

Anaphylaxis to winter melon due to cross-reactivity of sensitization to ragweed pollen

To the Editor:

Melon, watermelon, pumpkin, and zucchini are foods that belong to the Cucurbitaceae family and are causative agents of allergy; most cause oral allergy, whereas some result in systemic symptoms.¹⁻³ In most cases, patients are sensitized to allergenic molecules of pollen and subsequently develop highly cross-reactive sensitization to the causative foods.⁴ Winter melon (*Benincasa hispida*) is a member of the Cucurbitaceae family of plants consumed in Europe, America, Egypt, Australia, and particularly in East Asia. However, no case of anaphylaxis with ingestion of winter melon has been described, nor has any allergen been identified in the fruit.⁵ Here, we report the first case of anaphylaxis after ingestion of winter melon, presumably due to cross-reactive sensitization to ragweed pollen (*Ambrosia artemisiifolia*).

The patient was a 4-year-old boy. He could ingest winter melon and watermelon asymptotically at age 3. At age 4, he ingested miso soup containing winter melon during a kindergarten lunch. After 30 minutes from ingestion of winter melon, he developed swelling of both the eyelids, general urticaria, and dyspnea and was treated by a local clinic physician. One month later, he developed swelling of both the eyelids, cough, and dyspnea after 30 minutes from ingesting miso soup containing winter melon. All foods served in the kindergarten lunch except for winter melon were available for consumption after the two anaphylaxis episodes, and the only common food consumed in the two episodes was winter melon. Additionally, the patient did not consume any winter melon between the two episodes. During the same period in which he had winter melon anaphylaxis, he presented with facial swelling after consuming watermelon.

At age 1, he developed hives after consuming baked eggs; then, he was diagnosed with an egg allergy. At age 4, he could consume processed foods using egg binders. He had not developed atopic dermatitis, allergic rhinitis, or bronchial asthma. He could consume Cucurbitaceae family vegetables (cucumber, pumpkin, and melon), except winter melon and watermelon, without developing symptoms. There were no fields containing plants from the Cucurbitaceae family near his living environment.

The total IgE level was 990 IU/ml. Specific immunoglobulin E (IgE) measurement using the ImmunoCAP (Thermo Fisher Scientific/Phadia AB, Uppsala, Sweden) showed positivity to watermelon

(0.84 kU_A/L), melon (0.20 kU_A/L), Japanese cedar pollen (64.3 kU_A/mL), ragweed pollen (1.11 kU_A/mL), mugwort pollen (0.16 kU_A/mL), orchard grass pollen (0.24 kU_A/mL), and Japanese alder (0.51 kU_A/mL).

Prick-to-prick tests revealed positivity to winter melon pulp, creating a 3-mm wheal, and winter melon peel, creating an 8-mm wheal. The resulting wheal of a skin prick test with the positive control (histamine) was 5 mm and with the negative control (saline) was 1 mm (Figure 1). We diagnosed him with winter melon anaphylaxis due to his prior history of anaphylaxis after ingestion of winter melon on two occasions and his sensitization to winter melon. Because we could diagnose based on a convincing clinical history and sensitization, we did not perform an oral food challenge test for ethical reasons. We complied with the Declaration of Helsinki and obtained approval from Sagami-hara National Hospital Ethics Committee (Approval No.: 2016-064) and written consent from the patient's guardian.

To identify the cause and potential allergens of this reaction, inhibition ELISA and western blotting were performed with winter melon pulp extract, Japanese cedar pollen, and ragweed pollen, which were sensitized by specific IgE measurement, using the patient's serum. Ragweed pollen extract inhibited binding of serum IgE to the solid phase of winter melon using inhibition ELISA, whereas Japanese cedar pollen did not (data not shown). Western blotting assays with extracts of winter melon and ragweed pollen revealed IgE reactivity bands of approximately 23 kDa. No other IgE binding was detected. Furthermore, the approximately 23 kDa band of winter melon was completely inhibited by patient serum pretreated with ragweed pollen (Figure 2).

We report the first case of winter melon allergy presenting with anaphylaxis and have identified the causative 23 kDa protein. The patient could ingest winter melon without symptoms up to 3 years of age, and there was no environmental exposure to the Cucurbitaceae family; therefore, we determined that cross-reactivity related to the 23 kDa protein of ragweed pollen caused the allergy to winter melon. The sensitization rate of ragweed is reported to be 17.5% in Japanese schoolchildren⁶; therefore, it is not uncommon for Japanese children to be sensitized to ragweed.

Several articles have reported systemic allergic reactions due to the Cucurbitaceae family. Gandolfo-Cano et al. reported the case of

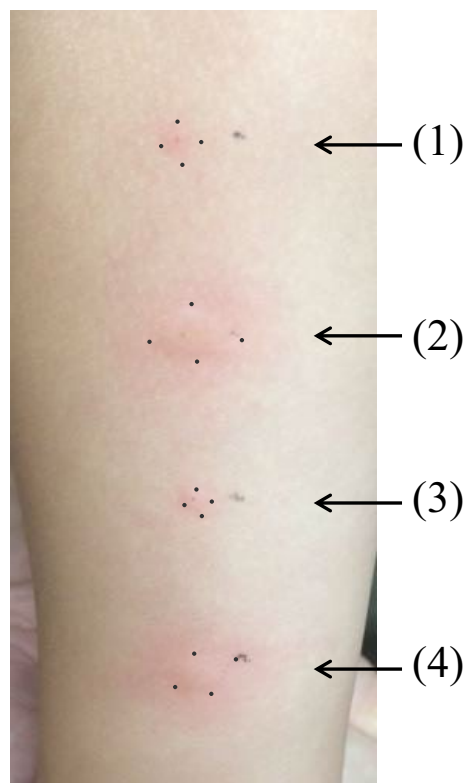


FIGURE 1 Skin prick test on the right forearm. (1) Prick-to-prick test for winter melon pulp, (2) prick-to-prick test for winter melon peel, (3) negative control (saline), (4) positive control (histamine 10 mg/mL). Wheal diameters measured 15 minutes post-skin-prick test

a 15-year-old girl who developed a melon allergy and presented with a 7–8 kDa protein as a lipid transfer protein (LTP) and a 28–29 kDa protein as a thaumatin-like protein (TLP) for the relevant allergens.¹ Other case reports of melon or pumpkin allergy with systemic symptoms showed 8–9 kDa proteins or 14–15 kDa proteins as profilins or LTPs for the allergens.^{2,7,8} In the current study, there were no IgE reactivity bands at 8–9 kDa or 15 kDa; only a 23 kDa protein was revealed. This led to the deduction that TLP was the causative protein. TLP is a very stable protein belonging to the pathogenesis-related protein 5 (PR-5) family and has a molecular weight of 23 kDa.¹ It has also been reported as an allergen in various fruits, such as apple, kiwi, cherry, banana, olive, and the Cucurbitaceae family, and it is thought to be a panallergen responsible for cross-reactivity between pollen and fruit.⁹ It has been suggested that TLP shows thermostability,¹⁰ and patients showed anaphylactic symptoms after ingesting heated winter melon. At present, allergens in ragweed pollen have been identified from Amb a 1 to Amb a 12, but allergens around 23 kDa and TLP have not been identified. Further studies are needed to identify this 23 kDa protein.

In summary, we describe, for the first time, a patient who developed anaphylaxis due to winter melon. We identified a 23 kDa protein as the causative allergen and deduced that its development was due to cross-reactivity with ragweed pollen sensitization.

Sincerely,

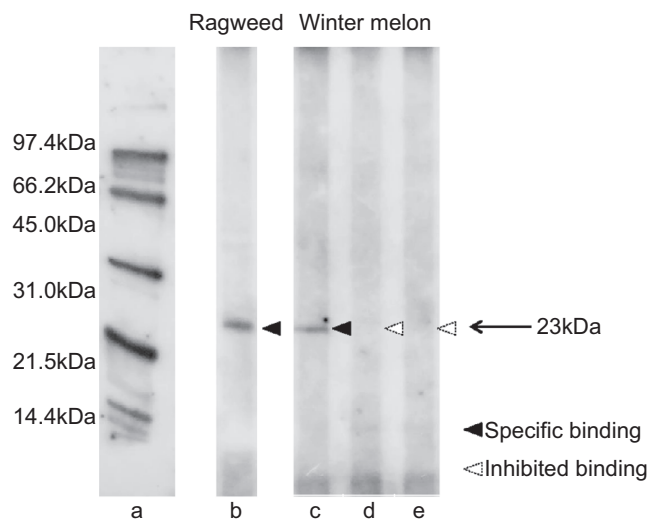


FIGURE 2 Immunoblotting and blotting inhibition analysis of ragweed pollen and winter melon pulp. Transferred ragweed (B) and winter melon pulp (C–E) reacted with the serum-containing phosphate-buffered saline or each extract as inhibitors (1 mg/mL dry weight). (A) Molecular weight standard, (B, C) serum +phosphate-buffered saline, (D) serum +winter melon pulp as an inhibitor, and (E) serum +ragweed pollen as an inhibitor. (A) showed molecular weight standard. Transferred ragweed (B) and winter melon pulp (C–E) reacted with the serum-containing phosphate-buffered saline or each extract as inhibitors (1 mg/mL dry weight)

KEYWORDS

Anaphylaxis, Child, Cucurbitaceae, pollen food allergy syndrome, Ragweed, Thaumatin-like protein, Watermelon, Western blotting, Winter melon

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CONFLICTS OF INTEREST

Motohiro Ebisawa has received speaker honoraria from Mylan EPD. Sakura Sato had received speaker honoraria from Mylan EPD. The other authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTION

Ken-ichi Nagakura contributed to conceptualization (lead); data curation (lead); formal analysis (lead); funding acquisition (supporting); investigation (equal); methodology (supporting); project administration (lead); resources (supporting); software (supporting); supervision (supporting); validation (equal); visualization (equal); writing—original draft (lead); and writing—review and editing (lead).

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PEER REVIEW

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