

Letter

A PATIENT WITH SALMON ROE ALLERGY SHOWING TAXONOMY-UNRELATED CROSS-REACTIVITY WITH SEA URCHIN ROE

In Japan, salmon (*Oncorhynchus keta*; phylum Chordata, family Salmonidae) eggs (salmon roe [SR]) are commonly eaten raw in dishes such as sushi, and the number of patients who develop severe allergies after initial SR intake has been increasing in recent years. In Western countries, one patient developed unexpected anaphylaxis after consuming rainbow trout (*Oncorhynchus mykiss*; family Salmonidae) roe,¹ and another adult developed anaphylactic symptoms after initial SR intake.² On the basis of the induction of allergy by initial SR intake, there is a possibility that SR allergy develops through sensitization due to cross-reactivity with other foods. However, the source of such SR sensitization remains unclear.³

We encountered a patient with allergy to SR who developed a cross-reactive allergic reaction to the eggs of sea urchins (phylum Echinodermata; sea urchin roe [UR]), which are distantly taxonomically related. There have been no previous reports of cross-reactivity between the Chordata and Echinodermata phyla. We confirmed the cross-reactivity between them by inhibition enzyme-linked immunosorbent assay (ELISA) and immunoblotting.

Disclosures: Authors have nothing to disclose.

Funding Sources: This research was supported by a grant from the Ministry of Health, Labour, and Welfare and the Cabinet Office of Japan, 2010.

© 2011 American College of Allergy, Asthma & Immunology.

Published by Elsevier Inc. All rights reserved.

doi:10.1016/j.anai.2011.06.007

The patient first developed SR allergy at 4 years of age. He had previously tolerated chicken eggs and had also eaten fish meat, including salmon and the roe of other kinds of fish (herring and pollock roe), without any reaction. Immediately after first ingesting an SR egg, he became pale, experienced abdominal pain, vomited, and had diarrhea. His SR specific IgE antibody level was subsequently found to be high (91.9 UA/mL) using the ImmunoCAP test (Phadia AB, Uppsala, Sweden). At the age of 10 years, because he wished to eat UR, which is a popular sushi dish, we planned an oral challenge after skin prick tests. The oral challenge was performed without discontinuing the oral administration of pranlukast for his underlying asthma. Because the skin prick test result was positive (wheal diameters: UR extract, 3 mm; 10 mg/mL histamine, 4 mm; and saline, 0 mm), a very small amount (corresponding to 0.1 mg) of UR was orally administered using the open challenge method after preparing for his admission. He developed abdominal pain 15 minutes after the challenge, excreted soft feces, and experienced itching around his eyes. The oral challenge test result was regarded as positive, and the test was terminated. The above symptoms disappeared without any treatment. We subsequently realized that we could have obtained more objective data if we had measured plasma histamine levels.

To examine the cross-reactivity between SR and UR, we performed an inhibition ELISA study with the patient's sera, as described in a previous report.³ Extracts from UR, salmon meat, SR, herring roe, Alaskan pollock roe, and chicken egg yolk were obtained in the previously reported manner.³ Specific IgE to SR and UR almost completely inhibited each other's binding. Interestingly, other kinds of fish roe were not only poor inhibitors of IgE specific

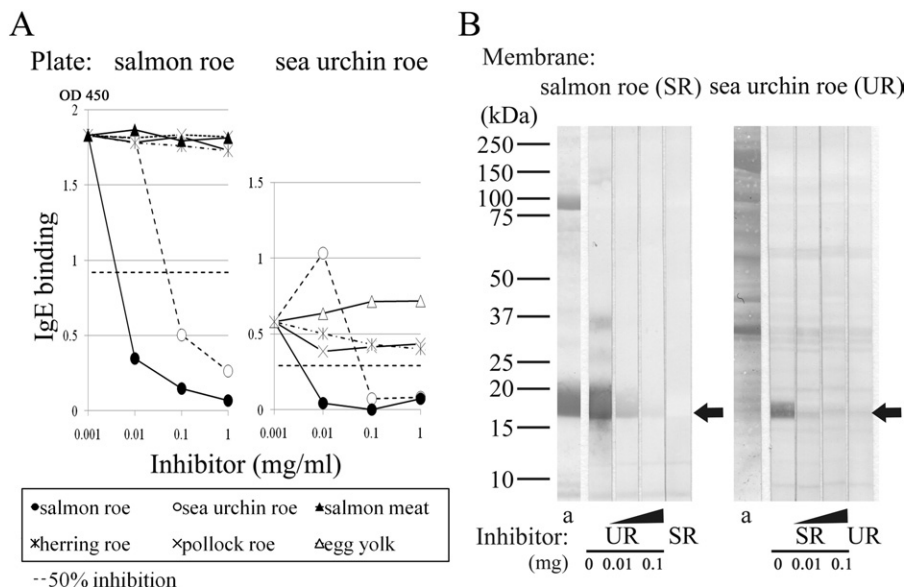


Figure 1. Inhibition assay and immunoblot results. A, Inhibition enzyme-linked immunosorbent assay between salmon roe (SR) and sea urchin roe (UR). Preincubation of the patient's serum with heterogeneous SR or UR extract induced more than 50% inhibition of the IgE specific to each extract. Other kinds of fish roe and chicken yolk did not affect IgE binding to either extract. B, Inhibition immunoblot between SR and UR. IgE specific to low-molecular-weight proteins (arrows) isolated from the 2 extracts mutually inhibited each other. Lane a: Amido black stained.

to UR, to which they were not taxonomically related, but also poor inhibitors of IgE specific to SR, to which they were closely related taxonomically (Figure 1A). This finding suggested that there was no correlation between taxonomy and allergenicity. Then, we attempted to identify the relevant allergen by performing an inhibition immunoblot study. Sodium dodecyl sulfate–polyacrylamide gel electrophoresis was performed in a 4% to 12% NuPAGE Novex Bis-Tris Mini Gel (Invitrogen, Carlsbad, California) under reducing conditions. Immunoblotting of the proteins and the detection of bound serum IgE were performed as previously reported.⁴ Specific IgE to 2 proteins of approximately 18 kDa that were isolated from UR or SR (1 protein was isolated from each roe) mutually inhibited each other (Figure 1B). We performed amino acid analysis of the N-terminal of the 18-kDa UR protein and identified an 18-kDa egg cortical vesicle protein (NP_999641). A search revealed homology with the complement C1q-like protein 4 precursor (ACM08719) of Atlantic salmon (*Salmo salar*) with a Basic Local Alignment Search Tool (BLAST) expected value of 2×10^{-10} . Both proteins belong to the C1q family, and a member of this family has been reported to be localized in mature eggs in the prespawning ovary.⁵ These findings suggest that the homology of these proteins could cause cross-reactivity.

There have been 3 case reports of UR allergy.^{6–8} As allergens, 2 high-molecular-weight proteins (118 kDa⁷ and 160 kDa⁸) have been reported, and the latter was identified as major yolk protein. However, these reports did not mention cross-reactivity. In Figure 1B, the patient's IgE did not react with these proteins. Therefore, the 18-kDa protein was considered to be a novel allergen that displays the unique characteristic of cross-reacting with SR.

This is the first study, to our knowledge, to demonstrate unexpected cross-reactivity between the Echinodermata and Chordata

phyla. It is important to bear in mind that cross-reactivity can occur in taxonomically unrelated species.

YASUTO KONDO, MD, PhD
KENICHI TANAKA, MD
CHISATO INUO, MD
IKUYA TSUGE, MD, PhD
ATSUO URISU, MD, PhD

Department of Pediatrics
Fujita Health University
Toyoake, Aichi, Japan
ykondo@fujita-hu.ac.jp

1. Mäkinen-Kiljunen S, Kiistala R, Varjonen E. Severe reactions from roe without concomitant fish allergy. *Ann Allergy Asthma Immunol.* 2003;91:413–416.
2. Flais MJ, Kim SS, Harris KE, Greenberger PA. Salmon caviar-induced anaphylactic shock. *Allergy Asthma Proc.* 2004;25:233–236.
3. Kondo Y, Kakami M, Koyama H, et al. IgE cross-reactivity between fish roe (salmon, herring and pollock) and chicken egg in patients anaphylactic to salmon roe. *Allergol Int.* 2005;54:317–323.
4. Kondo Y, Tokuda R, Urisu A, Matsuda T. Assessment of cross-reactivity between Japanese cedar (*Cryptomeria japonica*) pollen and tomato fruit extracts by RAST inhibition and immunoblot inhibition. *Clin Exp Allergy.* 2002;32:590–594.
5. Mei J, Chen B, Yue H, Gui JF. Identification of a C1q family member associated with cortical granules and follicular cell apoptosis in *Carassius auratus gibelio*. *Mol Cell Endocrinol.* 2008;289:67–76.
6. Hickey RW. Sea urchin roe (uni) anaphylaxis. *Ann Allergy Asthma Immunol.* 2007;98:493–494.
7. Rodriguez V, Bartolomé B, Armisén M, Vidal C. Food allergy to *Paracentrotus lividus* (sea urchin roe). *Ann Allergy Asthma Immunol.* 2007;98:393–396.
8. Yamasaki A, Higaki H, Nakashima K, et al. Identification of a major yolk protein as an allergen in sea urchin roe. *Acta Derm Venereol.* 2010;90:235–238.