

CONCISE COMMUNICATION



Lipid transfer protein syndrome due to wild grape juice and various vegetables: A life-threatening food allergen

Miho Hanada | Michiyo Nakagawa | Akemi Hamabata | Hiroo Amano

Department of Dermatology, Iwate Medical University School of Medicine, Shiwa-gun, Japan

Correspondence

Miho Hanada and Hiroo Amano, Department of Dermatology, Iwate Medical University, 2-1-1 Idaidori, Yahaba-cho, Shiwa-gun, Iwate 028-3695, Japan. Emails: hadacare@yahoo.co.jp; hamano@iwate-med.ac.jp

Abstract

We report a 16-year-old Japanese male with mugwort pollinosis in whom ingestion of wild grape juice and various vegetables caused recurrent general urticaria, abdominal pain, dyspnea, and loss of consciousness. A skin prick test demonstrated positive reactions to a wide variety of both non-heated and heated vegetables and fruits such as wild grape, bell pepper, onion, Chinese cabbage, tomato, eggplant, and broccoli. The serum immunoglobulin E levels (ImmunoCAP ISAC[®]) for Art v 3, Pla a 3, Pru p 3, and Jug r 3, which are lipid transfer protein (LTP) homologs, were positive but those for Bet v 1 and Bet v 2 were negative. We diagnosed the patient as having LTP syndrome, a condition in which additional factors such as exercise, non-steroidal anti-inflammatory drugs, or alcohol may trigger an allergic reaction. Wild grapes contain a large amount of salicylic acid, and in our patient ingestion of wild grape juice led to immediate loss of consciousness in the absence of exercise. This suggests that salicylic acid contained in fruits and vegetables may act as an important cofactor in LTP syndrome. Although sensitization to LTP is rarely reported in Asia, LTP are considered to be potentially life-threatening food allergens, and therefore warrant attention.

KEYWORDS

Art v 3, lipid transfer protein, mugwort pollinosis, salicylic acid, wild grape

1 | INTRODUCTION

Lipid transfer proteins (LTP) are allergens contained in the outer layer of many plants.¹ While some patients with food allergy are sensitized to only one plant-derived substance, most tend to develop allergy to a wide variety of such foods and/or pollens, irrespective of botanical classification. This condition termed LTP syndrome² is considered to be related to primary sensitization to a food LTP allergen in the absence of both pollinosis^{3,4} and a pollen source.^{5,6} While LTP are common causes of food allergy in the Mediterranean area,^{1,2} LTP syndrome is reported only rarely in Asia, where the habit of eating fruits and vegetables with the peel is unusual. Here, we report a case of LTP syndrome due to wild grape juice and various vegetables in a patient with mugwort pollinosis. Clinicians should be aware of LTP syndrome when making differential diagnosis, and take measures to prevent symptoms in patients.

2 | CASE REPORT

A 16-year-old Japanese male was referred to our department because of general urticaria, abdominal pain, and dyspnea that had occurred during exercise 30 min after eating a lunch box containing Chinese cabbage, bell peppers, and onions. Eight months after this first visit, the patient developed general urticaria, abdominal pain, and loss of consciousness immediately after drinking 50 mL of wild grape juice. Anamnesis revealed that he had sometimes experienced pruritic urticaria, sickness, and nausea after eating broccoli, tomato, and eggplant. His medical history included mugwort pollinosis from 13 years of age. The patient's total serum immunoglobulin (Ig)E level was 251 IU/mL, and specific IgE positivity for mugwort (16.7 UA/mL, class 4), ragweed (5.2 UA/mL, class 3), and duckweed (0.6 UA/mL, class 2) was detected, but that for birch, alder, cedar, cypress, and timothy grass was negative. Mugwort pollinosis in this patient was

severe, and there was quite a large amount of mugwort growing near his house. Plane trees also grew naturally in the neighborhood. He actively consumed vegetables and fruits, and especially liked to eat Chinese cabbage, peppers, and tomatoes. He preferred to eat fruits and vegetables without peeling.

A skin prick test (SPT) was performed using the prick-prick method and the patient showed positive reactions to a wide variety of both non-heated and heated vegetables and fruits such as wild grape (Figure 1a), bell pepper (Figure 1b), onion, Chinese cabbage (Figure 1c), tomato (Figure 1d), eggplant, and broccoli. Positive reactions were also elicited by both non-heated and heated sweet pepper (Figure 1b), mizuna green, cabbage, radish, turnip, wasabi, lettuce, peanut, and kidney bean, although the patient did not develop allergic symptoms. Positive reactions were also elicited by mugwort and ragweed, but not by cedar pollen. Mugwort, ragweed, and cedar pollen antigens were obtained from Torii Pharmaceutical.

The serum IgE levels (ImmunoCAP ISAC[®]; Thermo Fisher Scientific) for Art v 3 of mugwort (31.9 ISU-E, class 3), Pla a 3 of plane-tree (1.0 ISU-E, class 2), Pru p 3 of peach (2.0 ISU-E, class 2), and Jug r 3 of walnut (0.5 ISU-E, class 1) which are LTP homologs were positive, but those for Bet v 1, Bet v 2, and Art v 1 were negative.

Based on these results, we diagnosed the patient as having LTP syndrome. This case showed a number of features that are typical of LTP syndrome, namely an unstable clinical course, the role of cofactors, and recurrent symptoms after consumption of fruits and vegetables from different sources. SPT showed positive reaction to both non-heated and heated vegetables and fruits, which support the diagnosis of LTP syndrome.

We deduced that Art v 3 was the primary sensitizer for mugwort pollen-related food allergies in this case.

We advised the patient to refrain from eating any processed or unprocessed foods that may have caused systemic reactions in the past, especially wild grape, bell pepper, onion, Chinese cabbage, tomato, eggplant, and broccoli.

3 | DISCUSSION

Fruit and vegetable allergy is the most prevalent form of food allergy in adolescents and adults. Pollen food allergy syndrome and LTP syndrome tend to be overlooked as causes of such systemic allergic reactions.¹ In regions where there is high peach consumption, such as the Mediterranean region, primary sensitization to the peach LTP Pru p 3 may be causative.^{3,4} In China, mugwort pollen antigen Art v 3 may underlie LTP.⁵ In Japan, large amounts of airborne mugwort pollen are present from late summer to autumn. In the present case, mugwort pollen may have been related to the patient's food allergies.

ImmunoCAP ISAC was useful for diagnosis and a closer examination of allergen components. In this case, peach antigen-specific IgE (ImmunoCAP) and peach SPT were negative, but Pru p 3 was positive. Pru p 3 may therefore represent a potential risk factor for development of peach allergy.

Lipid transfer proteins are proteins belonging to the prolamin family, responsible for transport of 6–13-kDa lipid. The amino acid sequences of LTP have high homology in various plants, and various degrees of cross-reactivity among plants. Foods triggering LTP syndrome.^{1–6} Dietary advice recommends avoiding foods that cause systemic reactions even when heated or processed.

The pathogenic role of cofactors in food allergy is still unclear. One interesting theory suggests that changes in mucosal permeability induced by exercise, fasting, non-steroidal anti-inflammatory drugs and alcohol can enhance allergen absorption through the mucous membranes, thus enhancing exposure to allergens. Since beverages are absorbed quickly through the mucous membrane and wild grapes contain a large amount of salicylic acid, wild grape juice led to immediate loss of consciousness in the absence of exercise in our patient. This suggests that salicylic acid contained in fruits and vegetables may act as an important cofactor for LTP syndrome. Salicylic acid is abundant in strawberries, tomatoes, oranges, and pineapples as well as grapes.⁷ Patients should therefore avoid beverages made from trigger foods containing both LTP and salicylic acid. Our patient will need to be careful to exclude these items from his diet in the

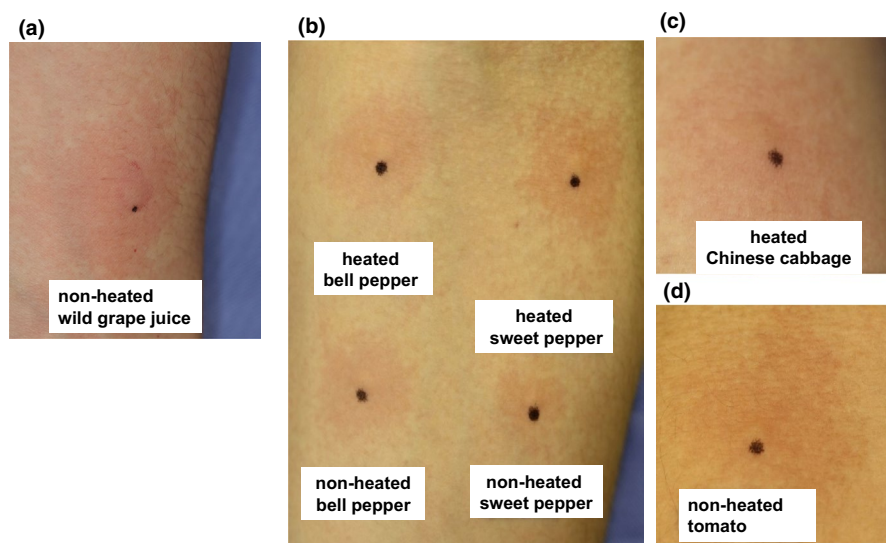


FIGURE 1 (a) Wild grape juice elicited a positive skin prick test (SPT) response. (b) Both heated and non-heated bell pepper and sweet pepper elicited positive SPT reactions. (c) Heated Chinese cabbage elicited a positive SPT response. (d) Non-heated tomato elicited a positive SPT response

future. The natural history of LTP has not been reported, but most reports suggest that relapse was decreased by following a diet.

The cause of the geographic bias of LTP syndrome is still unknown, but people living in Asia prefer to eat fruits and vegetables after peeling. In Europe and the USA, where a lot of fruits, dried fruits, and nuts are consumed, people may become easily sensitized to LTP. However, in Japan, it is customary to peel and eat fruits in view of concern about texture and residual pesticides, so this may explain the relatively few reports of LTP syndrome. No genetic involvement has been reported.

Collectively, although sensitization to LTP is rarely reported in Asia, LTP are considered to be potentially life-threatening food allergens, and therefore warrant attention.

CONFLICT OF INTEREST

None declared.

ORCID

Miho Hanada  <https://orcid.org/0000-0001-6885-3657>

Michiyo Nakagawa  <https://orcid.org/0000-0003-4569-2453>

REFERENCES

1. Asero R, Piantanida M, Pinter E, Pravettoni V. The clinical relevance of lipid transfer protein. *Clin Exp Allergy*. 2018;48:6–12.
2. Pascal M, Muñoz-Cano R, Reina Z, Palacín A, Vilella R, Picado C, et al. Lipid transfer protein syndrome: clinical pattern, cofactor effect and profile of molecular sensitization to plant-foods and pollens. *Clin Exp Allergy*. 2012;42:1529–39.
3. Pastorello EA, Pravettoni V, Farioli L. Hypersensitivity to mugwort (*Artemisia vulgaris*) in patients with peach allergy is due to a common lipid transfer protein allergen and is often without clinical expression. *J Allergy Clin Immunol*. 2002;110:310–7.
4. Azofra J, Berroa F, Gastaminza G. Lipid transfer protein syndrome in a Non-Mediterranean area. *Int Arch Allergy Immunol*. 2016;169:181–8.
5. Deng S, Yin J. Mugwort pollen-related food allergy: Lipid transfer protein sensitization and correlation with the severity of allergic reactions in a Chinese population. *Allergy Asthma Immunol Res*. 2019;11:116–28.
6. Lombardero M, García-Sellés FJ, Polo F. Prevalence of sensitization to *Artemisia* allergens Art v 1, Art v 3 and Art v 60 kDa. Cross-reactivity among Art v 3 and other relevant lipid-transfer protein allergens. *Clin Exp Allergy*. 2004;34:1415–21.
7. Chiang HL, Venter C, Syue PC, Ku K-L, Wu C-H. Which fruits and vegetables should be excluded from a low-salicylate diet? An analysis of salicylic acid in foodstuffs in Taiwan. *Int Arch Allergy Immunol*. 2018;176:198–204.

How to cite this article: Hanada M, Nakagawa M, Hamabata A, Amano H. Lipid transfer protein syndrome due to wild grape juice and various vegetables: a life-threatening food allergen. *J Dermatol*. 2021;00:1–3. <https://doi.org/10.1111/1346-8138.16010>