Anaphylaxis to mango fruit

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Mangifera indica (commonly known as mango) is a species of the flowering plant which bears juicy stone-fruits (drupes) and belongs to the family of Anacardiaceae. The most prominent countries for the cultivation and production of mango fruits are India and China. During recent years, mango fruit has enjoyed increasing popularity in Western Europe and elsewhere. Anaphylaxis induced by mango ingestion has been rarely reported [1–5]. Besides anaphylaxis, also delayed hypersensitivity reactions to mango have been reported anecdotally [2].

We report the case of a 16-year-old girl who presented with anaphylaxis to our emergency department. Thirty minutes after ingestion of a fruit salad (apple, kiwi, mango, grapes), she developed generalized pruritus, facial angioedema, abdominal pain, and dyspnoea. After admission to the hospital, she recovered after treatment with adrenaline, antihistamines, and corticosteroids. She had no history of any allergy, anaphylaxis, or atopy. She also denied previous food allergies or allergy on contact with latex products. Some months later, the patient experienced another event of anaphylaxis after ingestion of mango with pruritus, urticaria, dyspnoea, and vomiting. Allergological workup of this case included skin-prick tests (SPTs) with commercial extracts of aeroallergens to diagnose atopy and possible cross-sensitizations. Histamine hydrochloride (10 mg/ml, Allergopharma, Reinbek, Germany) was used as positive control, and saline solution as negative control (Allergopharma). The results were read after 15 min, and a wheal size ≥ 3 mm was rated positive according to national guidelines. SPT was positive to tree pollen including olive tree, grass, and weed pollen (mugwort, ragweed, plantain). SPTs were found negative for house dust mites, animal and mould allergens. SPT with fresh pistachio was positive, while SPTs with commercial nut extracts were negative (hazelnut, peanut, walnut, Brazil nut, and almond). Serum analysis for total immunoglobulin (Ig) E was 453 kU/l. Specific IgE to mango was found to be 3.17 kU_A/l, apple 1.3 kU_A/l, kiwi 2.4 kU_A/l, and latex 2.68 kU_A/l. Negative results were obtained for pistachio nut, grapes, and the birch major allergen Bet v1. Extended blood testing by chip technology (ISAC, Thermo Scientific, Uppsala, Sweden) revealed positive Art v1 (12.0 ISU-E), Art v3 (0.4 ISU-E), Phl p1 (18.0 ISU-E), Hev b8 (10.0 ISU-E) and positive profilins (Table 1). To better classify the relevance of the results, an inhibition test with fresh mango fruit was performed as described previously [2]. Cross-reactivity to Art v1, Bet v2 and Hev b8 could be confirmed (Table 2). After finalization of blood and skin tests, the patient underwent single-blinded placebo-controlled food challenge tests in our department. A maximum challenge with 16.7 g of pistachio nuts (cumulative dose 24.8 g) was tolerated without any reaction. On the next day, after ingestion of a dose of 85.0 g of mango fruit (cumulative dose 151.0 g) the girl developed urticaria, facial angioedema, and dyspnoea. The symptoms diminished after administration of intravenous prednisolone and antihistamines. In conclusion, we diagnosed an isolated mango fruit allergy.

Besides genuine allergy, various cross-sensitizations may be responsible for a rare mango fruit allergy. Based on botanical similarities of the family of Anacardiaceae, cross-reactivity to latex (formerly described as "latex-fruit syndrome"), profilins and other pan-allergens, and cross-reactivity to birch and/or mugwort allergens need to be considered and evaluated:

1. Earlier inhibition tests demonstrated cross-reactivity between mango fruits, mugwort, and birch pollen, mediated by Bet v1 and/or Art v1 [3]. In our case presented here, sIgE to Bet v1 was negative and therefore, we hypothesized a cross-reaction of a primary mugwort sensitization to mango fruit mediated by the defensin Art v1, and/or by the non-specific lipid transfer protein Art v3 [2]. Other case reports supported cross-reactivity to mugwort in mango allergy as well [4, 6], and this is the most probable cause of the mango fruit allergy in our patient.

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Table 1. ImmunoCAP ISAC results of our patient. All positive results are depicted of the 112 allergens being routinely assessed. The data of this semi-quantitative test are scaled in ISAC Standardized Units (ISU-E), ranging from 0.3 to 100 ISU-E. ISU-E < 0.3 were assessed as negative

Allergen source	Allergen component	ISU-E
Timothy grass	Phl p1	18.0 ISU-E
	Phl p4	6.5 ISU-E
	Phl p5b	0.9 ISU-E
	Phl p12 (profilin)	1.8 ISU-E
Bermuda grass	Cyn d1	2.0 ISU-E
Mugwort	Art v1	12.0 ISU-E
	Art v3 (nsLTP)	0.4 ISU-E
Birch	Bet v2 (profilin)	9.4 ISU-E
Latex	Hev b8 (profilin)	10.0 ISU-E
Mercury annual	Mer a1 (profilin)	12.0 ISU-E

Table 2. Results of the inhibition test with fresh mango fruit in 1 M NaCl. Allergen components were analysed by ImmunoCAP (kUA/l). The patient's serum was incubated with mango fruit about 24 h

Allergen component	Patient serum + 1 M NaCl	Patient serum + mango fruit
Mango (f91)	0.33 kUA/l	0.01 kUA/l
Art v1 (w231)	2.84 kUA/l	1.70 kUA/l
Bet v2 (t216)	2.55 kUA/l	0.39 kUA/l
Hev b8 (k221)	2.84 kUA/l	0.51 kUA/l
Phl p1/p5 (g213)	4.94 kUA/l	4.55 kUA/l

2. Mango, pistachio, and cashew are botanically related, eatable fruits of the family Anacardiaceae, and serological cross-reactivity is possible [7]. A Dutch analysis with cashew-sensitized children revealed a serological IgE co-sensitization to pistachio nut of 98% [8]. In addition, they described a serological co-sensitization to mango in 21% of their patients. So far, we are not aware of any reports with food challenges in individuals with positive specific IgE to cashew nuts, pistachio nuts, and mango. Therefore, the clinical relevance of this serological co-sensitization remains unclear. Of note, our patient did not react to pistachio nuts in food challenge tests. Since there was no history of cashew allergy, and sIgE to Ana o2 was negative, we saw no need for food challenges with cashew nuts.
3. Cross-reactivity between mango and latex allergens is well-known [6]. Since sIgE to the latex allergens Hev b1, b3, b5, b6.01 were negative, and the patient denied any symptoms on contact with latex products, the mango allergy is very unlikely related to latex sensitization.
4. Sensitization to pan-allergens needs to be considered in this case, although the clinical relevance is still a matter of debate [9]. Recent investigations identified two major allergens in mango, Man i1 and Man i2 [7]. Man i1 (molecular weight of 40 kDa, glyceraldehyde 3-phosphate dehydrogenase) seems to be a relatively ubiquitous allergen. Man i2 has a molecular weight of 30 kDa and is not exactly assigned yet. Man i3 is a profilin allergen with structural similarity to Art v1 [2]. Profilins are ubiquitously distributed pan-allergens which may cause cross-reactions between pollen and food [9]. Additionally, allergens in mango may resemble three recently identified allergens in bananas [7]. Our patient described no allergic reactions to banana. Further, since our patient denied allergic reactions to any other fruit, a relevant allergy to pan-allergens is less likely (none of these allergens were commercially available for sIgE analysis).

In conclusion, cross-reactivity to mugwort seems to be the most probable cause of the mango fruit allergy in our patient, which was reported being associated with severe allergic reactions. Therefore, these patients should be evaluated for allergies especially to other foods such as celery, spices, and melon. A detailed history, skin tests, serological diagnostics, and subsequent food challenge tests are urgently needed for proper diagnosis and counselling, prescription of emergency self-administration drugs including epinephrine, and avoidance rules for the patient.

Conflict of interest

The authors declare no conflict of interest.

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