

Anaphylaxis/angioedema caused by honey ingestion

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ABSTRACT

Honey allergy is a very rare, but serious health condition. In this study, we presented six patients who described systemic allergic reactions after ingestion of honey. Three of the six patients had suffered from anaphylaxis. Honey-specific IgE was measured and skin-prick tests for honey were performed to diagnose honey allergy. The results of honey-specific IgE of all patients were positive. Four patients had high serum-specific IgE for honey bee venom and two of five patients had also experienced anaphylaxis due to bee stings. Skin-prick tests with honey and pollens were positive in five patients. Honey is one of the foods that can cause severe systemic reactions. Specific IgE and skin-prick tests are helpful for the diagnosis of honey allergy.

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Honey allergy is a rare form of food allergy and there are only a few cases reported in the literature.^{1–4} In a study performed on 10,000 adolescents in Turkey only 1 subject was shown to have honey allergy.⁵ None of the 3500 6- to 9-year-old children and none of the 11,816 adults were reported to claim honey allergy in two studies.^{6,7} To our knowledge, five adults and one infant were reported to have honey allergy from Turkey.^{3,8} Although it is a rare condition, it is important because ingested honey can cause reactions varying from cough to anaphylaxis.^{1,8}

Honey is a mixture of flower nectar, pollens, and components from bees.² Various studies have been performed in the literature for the identification of specific antigenic structures of the honey.^{1,2,4} Honey allergy may be caused by the honey itself, to pollens (especially Compositae), or even to bee secretions and some parts of the insect. Also, royal jelly, a secretion of worker honey bee venoms, is reported to cause anaphylaxis and asthma exacerbation.⁹ In the series of Helbling *et al.*,¹ 13 of their patients had sensitivity to pollens and 11 had sensitivity to bee venom and whole bee body extracts.

Because the allergenic part of honey is not well defined, the tools to investigate honey allergy are controversial. Detection of serum-specific IgE level and prick-to-prick skin tests with honey may be helpful. The gold standard test is still a standardized oral provocation test. Some of the patients reported in the literature were diagnosed according to history without further

investigation and some were diagnosed despite negative test results. The uncertainty of the antigenic part of honey may have resulted in negative tests or some reactions caused by honey may be caused by intolerance or non-IgE hypersensitivity.

Here, six cases are reported with systemic reactions after ingestion of honey. The patients were evaluated using skin-prick tests, specific IgE, and oral provocation test.

PATIENTS AND METHODS

Patients who attended our pediatric allergy clinic with a suspected honey allergy between July 2010 and February 2013 were evaluated retrospectively. Detailed medical history was taken from patients and/or parents. The diagnosis of anaphylaxis was defined and classified according to the criteria suggested by the European Academy of Allergology and Clinical Immunology Taskforce on the management of anaphylaxis in childhood.^{10,11} Physical examination was performed. Honey and honey bee venom-specific IgE in serum (Immuno Cap Phadia) were measured. Levels ≥ 0.35 kU/L were considered positive. Skin-prick tests for honey and pollens were performed. The tested allergens by prick test included grass mix (cocksfoot, rye-grass timothy, meadow grass, sweet vernal grass, oat grass, wild oat, meadow fescue, bent grass, Yorkshire fog Bermuda grass, and *Bromus*), pollens of cereal mix (oat, wheat, barley, and maize), weeds (*Plantago*, *Parietaria*, *Artemisia*, *Salsola kali*, *Ambrosia*, Compositae, and Chenopodiaceae), and trees (Fagaceae, plane, Oleaceae, Saliceae, and cypress; Stallergenes, Lyon, France). Patients with chronic or recurrent respiratory symptoms were also tested with mites (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*), molds (*Alternaria*, *Cladosporium*, and *Aspergillus* and cat and dog epithelia (Stallergenes). In all patients prick-to-prick tests with honey were performed for three different

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honey types (mix flower honey, chestnut honey, and thyme honey), which are frequently consumed in our country including eaten by our patients. Positive (histamine) and negative (saline solution) controls were included. The reactions were read after 15 minutes and were considered to be positive if there was a wheal 3 mm greater than the negative control. When appropriate, double-blind, placebo-controlled provocation was performed with honey. Provocation test was not performed for patients who had anaphylaxis after honey ingestion. A written informed consent form was taken from patients and/or caregivers. This protocol is a routine procedure used for evaluation of suspected honey allergy in our allergy clinic.

Oral provocation was performed with mix flower honey and honey essence as placebo. Provocation was started with $\frac{1}{10}$ of a portion of honey or equivalent dose of placebo and the dose was increased every 15 minutes.

Patients with positive oral provocation and when provocation could not be performed, patients with IgE-related symptoms within 1 hour of honey ingestion, and positive prick and/or specific IgE test for honey were accepted as having honey allergy.

RESULTS

Six patients who had reactions after honey ingestion were evaluated. Characteristics of patients are presented in Table 1. The duration between initial reaction and evaluation ranged between 6 weeks and 2 years. All patients had allergic rhinitis symptoms and parents of five patients had asthma and/or allergic rhinitis. The family of one patient was a beekeeper (patient 4). This patient was receiving immunotherapy for bee venom.

One patient reported thyme honey ingestion; type of ingested honey was not recorded for other patients. All patients had suffered from a systemic reaction. Three of them had suffered from anaphylaxis; they had fainting, urticaria, and vomiting within 1 hour after honey ingestion. One patient had urticaria/angioedema and two had itching throat, cough, and angioedema after honey ingestion. Two of the three patients with anaphylaxis had also anaphylaxis due to bee stings.

The results of honey-specific IgE in six patients were positive and five of these also had high serum-specific IgE for honey bee venom. Skin-prick tests could not be performed on one patient because of dermatographism. This patient had a history of anaphylaxis after both honey ingestion and honey bee venom sting. His honey-specific IgE and honey bee venom-specific IgE were positive (patient 3). All five patients tested had positive skin-prick tests with all three types of honey. Also, all tested patients had positive prick test with pollens. Three of five patients were positive for Compositae, one was positive for grass pollen, and one was positive for cereal pollen. Other airborne allergens

were tested for three patients with respiratory symptoms, only one of these patients had cockroach and *D. farinae* sensitization.

Double-blind placebo-controlled oral provocation test was performed on one patient who had declared angioedema and urticaria after honey ingestion. This test could not be performed on other patients because three of our patients had had anaphylaxis and two did not consent for testing. The test was performed with mix flower honey and honey essence as placebo. Provocation was started with $\frac{1}{10}$ of a portion of honey or equivalent dose of placebo and the dose was increased by doubling every 15 minutes. Urticaria and angioedema appeared on the second step; systolic blood pressure was not decreased and there were no any symptoms related to other systems.

All parents/patients were informed about honey allergy and the importance of honey avoidance. Epinephrine autoinjector was prescribed to patients who had anaphylaxis and parents/patients were educated on its use.

DISCUSSION

Allergy due to honey is a serious health problem because it can cause severe systemic allergic reactions. There are limited data about honey allergy in the literature. In this study we present six patients with systemic allergic reactions after honey ingestion. Honey allergy may be caused by the honey itself or many specific materials including pollen proteins (mainly from Compositae plants) and secretions and some body parts of Hymenoptera insects.¹

In the literature, allergy to honey is usually attributed to the pollen content. The pollen content of honey depends on the location and the season when the pollens are collected. The most common pollens responsible for the reactions are assumed to be those of the Compositae family.^{1,12,13} Lombardi *et al.*¹² reported two patients who had honey allergy and sensitivity to mugwort (*Artemisia*). Helbling *et al.*¹ reported that 13 of 22 patients with systemic reaction to honey also had sensitivity to pollens (*Artemisia*, Compositae, grass, and birch pollens). One of the four patients reported by Karakaya *et al.*³ from Turkey had pollen-induced rhinitis. In accordance with the literature, five of our patients had allergic rhinitis and three of them had positive skin test with Compositae pollen, one patient was sensitive to grass pollen, and one patient was sensitive to cereal pollen.

Some studies reported that honey allergy is related to the components of honey bee venom. In the aforementioned study by Helbling *et al.*,¹ 11 of 22 honey-allergic patients also had sensitivity to bee venom and bee whole body extracts. One of the cases reported by Karakaya *et al.* had developed urticaria and angio-

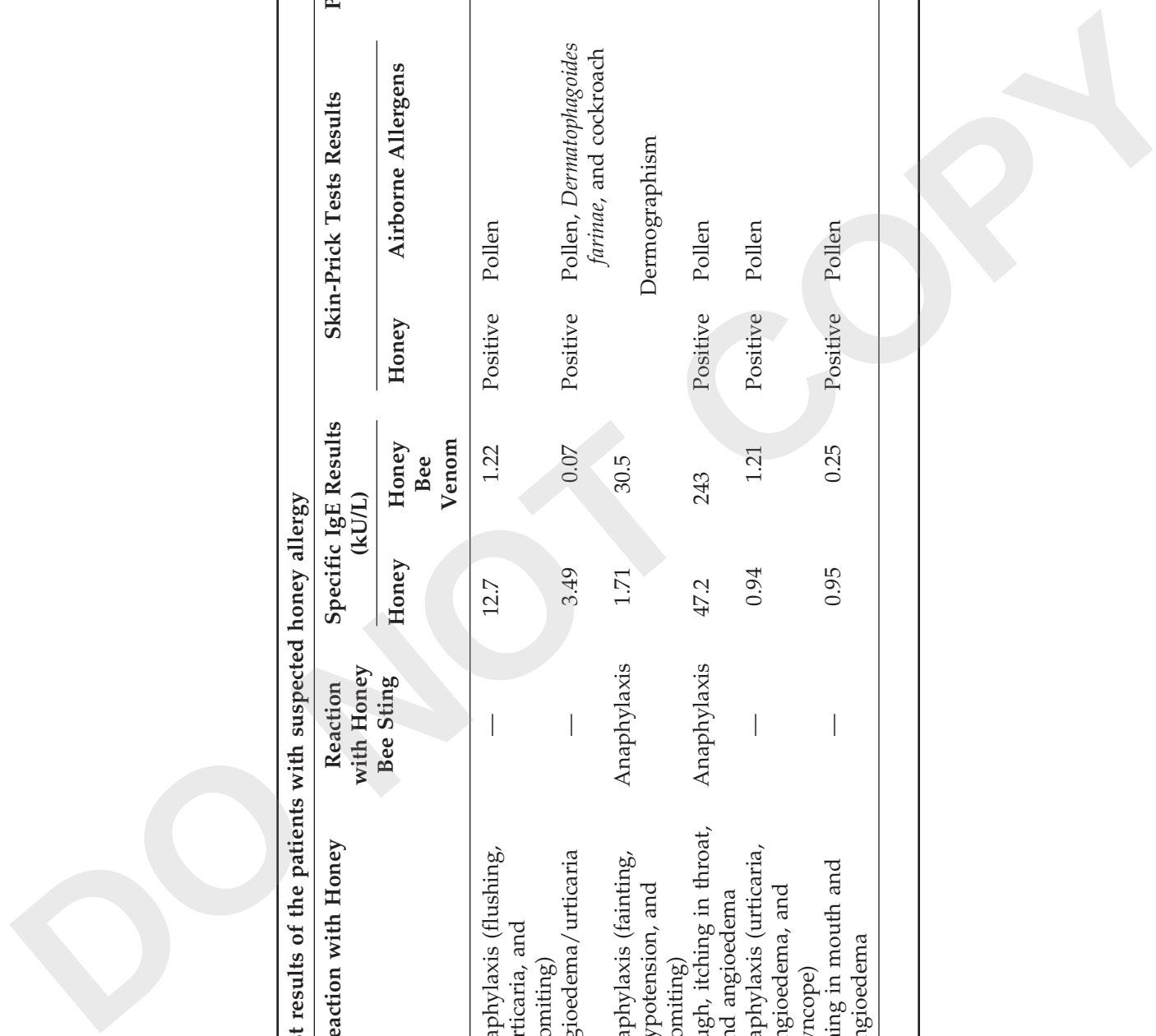


Table 1 Characteristics and test results of the patients with suspected honey allergy

Patient	Age (yr)	Gender	Reaction with Honey	Reaction with Honey Bee Sting	Specific IgE Results (kU/L)		Skin-Prick Tests Results		Provocation
					Honey	Honey Bee Venom	Honey	Airborne Allergens	
1	6.5	M	Anaphylaxis (flushing, urticaria, and vomiting)	—	12.7	1.22	Positive	Pollen	ND
2	12	F	Angioedema/urticaria	—	3.49	0.07	Positive	Pollen, <i>Dermatophagoides farinae</i> , and cockroach	Positive
3	8	M	Anaphylaxis (fainting, hypotension, and vomiting)	Anaphylaxis	1.71	30.5	ND	Dermographism	ND
4	12.5	M	Cough, itching in throat, and angioedema	Anaphylaxis	47.2	243	Positive	Pollen	ND
5	26	F	Anaphylaxis (urticaria, angioedema, and syncope)	—	0.94	1.21	Positive	Pollen	ND
6	29	F	Itching in mouth and angioedema	—	0.95	0.25	Positive	Pollen	ND

ND = not done.

edema after bee sting but their skin tests with bee venom were negative.³ Three of our patients had a history of anaphylaxis after a bee sting and positive specific IgE to hymenoptera venom. Two of these patients were receiving bee venom immunotherapy and their parents were beekeepers. Two of our patients had also positive specific IgE to bee venom but they did not report any reaction with bee sting.

Our study had some limitations. First, we could perform oral provocation test on only one of six patients because three of our patients had had anaphylaxis and two did not consent for testing. During provocation, urticaria occurred but arterial pressure was normal. Monitoring blood pressure during oral provocation is helpful for anaphylactic reactions but hypotension may not be seen in every case.¹⁴ Because history of these patients was compatible with honey allergy and they had evidence of IgE-mediated sensitization (skin-prick test and/or specific IgE positivity), these five patients were diagnosed as honey allergy. Second, we could not gather information about the type of ingested honey. As a matter of fact mix flower honey is the most frequently used type in our country and prick tests with all three types of honey were positive for all five patients (one could not be tested because of dermatographism).

In conclusion, despite being a rarely seen condition honey allergy has serious consequences. Allergic reactions to honey may be related to many factors including pollens, insect body components, and bee venom. For diagnosing honey allergy, skin tests and detection of serum-specific IgE levels are helpful. Patients with honey bee venom allergy and pollen allergy must be screened for honey allergy because of a potential risk.

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