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Case Report

A pediatric case of food-dependent exercise-induced anaphylaxis due to rice bran

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The authors have no financial conflicts of interest.

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ABSTRACT

Food-dependent exercise-induced anaphylaxis (FDEIA) caused by fruits and vegetables is increasing in recent years, but rice-induced FDEIA is rarely reported. The mechanism of FDEIA is unclear, although percutaneous sensitization occurs in some cases. A 14-year-old adolescent came our hospital who had 6 episodes of unknown FDEIA occurring from age 13. He affected atopic dermatitis in infancy, and he had been polishing rice daily to help with housework, and also had occasionally begun to observe urticaria while bathing after eating rice from 5 years old. Antigen-specific immunoglobulin E antibody titers (ImmunoCAP) were 1.35 UAmL for rice, 23.6 UAmL for orchard grass. Oral food challenge and exercise provocation test with polished rice were negative. An oral food challenge with rice bran was also negative, but exercise provocation test induced severe anaphylaxis. IgE immunoblotting with rice bran detected patient-specific bands, as 25-, 35-, 50-, and 60 kDa, and the 25- and 60-kDa bands were heat-resistant. In a suppression test using rice bran, these bands disappeared or diminished. In an inhibition test against orchard grass pollen with rice bran, inhibition was not observed. Conversely, an inhibition test against rice bran with orchard grass pollen, inhibition was observed in a concentration-dependent manner. This is extremely rare case of FDEIA in children, caused by rice bran. Furthermore, it might be induced by percutaneous sensitization. In FDEIA, it is necessary to scrutinize the possibility that rice bran may be the cause even in children.

Keywords: Food allergy; Food-dependent exercise-induced anaphylaxis; Exercise provocation test; Rice bran; Percutaneous sensitization; Pediatrics

INTRODUCTION

Food-dependent exercise-induced anaphylaxis (FDEIA) caused by fruits and vegetables is increasing in recent years, but rice-induced FDEIA is rarely reported [1, 2]. The mechanism of FDEIA is unclear, although percutaneous sensitization occurs in some cases [3]. We report a pediatric case of FDEIA, probably caused by percutaneous sensitization to rice bran. Informed consent was obtained from the patient's parents.

Asia Pacific allergy

CASE REPORT

A 14-year-old Japanese teenager visited Shimane University Hospital after 6 episodes of unknown FDEIA occurring from age 13. Since the age of 5 years, he had been polishing rice daily to help with housework and, occasionally, observed urticaria while bathing after eating rice. Despite being diagnosed with FDEIA for wheat using exercise provocation test a year later (at the age of 15), he experienced anaphylactic reactions (urticaria, wheezing, and dyspnea) iteratively after exercise (mostly outdoor running) without exposure to wheat products. He had atopic dermatitis in infancy and pollinosis caused by Japanese cedar and orchard grass since he was 8 years old, but no bronchial asthma or oral allergy syndrome.

To determine the cause of FDEIA excluding wheat, we focused on rice, carrot, and chicken, which were commonly contained in meals he had eaten just before anaphylaxis. We examined antigen-specific immunoglobulin E (IgE) titers using ImmunoCAP System (Thermo Fisher Scientific; Waltham, MA, USA). The levels were 1.35 U_A/mL for rice, 0.94 U_A/mL for carrot, <0.10 U_A/mL for chicken, 8.21 U_A/mL for wheat, 1.09 U_A/mL for omega5-gliadin and 23.6 U_A/mL for orchard grass at the first visit. Open oral food challenge with polished rice (cooked, 180 g, single dose), carrot (boiled, 50 g, single dose), and chicken (boiled, 50 g, single dose) were negative at the age of 15. Exercise provocation test (treadmill test, the standard Bruce protocol) was negative after ingesting these foods, with and without 300-mg preadministered acetylsalicylic acid. Previous reports showed that rice allergy could be induced by rice bran; therefore, we examined this further [4]. Open oral food challenge with rice bran (70% polished rice, total amount 150 g) was also negative. We performed exercise provocation test involving ingestion of rice bran without premedication with acetylsalicylic acid and observed severe anaphylaxis (urticaria, cough, wheezing, nausea, and hypotension) 15 minutes after exercise. These symptoms were ameliorated by intramuscular injection of adrenaline and antihistamine.

We performed IgE immunoblotting to identify the causative protein. Untreated rice bran was used as the solid phase and reacted with the patient's serum. A healthy subject, who provided written consent, was included as a negative control. We detected patient-specific bands of 25-, 35-, 50-, and 60 kDa (**Fig. 1A**). When heat-treated rice bran (95°C for 25 minutes) was used as the solid phase and reacted with the patient's serum, 25- and 60-kDa bands remained, while 35- and 50-kDa bands disappeared (**Fig. 1B**). In a suppression test using rice bran, these bands disappeared or diminished (**Fig. 1C**). In an inhibition test involving rice bran extract, inhibition was not observed in the solid phase of orchard grass pollen (**Fig. 2A**). Conversely, with orchard grass pollen extract, inhibition was partially observed in the rice bran solid phase in a concentration-dependent manner (**Fig. 2B**).

DISCUSSION

As exercise provocation test for rice was positive with 30% rice bran but negative with polished rice, the patient was diagnosed with FDEIA due to rice bran. Percutaneous sensitization was considered because the patient had been polishing rice and experienced atopic dermatitis for a long term. Inomata et al. [4] reported a case of epicutaneous sensitization woman, who developed rice bran allergy while handling rice bran paste. We estimated that direct cutaneous contact with rice-bran caused sensitization because the patient affected urticaria while bathing after eating rice since 5 years old. Patients with atopic

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Asia Pacific allergy

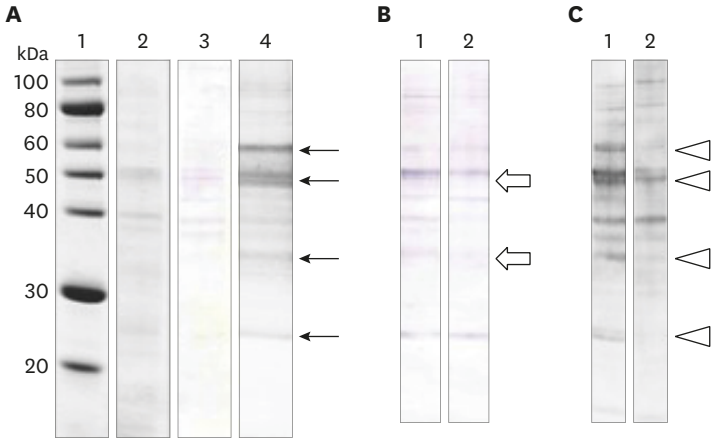

Fig. 1. (A) Immunoglobulin E immunoblotting using raw rice bran (3.5-μg protein/lane). Lane 1 = molecular weight marker, Lane 2 = rice bran extract, Lane 3 = healthy control, Lane 4 = patient's serum. Black arrows correspond to patient-specific bands. (B) Immunoglobulin E immunoblotting using raw and boiled rice bran conjugated with the patient's serum. Lane 1 = raw rice bran, Lane 2 = boiled rice bran (95°C, 25 minutes). White arrows correspond to bands that disappeared after conjugation with boiled rice bran. (C) Immunoglobulin E immunoblotting inhibition assay using raw rice bran. Lane 1 = untreated, Lane 2 = inhibited by raw rice bran. Triangle corresponds to inhibited bands. kDa; kilodalton.

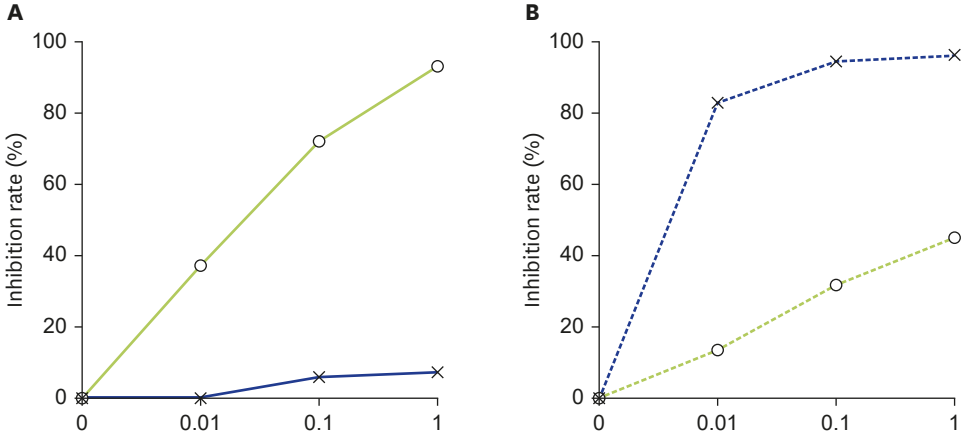

Fig. 2. Inhibition examination by ImmunoCAP. (A) Inhibited by rice bran extract. *X*-axis shows mixture of rice bran extract dilutions and patient's serum at 4:1 ratio. Rice bran extract is composed of 1-g rice bran + 10-mL distilled water and diluted with 0.1 M phosphate buffer solution. *Y*-axis shows inhibition rates. Each rate shows differences between absorbance of uninhibited samples (reacted solid phase and patient's serum only) and absorbance of inhibited by each extract. Solid phases are rice bran (○) and orchard grass (×) . (B) Inhibited by orchard grass extract. *X*-axis shows mixture of orchard grass (*Dactylis*) extract dilutions and patient's serum at 4:1 ratio. Orchard grass extracts were acquired from supernatant from 50-mg crude orchard grass pollen + 1.0 mL 0.1 M phosphate buffer solution after centrifugation (30 minutes, 10,000 g). *Y*-axis shows inhibition rates. Each rate show differences between absorbance of uninhibited samples (reacted solid phase and patient's serum only) and those inhibited by each extract. Solid phases are rice bran (○) and orchard grass (×).

dermatitis have high risk of developing food allergy due to percutaneous sensitization due to skin barrier dysfunction [5]. Togashi et al. [6] also indicated that atopic dermatitis may be a risk factor for percutaneous sensitization in rice bran allergy in a case of 5 years old boy, who raised in his grandparent's house served as family rice shop and might be exposed to rice bran for 1.5 years. In our case, rice proteins of 25-, 35-, 50-, and 60 kDa were the candidate antigens. Alpha-globulin (26 kDa) is a storage protein in the salt-soluble fraction, but there are few reports of it causing food allergy. Glyoxalase I (33 kDa) is a salt-soluble

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protein present in both rice bran and polished rice; however, polished rice did not induce any symptoms [7]. The 52-kDa-globulin, found mainly in rice bran, is unstable when exposed to heat or gastric acid and often induces symptoms like oral allergy syndrome; it is unlikely to cause reactivity in our case because the band disappeared after heat treatment. The 63-kDa-globulin, a member of the cupin superfamily with a heat-stable structure, is more likely to cause immediate hypersensitivity reactions, as seen in this case [8]. Rice is a seed from the genus *Gramineae* (scientific name: *Oryza sativa*) and belongs to the same genus as orchard grass (scientific name: *Dactylis glomerata*). As a result of the suppression test for common reactivity, orchard grass pollen and rice bran have common IgE epitopes. Although rice bran-specific IgE was reactive with this common IgE epitope, orchard grass-specific IgE was not reactive and reacted only with orchard grass-specific IgE epitope. It is unlikely that orchard grass sensitization preceded and was involved in disease onset in our case. We speculate that this is different from pollen-food allergy syndrome.

Despite some reports that rice bran antigen is responsible for rice allergy, polished rice allergy can often be asymptomatic because the content is affected by the rice polishing rate [4, 6]. Therefore, it can delay identification of the cause as seen in this case. In FDEIA, it is necessary to consider rice bran along with other causes. Additionally, health foods and cosmetics may contain rice allergen (rice bran) in daily life, with risk of exposure [9]. After identifying the causative food, it is necessary to avoid these allergens for safety.

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