

hypersensitivity reactions after *ingestion* of rice are scarce (4,5). Therefore, rice is commonly regarded as hypoallergenic and is frequently included in diets for allergic patients.

A 27-year-old woman without a history of atopy presented at the allergy unit because of

several episodes of rhinitis with sneezing, itching of the scalp and

A rare case of IgE-mediated food allergy

asthma within minutes after eating meals with seafood and rice. With each episode the symptoms became stronger and the last reaction was accompanied by acute urticaria. Six months before the first reaction she spent several months in the Far East without experiencing any symptoms after consuming this kind of food.

Skin prick tests (SPT) with a battery of common inhalant (ALK, Hørsholm, Denmark) and food allergen extracts (Stallergènes, Antony Cédex, France), including different fishes, seafood and rice were all negative, however, 'prick-prick' and scratch tests were clearly positive with 'native' cooked rice. SPT with rice extract from another manufacturer (Bencard) elicited a positive wheal-and-flare reaction. The total IgE concentration was 55 kU/l, IgE specific to rice (CAP FEIA, Pharmacia) were 4.6 kU/l (CAP class 3), to oat 1.5 kU/l (CAP class 2), to wheat 0.9 kU/l (CAP class 2), to rye 0.7 kU/l (CAP class 2), to corn 0.56 kU/l (CAP class 1), to barley 0.36 kU/l (CAP class 1), to soy, buckwheat, fish and shrimps 0, respectively.

Based on the patient's history, the positive prick-prick tests and presence of IgE antibodies to rice, the diagnosis of food allergy to rice was made. The patient refused an oral provocation. She was advised to avoid further rice consumption and she received an emergency kit consisting of histamines, steroids and epinephrine. Eighteen months later she experienced an allergic reaction with rhinitis and asthma after a vegetarian meal consisting of tofu and rice, although she removed the rice from her plate. The concentration of IgE specific to rice was still increased (10.5 kU/l) (CAP class 3) while no IgE antibodies could be detected to soy. Under elimination diet the patient remained asymptomatic during two years and the level of IgE antibodies to rice dropped to 2.3 kU/l (CAP class 2). During

travel in the USA she ate Chinese noodles without knowing that they were produced from rice. Immediately after ingestion of these noodles she developed generalized itching and dyspnea. After this allergic reaction the patient carefully avoided meals containing rice. Three years after the last episode IgE specific to rice has decreased strikingly to 0.5 kU/l (CAP class 1). The SPT to native cooked rice became negative.

Rice (*Oryza sativa*) belongs with other cultivated cereals to different tribes of the Poaceae family. As previously described (2,4), we also observed the presence of IgE specific to different cereals, but in lower concentrations than to rice. The existence of close allergenic cross-reactivity between different cereal grains has already been demonstrated by RAST inhibition studies (4,6). A 16-kDa rice protein (RP) was identified as a cross-reactive IgE binding structure that fulfilled the criterion of a major allergen (6). Recently, a 33-kDa rice allergen, designated Glb33, was identified as a novel plant glyoxalase I (7). Our patient had no problems when eating other cereals nor she suffered from hay fever to grass pollen. A study from Japan described cross-allergenicity between rice and buckwheat antigens (8), but IgE antibodies to buckwheat were not found in our patient. Mücken et al. (4) found similar allergenic potency of different sorts of rice all containing allergens of low molecular weight (14.4 and 28 kDa) as detected by western blotting.

In conclusion, our patient demonstrated that in a nonatopic person ingested rice can produce IgE-mediated allergic reactions and therefore should be regarded as a potential cause of food allergy. The strict avoidance over years may lead to loss of the sensitization.

*Allergy Unit
Department of Dermatology
University Hospital Zürich
Gloriastrasse 31
CH-8091 Zürich
Switzerland
Fax: +41 1255 4431
E-mail: wuethric@derm.unizh.ch

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References

1. WHITE P. Rice the essential harvest. Natl Geographic 1994;185:48–79.
2. DI LERNIA V, ALBERTINI G, BISIGHINI G. Immunologic contact urticaria syndrome from raw rice. Contact Dermatitis 1992; 27:196.
3. LEZAUN A, IGEA JM, QUIRCE S, CUEVAS M, PARRA F, ALONSO MD. Asthma and contact urticaria caused by rice in a housewife. Allergy 1994;49:92–95.
4. MÜSKEN H, SCHWARZ H, WAHL R, KLEINE-TEBBE, J. Nahrungsmittelallergie auf Reis. Allergologie 1991;14:239–242.
5. ARAI T, TAKAYA T, ITO Y, HAYAKAWA K, TOSHIMA S, SHIBUYA C, NOMURA M, YOSHIMI N, SHIBAYAMA M, YASUDA Y. Bronchial asthma induced by rice. Intern Med 1998;37: 98–101.
6. URISU A, YAMADA K, MASUDA S, KOMADA H, WADA E, KONDO Y, HORIBA F, TSURUTA M, YASAKI T, YAMADA M, TORII S, NAKAMURA R. 16-kilodalton rice protein is one of the major allergens in rice grain extract and responsible for cross-allergenicity between cereal-grains in the Poaceae family. Int Arch Allergy Appl Immunol 1991;96:244–252.
7. USUI Y, NAKASA M, HOTTA H, URISU A, AOKI N, KITAJIMA K, MATSUDA T. A 33-kDa allergen from rice (*Oryza sativa* L. Japonica) – cDNA cloning, expression, and identification as a novel glyoxalase I. J Biol Chem 2002;276:11376–11381.
8. YAMADA K, URISU A, KONDOU Y, WADA E, KOMADA H, INAGAKI Y, YAMADA M, TORII S. Cross-allergenicity between rice and buckwheat antigens and immediate hypersensitive reactions induced by buckwheat ingestion. SO Arerugi 1993;42:1600–1609.

Anaphylaxis to celecoxib

M. Grob*, W.J. Pichler, B. Wüthrich

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● CELECOXIB, a cyclooxygenase-2 inhibitor (Celebrex[®], GD Searle and Co, Skokie, IL), is increasingly being used for the relief of pain and inflammation in patients with osteoarthritis and rheumatoid arthritis. Elsewhere we reported on two patients with a

generalized delayed-type exanthema after celecoxib intake (1). To our knowledge we present here the first patient who developed a celecoxib-induced anaphylaxis.

The past history of a 56-year-old, nonatopic, female patient revealed an episode of rhinitis and itching of the throat after taking indomethacin.

**Probably a
nonallergenic
hypersensitivity to the
cyclooxygenase-2
inhibitor.**

Because of a coxarthrosis the patient was switched to celecoxib. She took more than sixty 200 mg celecoxib capsules within three months without any adverse reaction. After an interruption of two months the patient took again a 200 mg celecoxib capsule together with a multivitamin tablet (Wyciąge Skrezytu Polnego Zwitaminami®). Thirty minutes later, she developed a severe, life-threatening anaphylactic reaction with urticaria, angioedema, bronchospasm and vomiting, followed by syncope. The shock subsided after intravenous therapy with antihistamine, steroids and epinephrine.

Skin scratch tests with celecoxib, other nonsteroidal anti-inflammatory drugs (NSAIDs) and the multivitamin compound were negative. During a first day of oral provocation test (OPT) with 5 mg, 10 mg, and 25 mg celecoxib every hour no symptoms occurred. On the second day, the patient developed urticaria, swelling of the hands and edema of the larynx 40 min after taking 50 mg celecoxib. The plasma histamine (Enzyme Immunoassay, Immunotech, Marseilles, France) was clearly elevated one hour after the adverse reaction (27 nmol/L; normal value <10 nmol/l) and became normal after three hours (3 nmol/l). The serum levels of tryptase (UniCAP, Fluoroenzymeimmunoassay, Pharmacia Diagnostic) remained within the normal range, being 9.02 µg/l resp. 11.8 µg/l (normal value: <13.5 µg/l). No symptoms occurred after an OPT with a multivitamin tablet, acetylsalicylic acid (500 mg), paracetamol (875 mg) and nimesulide (175 mg). The lymphocyte transformation tests (LTT) to celecoxib were clearly positive with stimulation indices of 5.40 at a drug concentration of 10 µg/ml and of 2.90 at concentration of

50 µg/ml (positive SI value >2.00) (2). Other patients with cell-mediated celecoxib allergy were positive in this assay, while three control persons, who tolerated celecoxib, were negative (1, 2).

A potentially life-threatening anaphylactic reaction to celecoxib in our patient was confirmed by an OPT. According to the revised nomenclature for allergy (3), the question arises whether this anaphylactic reaction should be referred to immunologic mechanisms, IgE- or not IgE-mediated, or to a nonallergic anaphylaxis. The adverse reaction described here was shown to be mast cell-mediated by an elevated level of plasma histamine an hour after starting of the anaphylaxis (4). A nonallergic drug hypersensitivity to aspirin (ASS) and other NSAIDs due to disturbance of the prostaglandin metabolism could be excluded by OPTs. However, the negative tryptase levels after the acute reaction and the relatively higher dose (50 mg) of the drug necessary to provoke the symptoms, would suggest a nonallergic hypersensitivity due to unknown mechanisms rather than an IgE-mediated allergic anaphylaxis. On the other hand, an immunologic sensitization to celecoxib could be demonstrated by a positive LTT, although the symptoms were not of the delayed type.

In 14 post-marketing, placebo controlled clinical trials involving 11 008 patients and various dose time schedules, 0.02% of the 6376 patients taking celecoxib were reported to have manifested hypersensitivity reactions, such as an urticaria, an angioedema, or an edema of the larynx. No anaphylactic shock was described (5). According to the package insert celecoxib should not be given to patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs (6). However, it has been recently reported that celecoxib is well tolerated in patients with nonallergic adverse reactions to other NSAIDs and this was also confirmed in our experience (7, 8).

In conclusion, patients who ever experience a hypersensitivity reaction to celecoxib need an exact diagnosis, including an allergy work-up, in order to understand more clearly the underlying pathomechanism. Challenge tests with celecoxib, aspirin and other NSAIDs

should be performed to classify the hypersensitivity type with the goal of preventing anaphylaxis in patients taking celecoxib.

Allergy Unit
University Hospital
Gloriastrasse 31
CH-8091 Zurich
Switzerland
Tel: +41 1255 3083
Fax: +41 1255 4431
E-mail: wuethrich@derm.unizh.ch

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References

1. GROB M, SCHEIDEGGER P, WÜTHRICH B. Allergic skin reaction to celecoxib. *Dermatology* 2000;**201**:383.
2. BRITSCHI M, STEINER UC, SCHMID S, et al. T cell involvement in drug induced acute generalized exanthematous pustulosis. *J Clin Invest* 2001;**107**:1433-1441.
3. JOHANSSON SG, O'B HOURIHANE J, BOUSQUET J, et al. A revised nomenclature for allergy. An EAACI position statement from the EAACI nomenclature task force. *Allergy* 2001;**56**:813-824.
4. LIN RY, SCHWARTZ LB, CURRY A, et al. Histamine and tryptase levels in patients with acute allergic reactions: An emergency department-based study. *J Allergy Clin Immunol* 2000;**106**:65-71.
5. PATTERSON R, BELLO AE, LEFKOWITH J. Immunologic tolerability profile of celecoxib. *Clin Ther* 1999;**21**: 2065-2079.
6. U.S. Prescribing information for Celebrex® (celecoxib capsules). Illinois USA: GD Searle and Company, 2001.
7. DAHLÉN B, SZCZEKLIK A, MURRY J. Celecoxib in patients with asthma and aspirin intolerance. *NEJM* 2001;**344**:142.
8. BALLMER-WEBER BK, WÜTHRICH B. Tolerance to celecoxib in patients with a history of adverse reaction to NSAID [abstract]. *Allergy* 2001;**56**:104-105.