

## Recurrent anaphylaxis in patient allergic to eggplant – a Lipid transfer protein (LTP) syndrome

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### Abstract

Eggplant allergy is rare and most of the previously described reactions were mild. In this case report, we present an interesting case of a 27-year-old male who experienced symptoms of anaphylaxis (shortness of breath, and swelling of the face, lips and tongue, which was followed by hypotension, tachycardia of 140/min and a sudden loss of consciousness) several minutes after eating a dish containing backed eggplant. Previously, the patient had experienced symptoms of allergy after eating different types of food, such as salad and chicken in spices. The symptoms were enhanced by co-factors. They were heterogeneous, ranging from oral symptoms to anaphylactic shock.

During the diagnostic pathway, skin prick tests (SPTs) were positive to grass and cat. Prick by prick skin tests were positive for eggplant, both cooked and fresh. In ImmunoCap ISAC, IgE specific to rPhl p 1 (1.7 ISU-E), rCan f 5 (1,2 ISU-E), Fel d 1 (9.6 ISU-E) and LTPs - nJug r 3 (0.5 ISU-E), rPru p 3 (0.6 ISU-E), rPla a 3 (1.3 ISU-E) were found.

Based on the clinical pattern of the disease and the results of component resolved diagnosis, we suspect that this complex case of anaphylaxis may be gathered with LTP syndrome.

**Keywords:** anaphylaxis, eggplant, allergy, component resolved diagnosis, lipid transfer protein

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### Introduction

Allergic reactions to eggplant (aubergine, *Solanum melongena*) have been rarely reported and are mainly attributed to cross-reactivity with proteins of other fruit and vegetables.<sup>1</sup>

It is widely known that the frequency of allergy to different types of allergens depends on a number of factors, including exposure to a given allergen, socioeconomic factors, comorbidities, the climate zone, and dietary habits.<sup>2,3</sup> The currently described patient is probably one of the first in Poland who has experienced anaphylactic reaction due to eggplant allergy.

The prevalence of IgE-mediated eggplant allergy is estimated at approximately 0.8%, with higher rates of sensitization in females.<sup>4</sup> Eggplant is generally eaten after cooking or baking.<sup>5</sup> Eggplant contains 48 proteins that can potentially be a source of allergic reaction, most of which are not yet fully described.<sup>6</sup> One of the most interesting known eggplant allergens is LTP (lipid transfer protein), which is potentially cross-reactive with allergens of other fruit and vegetables. Other allergens include a protein with weak homology to 7S vicilins,<sup>7</sup> lipoxygenase, protein proteinase inhibitor and 15kDa and 35 kDa heat stable proteins with unknown functions.<sup>8</sup>

In 2009, a very interesting work was published by Babu et al., in which the authors investigated sensitization to different parts of the eggplant fruit, and detected the allergens. It was noticed that most allergens were localized in the eggplant peel (9 allergens; 26–71 kDa range) rather than the pulp (3 allergens; 52–71 kDa); among these, the allergens with molecular weights of 26, 28, 36, and 71 kDa seemed to be heat-stable, and the authors detected the allergens with molecular weights of 43, 45, 64, and 71 kDa to be glycoproteins.<sup>5</sup>

Lipid transfer proteins (LTPs) are plant panallergens, which are described as pure food allergens, and are capable of sensitizing through the gastrointestinal tract. LTPs have been found in many plant-related foods, particularly in those belonging to the *Rosaceae* family, for example peach (Pru p 3) and apple (Mal d 3), but also hazelnut (Cor a 8) from the *Betulaceae* family, walnut (Jug r 3) from the *Juglandaceae* family, peanut (a legume crop, from the *Fabaceae* family), sesame (*Pedaliaceae* family), and celery (*Apiaceae* family).<sup>9,10</sup>

nsLTPs (non-specific LTPs) are mostly present in the peel of fruits, rather than the pulp.<sup>11,12</sup> Interestingly, symptoms after

the consumption of LTP-containing foods can differ. In 2006, Sancho et al. showed that nsLTP levels in apple are greatly dependent on maturity, storage conditions and cultivar.<sup>13</sup>

LTP syndrome is a relatively new name for a clinical pattern of symptoms and natural course of allergy to this panallergen. We now know that there are different recognition patterns of LTPs – some patients only react to peach and apple (*Rosaceae* fruit, where sensitization to peach LTP Pru p 3 can be a marker), while others react to a wide range of foods, including hazelnut or walnut (where mugwort Art v 3 can be a marker).<sup>14,15</sup> Primary sensitization may result from exposure through the oral route, although skin contact may also lead to allergic reactions. This type of allergy is common in the Mediterranean, but not unheard of in other parts of the world. Peach is a typical primary sensitizer.<sup>10</sup> The symptoms may vary from mild oral allergy syndrome (OAS) to life-threatening anaphylactic reaction, even in a single patient.<sup>9,11</sup> The concentration of LTP differs in fruits and vegetables and increases with storage conditions and in certain cultivars.<sup>13</sup>

### A case study

Here, we present the case of a 27-year-old male admitted to the hospital with recurrent anaphylactic reactions of unknown cause.

The first allergic reaction appeared in summer 2012; the patient ate a seafood salad with a mixture of vegetables and then went for a fast walk, during which time he experienced swelling of the nose, cheeks, eyelids and tongue, tearing, rhinorrhea and tachycardia. The symptoms retreated after the administration of steroids and antihistamines.

On 31<sup>st</sup> October 2013, the patient ate fried chicken in a mixture of spices, with a tomato and cucumber salad. Immediately after ingestion he suffered an incident of dyspnea, with swelling of the face and severe pruritic urticaria on his back and upper limbs. In the emergency room, he received steroids and antihistamines with good clinical effect.

On 14<sup>th</sup> October 2014, the patient ate a homemade dish with pork and eggplant, and drank one beer. Initially, he experienced shortness of breath, and swelling of the face, lips and tongue, which was followed by hypotension, tachycardia of 140/min and a sudden loss of consciousness. He was given epinephrine, crystalloid fluids, steroids and antihistamines, was hospitalized and then discharged with a recommendation to use adrenaline in an auto-injector in the case of anaphylactic reaction.

During the diagnostic pathway, skin prick tests (SPTs) were performed with common inhalant and food allergens (Allergopharma, Nexter); also, prick by prick skin tests were undertaken with selected foods (raw and cooked eggplant pulp and peel, shrimp, banana, scallops, crab, beer, lettuce, tomato, cucumber, chicken meat, pork). The concentrations of IgE against selected food allergens was measured using the ImmunoCap system and the levels of IgE specific to allergen components was established using ImmunoCap ISAC; a value  $\geq 0.35$  kU/l was considered positive, in accordance with practice commonly accepted in other studies.<sup>16</sup>

The patient had a positive (interpretation according to The Global Allergy and Asthma European Network (GA<sup>2</sup>LEN))<sup>17</sup> SPT to allergens of grass and cat dander, but negative results for

birch, alder, hazel, weeds, dust mites, molds, and dog dander. Food SPTs were positive to peach, but negative to apple, orange, strawberry, banana, carrot, tomato, celery, potato, hazelnut, peanut, wheat flour, rye flour, rice, soybean, egg, cod, cocoa, and pork.

Results of the prick by prick tests with fresh and cooked eggplant were positive - raw eggplant peel 30/30 mm, pulp 10/10 mm, cooked eggplant peel 7/8 mm, pulp 4/4mm (histamine 4/4mm, control 0/0 mm) and negative with other tested native allergens. Specific IgE concentration was elevated against grass mix (Orchard-, Meadow Fescue, Perennial Rye-, Timothy-, Bluegrass) - 1.63 IU/ml and cat - 0.96 IU/ml. In Poland, it is not possible to estimate IgE to eggplant due to a lack of allergen extract.

The results of ImmunoCap ISAC are displayed in **Table 1**. In ImmunoCap ISAC, there are no allergen components of eggplant available.

**Table 1. ImmunoCap ISAC results, only positive results acknowledged**

Allergen component	Level of asIgE (ISU-E)	Allergen source
rPhl p 1	1.7	Timothy
rCan f 5	1.2	Dog
Fel d 1	9.6	Cat
nJug r 3	0.5	Walnut (LTP)
rPru p 3	0.6	Peach (LTP)
rPla a 3	1.3	Plane-tree (LTP)

**Negative results to following allergen components:** nGal d 1, nGal d 2, nGal d 3, nGal d 5, nBos d 4, nBos d 5, nBos d 6, nBos d 8, nBos d lactoferrin, rGad c 1, nPen m 1, nPen m 2, nPen m 4, rAna o 2, rBer e 1, rCor a 1.0401, rCor a 8, nCor a 9, nJug r 1, nJug r 2, nSes i 1, rAra h 1, rAra h 2, rAra h 3, nAra h 6, rAra h 8, rAra h 9, rGly m 4, nGly m 5, nGly m 6, nFag e 2, rTri a 14, rTri a 19.0101, nTri a aA\_TI, nAct d 1, nAct d 2, nAct d 5, rAct d 8, rApi g 1, rMal d 1, rPru p 1, nCyn d 1, rPhl p 2, nPhl p 4, rPhl p 5, rPhl p 6, rPhl p 7, rPhl p 11, rPhl p 12, rAln g 1, rBet v 1, rBet v 2, rBet v 4, rCor a 1.0101, nCry j 1, nCup a 1, nOle e 1, nOle e 7, rOle e 9, rPla a 1, nPla a 2, nAmb a 1, nArt v 1, nArt v 3, rChe a 1, rMer a 1, rPar j 2, rPla l 1, nSal k 1, rCan f 1, rCan f 2, nCan f 3, rEqu c 1, nEqu c 3, nFel d 2, rFel d 4, nMus m 1, rAlt a 1, rAlt a 6, rAsp f 1, rAsp f 3, rAsp f 6, rCla h 8, rBlo t 5, rDer f 1, rDer f 2, nDer p 1, rDer p 2, rDer p 10, rLep d 2, rBla g 1, rBla g 2, rBla g 5, nBla g 7, rApi m 1, nApi m 4, rPol d 5, rVes v 5, rAni s 1, rAni s 3, rHev b 1, rHev b 3, rHev b 5, rHev b 6.01, rHev b 8, nMUXF3

### Discussion

Based on the medical interview and the results of *in vitro* and *in vivo* tests, we established that the patient is strongly allergic to eggplant, grass and cat dander, although it does not explain all of the symptoms. The fourth anaphylactic reaction was clear, with anaphylaxis due to eggplant consumption. All other reactions were related to different kinds of food, in particular vegetables.

The clinical pattern of the disease and low, but still present levels of asIgE (antigen specific immunoglobulin E) directed against LTPs from different plant sources may suggest that this patient suffers from LTP syndrome. It is worth emphasizing the features of this case typical for LTP syndrome – unstable clinical course, role of co-factors (exercise, alcohol) and recurrent symptoms after the consumption of fruits and vegetables from

different sources.

There may be several reasons for low levels of LTPs in our patient. An important factor is the time between exposure to LTPs and an examination of the patients' blood serum. In 2011, Asero et al. found that specific IgE levels are only partially predictive of clinical allergy in LTP allergic patients.<sup>18</sup>

Similar results were published in 2012 by Pascal et al., who also found that there was no correlation between LTP-specific IgE levels and the severity of symptoms. In their research, the main offending foods reported by LTP allergic patients and confirmed by SPTs were peach, lettuce, walnut, hazelnut, peanut and green bean. In 40% of patients, cofactors were necessary to induce symptoms.<sup>19</sup> In the present case, cofactors (exercise and alcohol) played an important role in the development of anaphylaxis.

The pathogenic mechanism of cofactors in food allergy is still unclear. An interesting theory suggests that changes in mucosal permeability induced by exercise, medication or other cofactors can enhance allergen absorption through the mucous membranes, and, as a result, enhances exposure to allergens.<sup>20</sup>

Cases of cross allergy between eggplants and latex allergens were described.<sup>21</sup> In the case of our patient, there were no symptoms related to latex and skin prick tests with latex allergen extracts were negative.

The management of patients allergic to LTP is very important, due to large number of anaphylactic reactions in patients with this type of allergy. In 2014, it was emphasized that in the apple allergic population, LTP is most often involved in the occurrence of generalized symptoms in patients.<sup>22</sup> The current patient was advised to carry adrenalin in an auto-injector after his 3<sup>rd</sup> emergency room visit. It is unfortunately not surprising; there have been researches which state that the majority of patients with anaphylaxis do not receive self-injectable adrenaline to prevent future anaphylactic shock.<sup>23</sup>

Avoidance of sensitizing products is a key part in the management of food allergy. Due to cross-reactivity of nsLTPs, symptoms may appear after the ingestion of fruit and vegetables which previously seemed safe. Patients at risk of anaphylaxis, should carry a rescue set, including adrenaline in an auto-injector. Some patients that are allergic to the LTPs of Rosaceae fruits (around 1/3) may tolerate the pulp of these fruits. Unfortunately, reactions can still be observed when a cofactor is associated. Therefore, as a general recommendation, patients should avoid peeled fruits as well.<sup>19</sup>

In 2007, Asero et al. searched for safe plant-derived foods for LTP-allergic patients. He came to the conclusion that carrot, potato, banana and melon seem safe.<sup>24</sup>

The future for LTP syndrome patients definitely involves a specific immunotherapy developed according to the patient-specific sensitivity profile. There are some interesting cases showing the efficiency of this treatment, but there are no commercially available immunotherapies for these patients.<sup>25</sup>

Knowledge of the clinical pattern of allergy may help patients to understand their disease and prevent life-threatening anaphylactic reactions.

## Conclusion

The described patient suffers from a life threatening food allergy. Eggplant allergy, which is very rare in Europe, was confirmed by prick by prick tests. The patient was advised to carry adrenaline in an auto-injector, as well as steroids and antihistamines in case of an anaphylactic reaction.

The clinical pattern of the disease and low, but still present levels of asIgE directed against LTPs from different plant sources, may suggest that this patient suffers from LTP syndrome.

## List of abbreviations

Lipid transfer proteins – LTPs  
nsLTP – non-specific LTS  
Skin prick test – SPT  
Oral allergy syndrome - OAS  
Antigen specific immunoglobulin E - asIgE  
Component resolved diagnosis - CRD

## Competing Interests

The authors declare that they have no competing interests.

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## Authors' Contributions

Natalia Ukleja-Sokołowska - interviewed the patient, performed skin prick tests with native allergens, obtained patient permission and drafted the manuscript.

Ewa Gawrońska-Ukleja - designed and coordinated the study, and reviewed the manuscript

Magdalena Żbikowska-Gotz - performed the immunoassays.

Łukasz Sokołowski - reviewed the manuscript, drafted necessary corrections

Zbigniew Bartuzi - reviewed the manuscript, study design and patient diagnosis.

All authors read and approved the final manuscript.

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