
Fig and mulberry cross-allergy

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Background: Hypersensitivity reactions to ingestion of figs (*Ficus carica*) and mulberries (*Morus nigra* and *Morus alba*) are considered uncommon and have never been reported as occurring in the same patient.

Objective: To determine whether hypersensitivity to figs and mulberries can induce cross-allergy.

Methods: We describe 3 cases of associated fig and mulberry allergy in 3 patients with multiple sensitizations to food allergens (mostly fruit) and airborne allergens. The presence of specific IgE was investigated by skin prick tests and radioallergen sorbent tests.

Results: The 3 patients had a convincing clinical history of food allergy caused by eating fresh figs, and in all 3 cases clinical and/or laboratory evidence of sensitization to mulberries was also collected.

Conclusions: We reason that *Ficus* and *Morus* are closely related genera of the Moraceae family and speculate that hypersensitivity to figs and mulberries might be associated as the result of allergen cross-reactivity rather than mere coincidence.

Ann Allergy Asthma Immunol. 2003;91:493–495.

INTRODUCTION

Accounts of allergic reactions to figs (*Ficus carica*) in literature have been rare.^{1–3} Even less frequent are the reports dealing with allergy to mulberries (*Morus* spp).^{4,5} To our knowledge, food allergy caused by these 2 kinds of fruit has never been reported to occur in the same patient. Recently, we observed 3 patients who complained of food allergy symptoms in connection with ingestion of fresh figs, and in all 3 cases we also collected clinical and/or laboratory evidence of sensitization to mulberries. Since *Ficus* and *Morus* are 2 closely related genera of the Moraceae family, we sought to determine whether hypersensitivity to figs and mulberries could induce cross-allergy.

CASE REPORTS

Case 1

In early June 2002, a 12-year-old girl with a clinical history of current asthma and rhinitis due to Gramineae pollen and *Olea europaea* pollen reported lip and oropharyngeal angioedema and pruritus a few minutes after eating white mulberries (*Morus alba*). These symptoms subsided spontaneously within a few hours. In summer 2001, she experienced a similar allergic attack after eating the same fruit. Only a few days after the first visit, the patient underwent a further, more severe food adverse reaction after eating fresh figs, which was characterized by shortness of breath, a sense of suffocation, and lip, tongue, and oropharyngeal swelling and pruritus. These symptoms were treated with loratadine (20 mg) and lasted 3 to 4 hours. Successively, the young patient reported several mostly oral allergic reactions, which oc-

curred after eating fruit belonging to the Rosaceae family (cherries, apricots, peach, and apple), sweet fennel (*Foeniculum dulce*), and raw chicory (*Cichorium intybus*). She had never previously experienced food allergy.

Case 2

In June 2002, a 43-year-old, female domestic worker with a clinical history of cypress and *O europaea* pollinosis (mild rhinoconjunctivitis) who had never experienced food allergy before complained of acute generalized urticaria with pruritus, flushing, sensation of heat, conjunctival injection, colic, and clouded sensorium approximately 2 hours after eating fresh figs. The patient was treated in the emergency department with parenteral antihistamines and corticosteroids. Symptoms subsided in approximately 1 hour. A few days earlier, the patient had also experienced colic after ingestion of figs. Furthermore, some weeks before, she had experienced another intensive food allergy reaction after eating peaches. She stated that she had not eaten mulberries since she was a child.

Case 3

A 47-year-old, male cleaner with mild symptoms of perennial allergic rhinitis (attributable to *Dermatophagoides pteronyssinus* sensitization) reported undergoing several episodes of generalized pruritus, acute urticaria, and attacks of severe abdominal pain after eating fresh figs. In many instances, treatment had involved parenteral administration of corticosteroids and antihistamines. Furthermore, he mentioned that similar reactions had occurred on various occasions after eating white mulberries and black mulberries (*Morus nigra*). He also had experienced urticaria after eating peaches, plums, cherries, strawberries, peanuts, and beans.

MATERIALS AND METHODS

Skin prick tests were performed by prick-by-prick technique with fresh and dried figs and mulberries by inserting a Mor-

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Received for publication May 10, 2003.

Accepted for publication in revised form July 11, 2003.

row Brown standardized needle perpendicularly into the skin through a fruit slice 2 mm thick. Commercial extracts were used in skin prick testing for other food and airborne allergens (Stallergenes, Saronno, Italy) and latex (ALK-Abelló, Lainate, Milan). The test results were considered positive when a wheal at least 3 mm greater in diameter than the negative control was observed. The erythema diameter was also measured. Total and specific serum IgE was detected by total IgE and specific IgE reagents (UniCAP; Pharmacia & Upjohn S.p.A, Milan, Italy). Values of specific IgE less than 0.35 kU/L were considered a negative radioallergosorbent test (RAST) result.

RESULTS

Skin Prick Testing

Skin reactivity to the 2 potential food allergens was investigated primarily by the prick-by-prick procedure. The 3 patients tested positive to both kinds of fruit (Table 1). The same procedure proved negative in 5 nonatopic control subjects (data not shown). Commercial extracts of figs and mulberries were not readily available.

Skin prick tests with commercial food and airborne allergens revealed multiple sensitizations in all 3 patients. Specifically, patient 1 tested positive for several food allergens, in particular, hazelnuts, peanuts, beans, peas, soy bean, maize, apple, peach, cherries, melon, tomatoes, potatoes, carrots, and celery. Furthermore, she had a positive skin reaction to Gramineae pollen, *Parietaria judaica*, *O europaea*, *Betula verrucosa*, *Corylus avellana*, *Fagus sylvatica*, and *Dermatophagoides farinae*. Patient 2 displayed positive skin reactions to peanuts, peach, *O europaea*, and *Cupressus arizonica*. Patient 3 tested positive to peanuts, beans, apple, plum, cherries, strawberries, oranges, *O europaea*, *P judaica*, *D pteronyssinus*, and *D farinae*. None of the patients had a positive skin prick test result for latex.

Studies on Serum IgE

Results of particular interest are shown in Table 2. RAST (UniCAP; Pharmacia) failed to detect specific IgE against *F carica* in serum samples from the 3 patients, whereas RAST

Table 2. Specific and Total Serum IgE Levels

	Serum IgE, kU/L		
	Case 1	Case 2	Case 3
<i>Ficus carica</i>	<0.35	<0.35	<0.35
<i>Ficus benjamina</i>	<0.35	<0.35	<0.35
Latex	<0.35	<0.35	<0.35
<i>Betula verrucosa</i>	19.7	<0.35	<0.35
<i>Morus alba</i> (pollen)	0.55	<0.35	<0.35
Total IgE	17.4	806	251

for mulberries could not be performed due to unavailability of the relevant commercial reagent at the time observations were performed. Also, RAST results for *Ficus benjamina* and latex were negative (Table 2). Only patient 1 had a positive RAST result for white mulberry pollen and birch pollen (Table 2).

Regarding other food allergens, patient 1 exhibited a positive RAST result for hazelnuts, peanuts, soy bean, bananas, apple, strawberries, tomatoes, carrots, and celery; patient 2 tested negative for 16 major food allergens, including peanuts and peach; and patient 3 had a positive response for apple, plum, peach, cherries, strawberries, oranges, and lettuce.

DISCUSSION

We report on 3 cases of fig allergy diagnosed on the basis of a convincing clinical history and positive skin test results. (The RAST result for *F carica* remained negative.) Two patients complained of severe abdominal and general symptoms, whereas the third cited only oral and pharyngeal symptoms. Interestingly, after eating mulberries, 2 of these 3 patients reported experiencing symptoms similar to those caused by the ingestion of figs, and all of them showed a positive skin response to black and white mulberries. (RAST was not performed because relevant commercial reagents were not readily available.) It is worth noticing that the only patient who had not experienced allergy symptoms after eating mulberries denied having eaten this fruit for decades.

We are aware that more laboratory work is needed to explain the reason for the negativity in the commercial RAST assay for *F carica*, in contrast to what others have found.^{2,3} In our opinion, this point should be addressed by using specific IgE determination techniques other than RASTs.¹ On the other hand, one should keep in mind that RASTs and other similar in vitro assays are generally considered less sensitive than skin tests.⁶ In any event, in vitro detection of specific IgE (either to figs or mulberries) would open the way to RAST inhibition experiments, which could prove our cross-reactivity hypothesis.

From a more general point of view, the 3 cases were distinctively characterized by multisensitization to fruits, although clinical and laboratory positivity to nuts and airborne allergens, particularly pollen allergens, was also detected. Cross-reactivity between various pollen allergens and plant-derived food allergens has been proposed as the basis for the pollen-food allergy syndrome or oral allergy syndrome.⁷⁻⁹

Table 1. Diameters of Wheals Resulting From Prick-by-Prick Procedure With Figs and Mulberries*

Fruit	Wheal diameter, mm		
	Case 1	Case 2	Case 3
Fig, flesh	4 (12)	13 (32.5)	6.5 (15)
Fig, skin	3.5 (18)	5.5 (21.5)	2.5 (10.5)
Dried fig	ND	5.2 (18)	3 (16.5)
White mulberry	5 (22)	3 (0)	3.5 (10)
Black mulberry	6.5 (15)	3.5 (21)	9.5 (45)
Histamine hydrochloride, 10 mg/mL	5 (24)	4.2 (25)	5 (20)

Abbreviation: ND, not determined

* The diameters of the relevant erythematous reactions are presented in parentheses.

Hypersensitivity to Moraceae fruits might appropriately be considered in the context of this syndrome. One patient had a positive skin prick test result and a positive RAST result for birch pollen, an airborne allergen absent in the environment of residence, which has been reported to cross-react with different food allergens, particularly fruit.^{7,10}

Finally, none of the patients had a clinical history suggestive of sensitization to *F benjamina*, and the RAST results for this airborne allergen were negative. Furthermore, the patients denied symptoms of latex allergy and had negative skin prick test results and RAST results for latex. Both *F benjamina* allergy and latex allergy have been implicated in fig allergy.¹⁻³

We find it intriguing that 2 rather uncommon types of food allergy occurred in the same 3 patients (the only ones found by us with a positive skin prick test result to either figs or mulberries in the last few years). Although we are aware that the evidence we are able to provide is circumstantial, we speculate that these 2 fruits might induce cross-allergy, in consideration of the taxonomic affinity between *F carica* on the one hand and *M nigra* and *M alba* on the other. The prevalence and magnitude of clinical allergy caused by cross-reacting proteins and pan-allergens appear to be on the rise, perhaps reflecting an increased prevalence of atopy and allergen sensitization. Although molecular biology studies have investigated the nature of these allergens, clinical studies are also required to focus on as yet unrecognized food allergens.⁷

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