

Asthma and contact urticaria caused by rice in a housewife

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We report the case of an atopic housewife who presented with rhinoconjunctivitis-asthma and contact urticaria from handling rice and other cereals. She tolerated cooked cereals. Both skin prick tests with a rice extract (20% w/v) and a rub test with raw rice gave positive results. Bronchial challenge test with methacholine revealed a PC_{20} of 0.45 mg/ml. The challenge test with raw rice resulted in immediate and late clinical and spirometric responses; pretreatment with DSCG inhibited both responses. The histamine release test (HRT) with rice was positive, and we detected rice-specific IgE antibodies by REIA in the patient's serum. Skin prick tests, HRT, and RAST with a battery of cereals gave positive results. Finally, the rice REIA was inhibited by rice (75%), rye (63%), corn (64%), and wheat (51%) extracts.

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Cereals, plants belonging to the Gramineae family, have been cultivated since ancient times and their flour has long constituted an essential component of human diet. Cereal flours stand preeminently among plant-derived products able to induce occupational diseases (7). Rice (*Oryza sativa*) is commonly regarded as hypoallergenic and is frequently included in diets for allergic patients. There are only two reports in the literature describing immediate hypersensitivity reactions to rice despite its worldwide consumption (13, 23). We describe a housewife with IgE-mediated rhinoconjunctivitis-asthma (RCA) and contact urticaria (CU) caused by rice.

Case report

The patient was a 27-year-old housewife with a history of RCA caused by olive-pollen hypersensitivity. During the last 5 years, she had presented with respiratory and cutaneous symptoms related to exposure to several cereals. On the first occasion, she had suffered nose and eye itching, nasal obstruction, conjunctival reddening, and serial sneezing at a wedding when rice was thrown over the bride and groom. Later, she continued to experience nasal and conjunctival symptoms, as well as dry cough, chest tightness, dyspnea, wheezing, and hand itching and erythema whenever she handled raw rice. Nonetheless, this type of activity never caused her to require emergency treatment. Similar, though less intense,

symptoms occurred when she handled flour from other cereals such as corn or wheat. She also had respiratory symptoms when walking in the vicinity of grainfields or silos. On one occasion, she presented with systemic anaphylaxis within a few minutes of eating "migas" (a typical Spanish dish prepared with undercooked wheat flour), and she was treated with epinephrine, bronchodilators, and pressor agents at an emergency clinic. She regularly consumed cooked rice, bread, and pastries without symptoms.

In the routine clinical study that was performed out of the pollen season, the patient's physical examination, serum biochemistry, and urine analysis were all normal. The blood count showed 400 eosinophils/mm³. Total IgE was 160 kU/l. Paranasal sinus and chest radiographs were normal. Spirometry revealed an FEV₁ of 101% and an FVC of 106% of predicted. An allergic study was performed out of the olive-pollen season.

Material and methods

Cereal flour extracts for in vivo and in vitro tests

Extracts of different cereal flours (rice, wheat, rye, oats, barley, and corn) were prepared by mixing 2 g of flour in 10 ml of PBS (phosphate-buffered saline, pH 7.3) at laboratory temperature. After it had been stirred for 60 min and passed through filter paper, the solution was dialyzed against PBS for 24 h, and afterwards was passed through a 0.22-µm Millipore

filter (Millipore, Bedford, MA, USA) for sterilization. The extracts had a final concentration of 1:5 w/v. The rice extract had a final protein content of 0.52 mg/ml, as determined by Bradford's method (5) (Bio-Rad, Munich, Germany).

Skin prick test (SPT)

SPT were done with the extracts above mentioned. Ten normal persons and 15 atopic subjects served as controls. A battery of commercially available common inhalant and food allergens (Bencard, Worthing, UK), including storage mites (*Lepidoglyphus destructor*, *Acarus siro*) and pollen of trees (*Olea europaea*, *Betula verrucosa*) and weeds (*Ambrosia elatior*, *Artemisia vulgaris*), was also tested. We measured the largest wheal diameter, and considered a reaction to be positive if the wheal size induced by the allergen was 3 mm greater than negative control (PBS). Histamine chlorhydrate 10 mg/ml was used as positive control.

Rub test

The patient's forearm was rubbed with raw rice for 30 s and examined 15 min later. Two atopic subjects were also tested as controls.

Bronchial provocation test (BPT) with methacholine

The methacholine inhalation test was performed according to the method of Cockcroft (8), with some modifications. The aerosolized particles were generated by a continuous pressurized nebulizer, model De Villbis 646, with a fixed output of 0.28 ml/min.

Challenge test with raw rice

Ambulatory peak expiratory flow rates were recorded at 2-h intervals for 3 d before challenge with raw rice. No significant variability was noted. The patient, who had normal basal spirometry values, was placed in a closed room and asked to handle rice for 10 min, mimicking usual household conditions. Pulmonary function measurements of FEV₁ and FVC were performed at base line and at 5, 10, 15, 20, 30, 60, and 120 min after challenge. A positive response was defined as a >20% fall in FEV₁ with respect to base-line values. Peak-flow measurements were recorded thereafter at 2-h intervals for 24 h to detect a possible late response. A positive response was defined as a >25% fall in PEFR from base line (21). The inhibitory effect of disodium cromoglycate (DSCG) on the test was also studied. DSCG (40 mg) was given by inhalation by spinhaler 30 min before the challenge. Three unexposed asthmatic patients with similar nonspecific reactivity

were challenged with raw rice under the same conditions after giving their informed consent.

Histamine release test (HRT)

HRT was performed by an automated fluorometric method according to Siraganian (20) with the modifications previously described (16), with four different fivefold dilutions (1:5, 1:25, 1:125, 1:625) of the cereal flour extracts and *Lolium perenne* and *O. europaea* pollens. A release greater than 10% was considered to be positive.

Specific IgE determination

Specific IgE antibodies against wheat, rye, and barley flour, and *L. perenne* and *O. europaea* pollen, were measured by RAST according to the manufacturer's instructions (Pharmacia Diagnostics AB, Uppsala, Sweden). The determination of specific antirice flour IgE antibodies was performed by reverse enzyme-immunoassay (REIA).

REIA assay

Rice flour extract was conjugated with peroxidase that was activated according to the method of oxidation of Nakane (17), following the procedure previously described (9). M 24 AR microplates (Dynatech Lab, Mountain View, CA, USA) were coated with a monospecific antihuman IgE (Tago, Inc., Burlingame, CA, USA), as previously described (15). A volume of 0.05 ml of serum mixed with an equal volume of PBS-Tw was incubated in each well at 4°C for 18 h. After several washes, 0.2 ml of a dilution of the allergen-enzyme conjugate made in PBS-Tw 25% fetal calf serum, containing 1 µg of peroxidase, was added to each well and shaken for 2 h at room temperature. After 10 alternative washings with PBS-Tw and tap water, the substrate (0.1 ml per well) was added and left for 30 min. The reaction was arrested with 1 M H₂SO₄, and the plates were read on a Titertek Multiskan (Flow Lab, Irvine, UK) at 492 nm. The substrate was composed of 1.2 phenylene diamine (2 mg/ml) citrate phosphate buffer 0.1 M, pH 5, 0.03% H₂O₂. Any result higher than the mean + 2 SD of six control subjects was considered to be positive.

REIA inhibition

REIA inhibition assays for the determination of cross-reacting antigenic determinants were performed as follows: patient's serum was incubated as described. Afterwards, the same amounts of the conjugate were mixed with increasing amounts of the different allergens and added to the wells for 2 h

at room temperature while they were being shaken. The allergens tested were rice, rye, corn, and wheat flour extracts and *L. perenne* pollen.

Results

SPT results with all the cereal flour extracts and with olive pollen were positive in the patient (Table 1). All other allergens tested gave negative results. SPT results were negative in control subjects.

The rub test was positive, producing erythema, wheals, and pruritus on the contact area 5 min after rubbing raw rice on the patient's right forearm. This test was negative in control subjects.

Bronchial challenge with methacholine revealed bronchial hyperreactivity, with a PC_{20} value of 0.45 mg/ml.

The challenge test with raw rice resulted in immediate and late clinical and spirometric responses. After 10 min of handling raw rice, the patient developed serial sneezing; nasal obstruction; pruritus in eye, nose, and face; aqueous rhinorrhea; dry cough; chest tightness; and mild dyspnea. Physical examination disclosed conjunctival erythema, congestive nasal mucosa, and hand urticaria. A 27% decrease in FEV_1 was detected at 5 min; it persisted for 10 min before FEV_1 returned spontaneously to normal values in 30 min (Fig. 1). On follow-up, peak-flow determinations showed a 25% decrease 12 h after challenge, reached a maximal 50% decline at 18 h, and reverted to normal values at 20 h with oral prednisone and inhaled salbutamol treatment. Throughout this period, the patient experienced rhinoconjunctivitis, cough, and chest tightness. Control subjects showed no reaction to the challenge. The same test was negative after prior inhalation of 40 mg

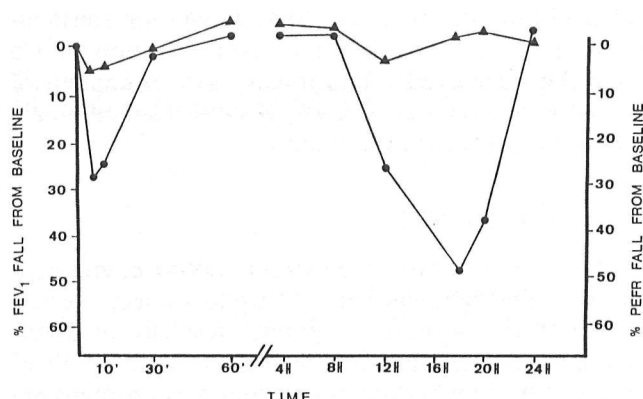


Fig. 1. Challenge test with raw rice (●—●) and same test after inhalation of 40 mg of DSCG (▲—▲).

of DSCG (Fig. 1). Under these conditions, she presented with only mild rhinoconjunctivitis after 2 min of exposure. Therefore, preinhalation of DSCG inhibited the immediate and late responses.

HRT results were positive with all cereal flour extracts and *O. europaea* pollen, and negative with *L. perenne* pollen (Table 1). HRT results in controls were negative.

Specific IgE antibodies against wheat, rye, and barley flour were found in the patient's serum by commercial RAST assays, as shown in Table 1. RAST for *L. perenne* pollen was negative.

The patient showed highly positive rice flour REIA values ($OD_{492\text{ nm}} = 1.320$). In contrast, the control subjects had negative REIA values ($OD_{492\text{ nm}} = 0.188 \pm 0.054$). The rice REIA values were inhibited by the extracts of rice flour (75% of inhibition), rye flour (63%), corn flour (64%), and wheat flour (51%). We could observe 25% inhibition with *L. perenne* pollen.

Discussion

Many types of organic allergens reported to cause IgE-mediated hypersensitivity are of vegetable origin (12). An interesting type of allergic food reaction is that caused by the inhalation of minute particles of foodstuffs in aerosol form. There are reports of housewives exhibiting RCA when handling and peeling potatoes (18, 19), and there are reported cases of asthma caused by the vapor from legumes and Swiss chard in which IgE-mediated mechanisms have been demonstrated (6, 10, 14).

In our patient, the positivity of SPT with the flour extracts, and the positivity of the rub test and the challenge test with raw rice, as well as the demonstration of specific IgE antibodies against rice and the other cereal flours by HRT, RAST, and REIA strongly suggest an IgE-mediated hypersensitivity mechanism. In this case, it is noteworthy that rice was the first and clinically most important cereal

Table 1. Results of skin prick tests, HRT, and RAST with cereal flours and pollens

	SPT*	HRT**	RAST (PRU/ml)
Cereal flours:			
Rice	11 ps	20	#
Wheat	13 ps	14	0.8
Rye	11 ps	11	5.68
Oats	11 ps	14	nd
Barley	15 ps	13	6.93
Corn	15 ps	14	nd
Pollens:			
<i>Olea europaea</i>	7 ps	25	1.09
<i>Lolium perenne</i>	0	2	<0.35
<i>Betula verrucosa</i>	0	nd+	nd
<i>Ambrosia elatior</i>	0	nd	nd
<i>Artemisia vulgaris</i>	0	nd	nd

* Wheal diameter in mm; ps=pseudopods. Histamine chlorhydrate 10 mg/ml=7 mm; negative control (PBS)=0 mm.

** Maximum release (%).

+nd=not done.

Antirice IgE antibodies were measured by REIA (see text).

causing symptoms, in spite of the generally low allergenic quality of this cereal. It is also of interest that the level of allergen exposure in this household environment was not nearly as intense or extended as in the more typical cereal-related occupational cases described in the literature (bakers, pastry cooks) (1, 2, 4). The rarity of our finding is illustrated by the fact that a literature survey revealed a single case of asthma caused by cereal flours in a housewife, probably attributable to wheat (22).

The existence of cross-reactivity among different cereals must be taken into account. RAST-inhibition studies have established that the degree of cross-reactivity is highly dependent on taxonomic proximity (3). This is a clinically important fact, since once patients become sensitized to one cereal, they are likely to develop symptoms upon exposure to others. In the case herein reported, the REIA inhibition tests demonstrated the existence of immunologic cross-reactivity among different cereals. A certain degree of cross-reactivity has been also observed between cereal flour and grass pollen (11). This could not be detected in our study.

Housewives are exposed to numerous potential food allergens that, acting as inhalants, can induce respiratory symptoms in sensitized patients, and could even be the source of the primary sensitization. Their role may be missed, but if we are able to identify them as the causative allergens of the respiratory or cutaneous symptoms, these patients may remain asymptomatic by avoiding exposure to them. We think that diagnosis and prevention in these cases are very important. However, if sensitized patients are unable to avoid very common foods, they should be treated with topical and inhaled DSCG or with other antiallergic drugs (mast cell stabilizers). Our patient has remained asymptomatic for 2 years since the study was performed by avoiding contact with rice, without requiring any treatment.

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