 3. Macrocytic anemia, low levels of B12 vitamin (146 pg/mL), and positive serum anti-parietal cells autoantibodies along with gastroscopy and biopsy eventually led to diagnose autoimmune chronic atrophic gastritis.

## DISCUSSION AND LITERATURE REVIEW

Data of systemic reactions induced by foods in patients sensitized uniquely to labile plant food allergens are sparse.<sup>3</sup> Under normal conditions, PR-10 allergens and profilin induce only local oropharyngeal symptoms. Notably, profilin hypersensitivity reduces the risk of systemic reactions to stable allergens such as seed storage proteins and/or lipid transfer proteins in co-sensitized patients.<sup>4</sup> The normal gastric digestion process will lead to the degradation of these allergens making them no longer recognizable by specific IgE.<sup>5</sup> Thus, the co-factors that pose these patients at risk of systemic reactions are all those conditions that favor labile food allergens to avoid gastric digestion, allowing them to reach the duodenum in a structurally unmodified form. The following conditions can be identified:

- a. High quantity of allergen in a brief time span. Gastric digestion ability and amount of the offending food are probably inversely related.
- b. Liquid state of the food. Liquids cross the stomach and reach the duodenum much more rapidly than solids, especially if ingested in large amounts.
- c. Fasting. An empty stomach could represent a risk factor for a rapid passage of food into the duodenum.<sup>5</sup>
- d. Antacids. Proton-pump inhibitors may theoretically facilitate food sensitization<sup>6</sup> and cause an insufficient degradation of labile allergens.
- e. Atrophic gastritis. Although no evidence is currently available that this may be a co-factor, this rare clinical condition is characterized by a severely compromised gastric secretion and hence by a markedly reduced capacity to digest foods.

In the first case, two combined co-factors (fasting and liquid state of the allergen) were present. Carrot has been reported to induce systemic reactions more frequently than Rosaceae fruits.<sup>7</sup> On the second occasion, the first patient was taking a proton-pump inhibitor at high dosage. Further, the patient suffered from moderate asthma that could also represent a risk factor.

In the second patient, the adverse reaction was associated with a huge consumption of melon. Melon has been recognized as a marker of profilin hypersensitivity and was recently shown as able to induce severe reactions in grass pollen-allergic patients.<sup>8</sup> However, that study suggests that profilin might also penetrate through the damaged oral mucosa of severely grass pollen-allergic patients.<sup>8</sup> Regarding alcohol as an augmentation factor of food allergy reactions, the results of a recent study show that its position is ambiguous.<sup>9</sup>

In the third patient, while a series of four spontaneous reactions seems rather unlikely, the co-factor was probably the severe atrophy of the stomach leading to a block of gastric secretion and of pepsin digestion, also associated with marked weight loss.

We must admit that the final proof of a causal relationship is missing in our patients as, also due to the severity of the allergic reactions they experienced, allergy was not confirmed by a double-blind, placebo-controlled food challenge (DBPCFC). However, we are quite sure that they were not sensitized to stable plant food allergens; further, all the reactions occurred after the intake of plant-derived foods known to contain the allergenic protein they were sensitized to. A differential diagnosis in case 1 might also be relapsing, acute spontaneous urticaria.

## CONCLUSIONS

Clinicians should be aware that also allergy due to pollen cross-reactive allergens, such as PR-10 and profilin, may cause systemic reactions under certain circumstances.

## CONFLICT OF INTEREST

All the authors declare the lack of any conflict of interest.

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Riccardo Asero<sup>1</sup> 

Giorgio Celi<sup>2</sup>

Enrico Scala<sup>3</sup> 

<sup>1</sup>Ambulatorio di Allergologia, Clinica San Carlo, Paderno Dugnano, Italy

<sup>2</sup>Ambulatorio di Allergologia, Clinica Villa Pia, Roma, Italy

<sup>3</sup>Ambulatorio di Allergologia, Istituto Dermatologico dell'Immacolata, Roma, Italy

## Correspondence

Riccardo Asero, Ambulatorio di Allergologia, Clinica San Carlo, Via Ospedale 21, 20037 Paderno Dugnano, Italy.

Email: r.asero@libero.it

## ORCID

Riccardo Asero  <https://orcid.org/0000-0002-8277-1700>

Enrico Scala  <https://orcid.org/0000-0002-9391-9168>

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