

Short communication

Mustard allergy in children

Background: Mustard allergy is not well known. This study aimed to assess its clinical features and other associated allergies, and to define skin prick tests (SPT), specific IgE, and dose response by oral food challenge.

Methods: Our study investigated 36 children with positive mustard SPT. The diagnosis of mustard allergy was based on open or single-blind, placebo-controlled food challenge (SBPCFC). We compared the subjects to 22 controls.

Results: The initial clinical features were atopic dermatitis (51.8%), and urticaria and/or angioedema (37%). Fifteen children were allergic (positive SBPCFC) and 21 children were nonallergic (negative SBPCFC). Symptoms after mustard ingestion started under 3 years of age in 53.3% of the subjects. There was no significant difference in the food allergies and associated inhalant allergen sensitizations between the two groups. In the allergic group, the mean wheal diameter for mustard SPT was 8.8 mm and the median concentration of mustard serum (s) IgE 14.8 kU/l. The mean cumulative reactive dose were 153 mg.

Conclusions: Allergic reactions to mustard started early in life. Clinical symptoms were not severe in children. Mustard should be included in screening tests of food allergy in children.

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The prevalence of food allergy is great. Using double-blind, placebo-controlled food challenges (DBPCFC) to confirm patients' reports, Young et al. (1) found adverse food reaction in 1.4–1.8% of the general population in the UK. In France, the estimated prevalence of food allergy is higher; 2.4–3.8% (3). Food allergy is more frequent in children, particularly before school age, affecting 6–8% of young children (3, 4).

The prevalence of allergy to individual foods varies with the dietary practices of different populations. A recent study performed in France and validated by standard procedures (5) ranks mustard in fourth place in children's food allergies, behind eggs, peanuts, and cow's milk. However, mustard allergy is not well known. Descriptions in the literature of observations of anaphylaxis after ingestion of mustard is proof of the seriousness of this allergy (6–10).

DBPCFC have been regarded as the reference standard for the diagnosis of food allergies. However, we based clinical diagnosis on open or single-blind, placebo-controlled food challenge (SBPCFC) because the strong taste of mustard makes it impossible to perform DBPCFC, and use of lyophilized capsules prevents the first oropharyngeal contact.

In this study, we examined 36 children with positive mustard skin prick test (SPT). The age of onset of allergic reaction, clinical manifestations, and other

associated food allergy and/or inhalant sensitizations were evaluated. We reported data for SPT, specific IgE, and dose response by oral food challenge. Mustard dose response has never been reported, as far as we know. We compared allergic patients (positive SBPCFC) and sensitized patients (negative SBPCFC) to 22 controls.

Material and methods

Study subjects

From April 1997 to April 1999, 36 consecutive patients with positive mustard SPT, selected from the 3600 mustard SPT performed (1%), were enrolled in the study. The mustard SPT is systematically performed on atopic children attending the hospital as outpatients with a clinical history suggesting food allergy. The diagnosis of mustard allergy was based on SBPCFC with positive SPT and/or specific IgE to mustard. The study population consisted of 36 children, 22 boys and 14 girls (sex ratio M/F 1.5), aged 10 months to 15 years (average age 5.5 years). The allergic group comprised 15 children with positive open or SBPCFC. The non-allergic group comprised 21 children with positive SPT and negative SBPCFC (Table 1). We compared all our patients to 22 controls without history of food allergy. We assessed mustard SPT and serum (s) IgE in the control group.

Methods

SPT. Fresh extracts (mustard-seed powder, including *Sinapis alba* and *Brassica juncea*, 1:10 w/v, protein concentration 5 mg/ml) were used for SPT. With this extract, mustard SPT were negative in the control group. SPT were done on the volar side of the forearm with a lancet (Dome Hollister-Stier, Slough, UK, 1-mm tip). We used the prick plus prick method of Dreborg & Foucard (11). We also systematically tested the following allergens (Stallergènes, Fresnes, France): *Dermatophagoides pteronyssinus*, *D. farinae*, *Alternaria alternata*, cat and dog epithelial danders, grass pollens (orchard and timothy grass), cockroach (*Blatta germanica*), latex, cow's milk, egg white, egg yolk, peanut, cod, wheat, and soy. Other SPT were

carried out as appropriate to the clinical context. The results were assessed by relating wheal area to that induced by histamine at 10 mg/ml histamine base. We excluded a dermographic reaction by using a negative control, 50% glycerosaline solution. Only wheals half the average of the positive control or more, and equal to or larger than 3 mm were scored as positive.

Serum IgE (mustard sIgE). Mustard-specific IgE were determined by enzymatic immunoassay (CAP System, Pharmacia, St Quentin en Yvelines, France). For children with IgE concentration measured by another method, we assessed sIgE by the CAP System. A child was considered allergic if the IgE antibody concentration was greater than 3.5 kU/l.

Table 1. Individual data of 36 patients with positive mustard skin prick test

Patient no.	Sex	Age (years)	SPT (mm)	Mustard sIgE kU/l	CRD (mg) SBPCFC	Symptoms SBPCFC	Other food allergies
<i>Group 1</i>							
1	F	7.4	5	11.64	36	U, RC	
2	M	2.8	7	58.08	6	U	Peanut, egg
3	M	8.5	10	*11.72	86	U, RC, OAS	
4	M	1.5	5	5	16	U	Egg
5	M	6.7	10	3.57	1	U	Peanut
6	F	5.10	12	100	16	U	Peanut, egg, kiwi fruit
7	M	8.1	15	19.86	36	A	
8	M	2.4	10	17	936	U	
9	M	2.6	15	9.08	436	U, RC	Peanut
10	M	11	5	1	186	U	Avocado
11	F	2.7	16	> 100	86	U, AD	Peanut, egg, soy, beef
12	F	1.8	12	13.5	6	U	Peanut, egg
13	M	2.6	5	3.38	1	U	Egg
14	M	1.7	3	2.75	436	U	Egg, wheat
15	F	11.4	3	0.89	16	U	
<i>Group 2</i>							
16	M	1.8	4	9.69	N		Peanut, egg, shrimp, hazelnut
17	M	2.5	6	4.36	N		Hazelnut
18	M	9.11	3	0.35	N		
19	M	2.9	3	3.19	N		
20	F	3.11	3	6.81	N		
21	M	12.8	3	3.95	N		Peanut, sesame, hazelnut
22	M	7.9	10	2.78	N		Shrimp, kiwi fruit
23	F	2.8	5	0.35	N		Peanut
24	F	6	3	1.36	N		Peanut
25	M	15	6	26.11	N		Cod
26	M	0.10	4	0.35	N		
27	M	4	8	19.42	N		Peanut, egg
28	M	2.3	5	1.56	N		Peanut, egg
29	F	4.5	11	0.35	N		Peanut
30	M	4	5	2.78	N		Egg, shrimp
31	F	7.2	4	0.58	N		
32	F	7.4	5	0.45	N		
33	M	1.3	15	19.3	N		Peanut, egg, cow's milk
34	F	2.1	10	0.35	N		Egg
35	M	6.4	6	0.35	N		
36	F	14.5	8	0.35	N		Peanut, shrimp

U: generalized urticaria; A: angioedema; RC: rhinoconjunctivitis; AD: eczema; OAS: oral allergy syndrome; CRD: cumulative reactive dose; SBPCFC: single-blind, placebo-controlled food challenge; N: negative; P: positive.

Group 1: allergic patients with positive SBPCFC (patients 1–15).

Group 2: sensitized patients with negative SBPCFC to 936 mg cumulative dose (patients 16–36).

Food challenge. The methods used and the criteria for a positive result in oral food challenge were as described elsewhere (12, 13). We investigated by SBPCFC because it is impossible to mask the taste of mustard, and young children find it difficult to swallow lyophilized capsules. The food suspected was eliminated from the diet for 2 weeks before the challenge. Increasing doses from 1 to 500 mg of mustard powder were masked in stewed apple and administered over 20 min. The dose for progression is as follows: 1, 5, 10, 20, 50, 100, 250, and 500 mg. One challenge contained placebo and the other contained mustard. They were administered 4 h apart, and the number of doses administered was equivalent. It appeared that 500 mg was sufficient to test a child and was higher than the dose habitually consumed. All reactions were scored as to type, time of onset, severity, and duration. Only symptoms developed within a few minutes to 2 h after the last dose of the food challenge were considered for the diagnosis.

Statistical analysis. Student's *t*-test was used for the statistical analysis. We calculated sensitivity, specificity, positive predictive accuracy (PPA), and negative predictive accuracy (NPA) by Goldman's method (14). The sensitivity indicated the true positive and was the number of positive tests achieved with subjects allergic to mustard. The specificity was the number of negative tests among the nonallergic patients.

Results

Our study was performed on 36 children having positive mustard SPT. The 54 initial clinical features of the studied subjects were (sometimes in association) as follows: atopic dermatitis in 28 cases (51.8%); urticaria and/or angioedema in 20 cases (37%); asthma in five cases (9.2%); and, in one case, laryngeal edema with oral allergy syndrome and rhinoconjunctivitis (1.8%). No anaphylaxis was observed. First-degree family atopy was reported for 29 of the children (80.5%). In

the allergic group, symptoms after mustard ingestion started under 3 years of age for eight children (53.3%). Patients included 15 allergic patients and 21 nonallergic patients (Table 1).

The mean wheal diameter for mustard SPT and the median concentration of mustard sIgE are described in Table 2.

Associated food allergies affected 24 of the 36 patients (Table 1). Associated inhalant allergen sensitization affected 24 of the study group of 36: eight from group 1 (four cases of pollinosis), and 16 of the nonallergic children (eight cases of pollinosis). There was no significant difference in the food allergies and associated inhalant allergen sensitizations.

The cumulative reactive dose by open challenge or SBPCFC varied from 1 to 936 mg. No reactions to placebo were observed. The mean cumulative reactive dose was 153 mg. The reactions observed during the SBPCFC were urticaria (14 cases), rhinoconjunctivitis (three cases), angioedema (one case), oral allergy syndrome (one case), and eczema (one case).

The sensitivity of mustard sIgE was 80% (CI 95% 78.20–100), the specificity 66.6% (CI 95% 51.96–85.78), the PPA 63.1% (CI 95% 26.59–78.73), and the NPA 82.3% (CI 95% 88.78–100). The area under the receiver operating characteristic curve (ROC) was 0.891 (SD 0.019). The best PPA was 80% at levels of 19.8 kU/l for specific IgE antibodies. The mustard CAP System never reached a 95% predictive value in the study population.

Discussion

The mustard plant belongs to the Brassicaceae family. Mustard powder is a mixture of two species of Brassicaceae, *Sinapis alba* L. (yellow mustard) and *Brassica juncea* L. (oriental mustard). The major allergen of yellow mustard, Sin a 1, resists heating and degradation by proteolytic enzymes (15, 16). The major allergen in oriental mustard, Bra j 1, has been found to be closely related in structure to Sin a 1 (19). The Brassicaceae family includes green (cabbage, cauliflower, Brussels sprouts, turnips, radishes, and broccoli) and fodder (rape) crops (7). But cross-sensitivity between Brassicaceae species is rare (18). In our study, we noted a single sensitization to radishes, not expressed clinically. Caballero et al. found an association between mugwort pollen hypersensitivity and sensitivity to other edible plants including mustard (19). In our study, we did not observe any particular association with pollen.

Mustard allergy started early in life, usually before the age of 3 years: 8/15 allergic children were under 3 years of age. Mustard is considered a probable hidden allergen in the usual infant diet. This increased frequency of occurrence at early ages could be explained by sensitization *in utero* and also by the presence of

Table 2. Characteristics of patients with positive mustard SPT and controls. Group 1: allergic patients, group 2: sensitized patients, group 3: control patients

	Group 1	Group 2	Controls	P
No. of patients	15	21	22	
Mean age (years)	5	5.6	2.9	
SPT (mm) (mean wheal diameter)	8.8*	5.3*		<i>P</i> <0.05
Mustard sIgE (kU/l)	23.8*	4.9*	0.37*	<i>P</i> <0.001
(median concentration)	(SD 27.2)			
Other food allergies	10	14		NS
Sensitization to inhalant allergen	8	16		NS
Pollinosis	4	8		NS

NS: nonsignificant (*P*>0.05); SPT: skin prick test.

mustard in baby foods. Mustard is also present in commercial foods for toddlers. Contact with mustard is frequent in infancy. Niinimäki et al. report positive SPT to mustard in three infants aged 12–18 months, breast-fed until the age of 11 months, who had never consumed mustard before (20). A sensitization pathway *in utero* or through the mother's milk was suggested. Niinimäki & Hannuksela tested spices in a series of 1120 atopic and 380 nonatopic patients (21). Mustard was tested separately in patients with positive skin test reactions to curry. The mustard prick tests were positive in 23 of the 71 subjects tested (32.4% of cases). They were accompanied by clinical signs in two cases. They included two pediatric observations of erythema and pruritis in the perioral region and the sensation of a lump in the larynx after eating mustard. We did not observe anaphylaxis due to mustard, but a first case of anaphylaxis was described by Panconesi et al. in 1980 after the subject had eaten pizza (6). Since then, there have been several reports (6–10).

Mustard contains irritating substances such as isothiocyanates in *B. nigra*, sinalbin in *S. alba*, and capsaicin, the irritant ingredient of capsicum. Capsaicin also releases substance P, which may cause non-IgE-mediated mast-cell degranulation. Mustard contains irritants that may cause nonimmune reactions mimicking allergic reactions. It is important to base diagnosis on food challenge. In our study, the size of the mustard SPT wheal and the mustard sIgE concentration appear to be significant. The mean average mustard SPT wheal was 8.8 mm in the allergic group. The average concentration of mustard sIgE was 23.8 kU/l in the allergic group. DBPCFC is the reference standard for food allergy diagnosis. It is necessary to define an inert vehicle that masks the taste of mustard if true DBPCFC are to be performed. Protein extracts will probably need to be used, as reported for peanut (22). The dose response has never been reported for mustard, as far as

we know. It was not very high in our patients, the mean estimate being 153 mg. Panconesi et al. (6) and Wildström & Johansson (8) have shown that the amounts of mustard ingested were very small in the cases they observed. Two of the five cases arose from accidental contamination of food by cooking utensils.

The treatment of food allergy is the elimination of the offending food. Having the correct label on a food product is imperative. Unlike peanut (22), immunotherapy has not been tried with mustard.

In conclusion, our results demonstrate the important position mustard allergy occupies in France. At first, we wondered whether the increase in its prevalence was connected with difficulties in diagnosis due to irritation caused by the mustard allergen in SPT or even in oral food challenge. But the increased frequency of its occurrence is indeed real and is probably linked to early consumption in baby foods. As with peanut, sensitization certainly takes place *in utero* or through breastfeeding. The symptoms of this food allergy can be serious, as the instances of anaphylaxis show. The issue of the DBPCFC remains, with the problem of which vehicle to use to mask the mustard and avoid its irritating character. Protein extracts would probably be needed to perform DBPCFC.

These data suggest that screening tests for food allergies should be changed so that mustard is included systematically even before the age of 3 years, as was suggested for peanut a few years ago. The evolution of this food allergy needs to be clarified by further studies. It is difficult to eliminate mustard from the diet, as it is often hidden in food. The labeling of food must be improved. At the moment, the presence of mustard can be indicated simply by the general term "spices".

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