

Mustard allergy. Two anaphylactic reactions to ingestion of mustard sauce

P. Monreal, J. Botey, M. Pena, A. Marin, and J. L. Eserverri

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Two cases of anaphylactic reactions set off by the ingestion of a small amount of mustard sauce are described. Mediation by specific IgE to mustard was determined by skin prick tests and radioimmunoassay, which suggested a type I hypersensitivity mechanism.

Despite the antigenic potency of mustard, a spice that is consumed frequently, very few cases of hypersensitivity from ingestion have been described.

INTRODUCTION

This paper describes two cases of anaphylactic reactions in two adolescents after the ingestion of mustard sauce.

Allergy to mustard has been known for some time. Gervais,¹ Moneret-Vautrin,² and Brostoff³ have emphasized the antigenic potency of this vegetable, a member of the *Cruciferae* family, and have compared the severity of reactions to mustard with those to penicillin.

Commercial mustard sauces contain ground *Brassica* seeds among other ingredients listed below.

- Ground *Brassica nigra* seeds
- Water
- Salt
- Wine vinegar
- Sugar
- Starch
- Wheat flour
- Additives (stabilizers, preserving agents, colorants)
- Spices: tarragon, barberry, truffles, cinnamon, cloves and pepper

Brassica nigra (mustard) is a plant belonging to the *Cruciferae* family⁴ which includes the vegetables below.

- Greens and Forage Crops
 - Cabbage (*Brassica oleracea*)
 - Brussels Sprouts (*B. oleracea*)
 - Cauliflower (*B. oleracea*)
 - Broccoli (*B. oleracea*)
 - Kohlrabi (*B. oleracea*)
 - Rutabaga (*B. campestris*)
 - Turnips (*B. campestris* and *B. rapa*)
 - Radishes (*Raphanus sativus*)
- Oilseeds
 - Rape (*B. napus*)
- Spices
 - Black mustard (*B. nigra*)
 - White mustard (*S. alba*)

In spite of the fact that mustard frequently is eaten on sausages or hamburgers, or masked in sauces such as mayonnaise, cocktail sauce, and meat sauce, there are few bibliographic references to allergic reactions to mustard. Very few cases of anaphylaxis due to ingestion of mustard are described in the medical literature.^{3,4,5,6,7}

It is noteworthy that in all these cases the amount of mustard ingested was very small; in two of the five cases described^{5,6} it came from accidental contamination of the food by cooking utensils. Reactions have been so severe that they required urgent hospital attention, and one of the five patients required admission to an intensive care unit.⁷

An immediate exacerbation of eczema after mustard ingestion,⁸ suggesting Type I hypersensitivity, and contact dermatitis from mustard,^{9,10,11} suggesting Type IV hypersensitivity, have also been reported.

MATERIALS AND METHODS

Clinical History

Patient 1. The first patient was a 17-year-old boy. At 11 years of age, immediately after eating a sausage sandwich with a small amount of mustard sauce, he experienced pruritus and swelling of his lips and tongue, dysphagia, dysphonia, and progressive upper respiratory difficulty as well as intense facial and palpebral edema. He did not have hypotension, bronchospasm, or gastrointestinal symptoms. He received 0.5 mL of adrenaline 1/1000 subcutaneously and methylprednisolone intramuscularly at an emergency room resulting in remission of symptoms. He remained under observation for several hours in the emergency room.

He had eaten mustard on previous occasions and once several years earlier he reported having suffered immediate urticaria and intense facial angioedema.

He had a family history of atopy, a personal history of IgE-dependent asthma since 4 years of age (positive skin tests to molds and grasses) and recurrent urticaria-angioedema since 5 years of age.

Patient 2. The second patient was a 14-year-old girl. After one hour of physical exercise in a closed gymnasium with no reaction afterwards, she ate a sausage sandwich with a small amount of mustard sauce at a friend's house. While she was eating it she had a burning sensation, swell-

From the Allergy and Clinical Immunology Department, Micromethods Laboratory, Valle de Hebron Children's Hospital, Universidad Autónoma, Barcelona, Spain.

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ing of her lips and tongue, and intense facial edema, followed immediately by upper respiratory difficulty, difficulty in swallowing, nausea, and generalized urticaria. She was taken directly to the emergency room, and the acute symptoms remitted after she had received subcutaneous adrenaline and intramuscular methylprednisolone.

She had also eaten mustard several years earlier without any reaction.

One year after this anaphylactic episode, she ingested cocktail sauce in a restaurant and immediately experienced pruritus of the lips and tongue with swelling of the tongue, which remitted spontaneously.

She had a positive family history of atopy and a personal history of non-IgE-dependent asthma since the age of 4 years.

Skin Tests

Immediate hypersensitivity skin tests were performed by the prick test technique with Morrow-Brown lancets.

The patients were tested with the following inhalant allergens: *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Acarus siro*, dog, cat, hamster and horse epithelia, sheep wool, duck and goose feathers, silver thatch, *Alternaria*, *Cladosporium*, *Mucor*, *Penicillium*, elm, hazel-nut, olive, oak, *Phleum pratense*, *Lolium perenne*, *Dactylis glomerata*, *Cynodon dactylon*, *Triticum sativum*, *Parietaria judaica*, *Salsola kali*, *Artemisia vulgaris*, *Platago lanceolata* and *Chenopodium album* (Leti, Dome/Hollister-Stier, Bencard and Pharmacia).

They were also tested with several foods (milk, egg, dried fruits, fish, shellfish, cereals, and fruit) (Aristegui).

Skin tests were performed with mustard extract provided by Aristegui Laboratories (Madrid, Spain) and obtained from ground *Brassica nigra* seeds (concentration 20 mg/mL).

Skin tests for cabbage (20 mg/mL) (Leti) were also applied, but

tests for other vegetables of the *Cruciferae* family were not.

Physiologic serum was used as a negative control, and histamine, 1:100, as a positive control. Codeine phosphate at 9:100 was used to evaluate nonspecific cutaneous hyper-reactivity.

The skin tests were read after 15 minutes and were considered positive only if the largest diameter of the wheal obtained with the antigen was larger than the diameters obtained with histamine.

Skin tests for mustard were also performed on ten control patients, five nonatopic, and five atopic (three sensitized to mites and two to grasses), and in all cases were negative.

Additional Studies

Chest radiographs were obtained as well as spirometry using a Vicatest 5 Mijnhardt spirometer.

The second patient had reported dyspnea after physical exercise and had also experienced an anaphylactic reaction after exercise. Exercise challenge consisting of an 8-minute free run in an indoor hall 20 m long was to be considered positive if it elicited symptoms of asthma or decreases of 20% in the FVC, 15% in the FEV₁, and 30% in the FEF₂₅₋₇₅.

The second patient was also challenged orally to a series of additives that can be found in mustard sauces and in commercial sausages, tartrazine (1 and 10 mg), sodium benzoate (10 and 100 mg), sodium bisulfite (5 and 25 mg), and sodium nitrite (4 and 8 mg). Challenges were undertaken with patients fasting and after they had followed a diet that excluded additives. The tests began with the lowest dose of the additive and if after one hour no symptoms had appeared, the second dose of the additive was administered and the patient was observed for two more hours. Only one additive was administered daily and the next additive was not given until 48 hours later in order to detect possible delayed reactions. Previously, on a different day, patients

were challenged with a placebo (lactose 100 mg).

In Vitro Tests

Further studies included a complete hemogram, blood glucose, renal and hepatic function tests, IgG, IgM, and IgA concentrations (nephelometry).

Total serum IgE was determined by radioimmunoassay (PRIST) (Pharmacia).

Specific IgE was also determined by radioimmunoassay (Phadebas RAST) (Pharmacia) and results were measured in PRU units/mL.

Specific IgE was determined for all the inhalant allergens and foods tested as well as for mustard by RAST. The RAST discs labeled with mustard antigen were provided by Pharmacia Laboratories and were prepared with a mixture of seeds ground from both black (*Brassica nigra*) and white (*Sinapis alba*) mustards.

Given the high risk of an anaphylactic reaction and the fact that the *in vivo* and *in vitro* test results clearly showed an immediate hypersensitivity mechanism, no oral challenges were undertaken with mustard on either patient. Furthermore, both patients had had two immediate or Type I hypersensitivity reactions after ingestion of mustard from another source.

RESULTS

Skin tests for inhalant allergens in the first patient were positive to house dust mites (DPT and DF), grasses (Phleum, Lolium, Dactylis and Triticum), molds (Alternaria) and cat epithelium. Skin tests for foods including cabbage were all negative.

The prick test with mustard extract was positive, eliciting a 15-mm wheal with pseudopods, in comparison to a 5-mm wheal to the histamine control.

Total IgE was 668 U/mL.

Specific IgE levels (RAST) for inhalant allergens were DPT 1 PRU, DF 1 PRU, Triticum 2 PRU, Lol-

ium 7 PRU, *Alternaria* 2 PRU, and cat epithelium 4 PRU.

The specific IgE (RAST) for mustard was 50 PRU (a very high level of specific IgE).

The chest radiograph was normal. Complete blood count, blood chemistries and serum immunoglobulin concentrations were normal. Spirometry revealed small airway obstruction with FVC 89%, FEV₁ 85%, and FEF₂₅₋₇₅ 58% predicted normal.

Skin tests for inhalant allergens in the second patient were negative. Skin tests for foods including cabbage were also negative.

Oral challenges with sodium benzoate (10 and 100 mg), sodium bisulfite (5 and 25 mg), tartrazine (1 and 10 mg), and sodium nitrite (4 and 8 mg) were negative.

Spirometry was normal: FVC 107%, FEV₁ 107% and FEF₂₅₋₇₅ 80% predicted normal. Exercise challenge consisting of an 8-minute free run was negative.

The prick test with mustard extract was positive, eliciting a 10-mm wheal with pseudopods in comparison to a 4-mm wheal to the histamine control.

Total IgE was 166 U/mL.

Specific IgE (RAST) for mites, pollen, molds, epithelia, and foods was negative.

The specific IgE (RAST) for mustard was 43 PRU (a very high level).

The chest radiograph was normal. Complete blood count, blood chemistries, and total serum immunoglobulin concentrations were normal.

Both patients followed a mustard-free diet and also avoided eating the other vegetables in the Cruciferae family.

DISCUSSION

Of the IgE-dependent allergen that induce anaphylaxis, foods fall into fourth place in terms of frequency.⁷ Furthermore, food-induced anaphylaxis has been reported more common in childhood and adolescence.^{3,12} This study describes two

cases of food anaphylaxis in two adolescents.

The most highly allergenic foods are fish, shellfish, milk, egg, nuts, legumes such as peanuts and soybeans, mustard, and fungi.³

Mustard belongs to the Cruciferae family, which is composed of greens (cabbage, cauliflower, brussels sprouts, turnips, radishes, watercress), oilseeds (rape) and spices (white and black mustard).^{4,13}

Mustard, a spice used frequently in the urban environment, can produce violent symptoms of immediate hypersensitivity, especially in subjects with histories of pollinosis.^{7,14} In spite of the antigenic potency of this spice and the fact that its use has increased, reports of reactions after ingestion are still rare. This is probably due to a lack of knowledge of the antigen. Although Gervais¹ in 1976 and Brostoff³ discussed hypersensitivity to mustard and its great antigenic potency, very few cases of anaphylactic reactions due to the ingestion of mustard have been published in the medical literature and almost all of them have appeared within the last 6 years.^{4,6,7} Worthy of note in all these cases is the severity of the reactions and the fact that the amount of mustard was very small. Another common factor is that the patients were usually young.

Hypersensitivity to mustard is due to the protein in this vegetable and not to alyl-sulfocyanide as some authors believed.^{1,2} Leanizbarrutia et al⁴ have shown with a heat-treated mustard extract that sensitization persists even in the absence of alyl-sulfocyanide.

The diagnosis of these immediate hypersensitivity reactions is made by skin tests with mustard extract using the prick test technique and by the detection of the IgE specific to mustard.³ All patients mentioned in the existing literature were studied with these diagnostic methods and double-blind oral challenge was avoided because of the great risk of anaphylaxis.^{4-7,15} Furthermore,

Panconesi's patient⁵ experienced anaphylactic shock after the application of an intradermal skin test with mustard. It is dangerous to apply intradermal skin tests with any type of antigen without having previously performed a prick test, especially when dealing with an antigen as powerful as mustard.

Furthermore, oral challenges should be avoided in patients with histories of anaphylaxis and in patients with histories of reactions to antigens as potent as mustard. Violent anaphylactic reactions to mustard have been described, at times even due to amounts of antigen undetected by the patient since they came from accidental contamination of pizza during its preparation in the restaurant⁵ or from contamination of a hot dog in a sidewalk stand.⁶ Another patient experienced anaphylactic shock requiring admission to an intensive care unit after sucking on a fork stained with a small amount of mustard.⁴

The cross-sensitivity of mustard with other vegetables of the Cruciferae family has also been discussed, but not all authors have recognized it. Leanizbarrutia⁴ did not detect cross-sensitivity with other Cruciferae in either of his two cases. Panconesi⁵ found intradermal skin tests positive to turnips, cabbage, and cauliflower in his patient and Widstrom⁶ found a class 3 RAST to rape in his patient. Blaiss¹⁵ described a case of anaphylactic shock due to ingestion of cabbage in a pollen-sensitive patient; in this case, skin tests were positive for mustard, cauliflower, and broccoli.

Our two patients tolerated the ingestion of raw radishes and cooked cabbage, cauliflower, and watercress with no problem. They had not eaten other Cruciferae. We only studied cabbage by skin tests and results were negative in both patients.

In addition to anaphylaxis, other hypersensitive reactions to mustard have also been described: the immediate exacerbation of eczema

after ingestion of mustard (Type I hypersensitivity)⁸ and two cases of contact dermatitis from mustard (Type IV hypersensitivity) after handling sauces while making a salad⁹ and after the application of a mustard liniment.¹¹

Hypersensitivity reactions induced by other Cruciferae have been described: anaphylaxis due to ingestion of cabbage (Type I),¹⁵ inhalation allergy to turnip pollen (Type I),¹³ allergy to rape pollen (Type I),^{16,17} contact dermatitis from radishes,¹⁷ and contact dermatitis from cauliflower¹⁹ (both Type IV).

Although many articles refer to the cross-sensitivity between pollen and fruit, greens or nuts, and dried fruit (which are unrelated botanically), this possible cross-reactivity is still under discussion and is difficult to determine both *in vivo* and *in vitro*.^{3,4,14,20,21} The best recognized is the cross-sensitivity between grass pollen and cereals, however, others such as between birch pollen and apples have been described³ and the probability of cross-reactivity between grass pollen and mustard¹⁴ has been discussed. Our first patient is allergic to grass pollen and has had immediate anaphylactic reactions after ingesting mustard.

Various mechanisms have been discussed in an attempt to explain this cross sensitivity. Some authors speak of a cross-reactivity due to antigenic similarity or to shared antigens²⁰; others believe it is due to the carbohydrate fraction contained both in the pollen and the food.²¹ In the food, the carbohydrate fraction is destroyed at the gastric level by hydrochloric acid, but it is not destroyed in pollen since it enters the organism by inhalation. This would cause symptoms of pollinosis but not of food allergy. This latter hypothesis would explain the nu-

merous cases of skin sensitivity to mustard that Leanizbarrutia found in patients with pollinosis who had had no symptoms after ingestion.

REFERENCES

1. Gervais P. *Allergologie and Ecologie*. Paris: Masson, 1976:117-8.
2. Moneret-Vautrin D, Andre C. *Immunopathologie de l'allergie alimentaire et des fausses allergies alimentaires*. Paris: Masson, 1983:60.
3. Brostoff J, Challacombe SJ. *Food allergy and intolerance*. London: Bailliere Tindall, 1987:456-66, 945, 972-3.
4. Leanizbarrutia I, Muñoz D, Bernola G, et al. Reacción anafiláctica tras ingesta de salsa de mostaza. *Rev Esp Alerg Inmunol Clin Mayo* 1988;3:79-83.
5. Panconesi E, Sertoli A, Fabri P, Giorgini S, Spallanzani P. Anaphylactic shock from mustard after ingestion of pizza. *Contact Dermatitis* 1980;6:294-5.
6. Widstrom L, Johansson SG. IgE-mediated anaphylaxis from mustard. *Acta Derm Venerol (Stockh)* 1986;66:70-1.
7. Carrillo T, Cuevas M, Muñoz T, Ureña V, Moneo I. Pancreatitis aguda como complicación de anafilaxia por mostaza. *Rev Esp Alergol Inmunol Clin* 1987;2:388-90.
8. Meding B. Immediate hypersensitivity to mustard and rape. *Contact Dermatitis* 1985;13:121-2.
9. Leanizbarrutia I, Muñoz D, Fernandez de Corres L. Cutaneous allergy to mustard. *Contact Dermatitis* 1987;17:262-3.
10. Danaker CJ, White IR. Cutaneous allergy to mustard in a salad maker. *Contact Dermatitis* 1987;6:212-4.
11. Gaul EE. Contact dermatitis from synthetic oil of mustard. *Arch Dermatol* 1964;90:158.
12. Orange RP, Donsky GJ. Anaphylaxis. In: Middleton E Jr, Reed CE, Ellis EF, eds. *Allergy: principles and practice*. St. Louis: Mosby 1983;687-721.
13. Armentia A, Fernandez A, Quintero de Juana A, Salvador de Luna J. Alergia al polen de nabo. *Rev Esp Alerg Inmunol Clin (Febrero)* 1989; 4:37-42.
14. Leanizbarrutia I, Muñoz D, Bernola G, Fernandez E, Audicana M, Fernandez de Corres L. Sensibilizaciones cutáneas a mostaza. Frecuencia e implicación clínica. *Rev Esp Alergol Inmunol Clin* 1988;3: 113-9.
15. Blaiss M, McCants M, Lehrer S. Anaphylaxis to cabbage. Detection of allergens. *Ann Allergy* 1987;58: 248-50.
16. Bugur I, Arner B. Rape pollen allergy. *Scand J Respir Dis* 1978;59: 222-7.
17. Couturier P, Coste P, Mallea M, Soler M. Allergie aux pollens de colza. *Rev Fran Allergol* 1977;17: 51-2.
18. Mitchell J, Jordan WP. Allergic contact dermatitis from radish. *Raphanus sativus*. *Br J Dermatol* 1974;91:183.
19. Van Ketel WG. A cauliflower allergy. *Contact Dermatitis* 1975; 1:324.
20. Hernandez J, Garcia F, Pagan JA, Negro J. Hipersensibilidad inmediata a frutas, verduras y polinosis. *Allergol Immunopathol* 1985;13: 197-201.
21. Eriksson H, Formgren H, Svenonius E. Food hypersensitivity in patients with pollen allergy. *Allergy* 1982;37:437-43.
22. Hannuksela M, Lahti A. Immediate reactions to fruits and vegetables. *Contact Dermatitis* 1977;3:79-84.
23. Aalberse R, Koshte V, Clemens J. Immunoglobulin E antibodies that crossreact with vegetable foods, pollen and Hymenoptera venom. *J Allergy Clin Immunol* 1981;68: 256-364.

Request for reprints should be addressed to:
Dr J Botey
Chief, Allergy and Clinical Immunology
Children's Hospital
Valle de Hebron
Diagonal, 347, Entlo
Barcelona 08037
Spain