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Anaphylaxis caused by ingestion of jellyfish

Although anaphylaxis caused by foods is well known, an immediate allergic reaction due to jellyfish ingestion has never been reported. We report a 32-year-old Japanese female, who developed anaphylaxis after eating salt-preserved jellyfish. The patient was a surfer and had frequently been stung by jellyfish. Thirty minutes after eating salted jellyfish, she showed wheals and oral stinging sensation and 60 minutes later when she was dancing the hula, she showed an asthma-like attack, hypotension, nausea, vomiting and abdominal pain. Prick-to-prick test for the salted jellyfish produced a positive reaction as strong as that induced by histamine. Immunoblot analysis revealed that IgE antibodies in the patient serum reacted with an approximately 200 kDa protein in extracts from tentacle and umbrella of living jellyfish and in extract from the salted jellyfish, as well as a 25 kDa protein only in extracts from living jellyfish. This patient is considered to be the first reported case of anaphylaxis caused by intake of jellyfish. It is speculated that the patient was first sensitized through the skin by jellyfish stings and then jellyfish intake induced generalized attack of anaphylaxis. The 200 kDa unknown jellyfish protein may be the causative allergen.

Key words: jellyfish, anaphylaxis, food-allergy, immunoblotting, prick-test

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Skin disorders of jellyfish are caused by either toxic (irritant) or immunologic (allergic) effects [1]. Contact with jellyfish usually results in acute cutaneous inflammation with erythema, swelling, vesicles, and bullae, as well as some degree of burning pain [2]. Most skin lesions seem to occur due to the direct toxic effect of venoms in the nematocysts of jellyfish.

On the other hand, it is also known that jellyfish occasionally induces cutaneous lesions through delayed allergic mechanisms [1-4]. In contrast, immediate anaphylactic allergy to jellyfish is extremely rare and only two cases of anaphylaxis by jellyfish stings have been reported [5, 6]. Only one case has been reported showing gastrointestinal symptoms and urticaria after jellyfish ingestion [7], although the condition was not well confirmed to be anaphylaxis.

In this study, we report the first case of anaphylaxis, which was produced by the ingestion of salt-preserved jellyfish. Intriguingly, the patient was a surfer and had frequently been stung by jellyfish. The result of immunoblot analysis suggested that an unknown 200 kDa protein in the salt-preserved jellyfish was an allergenic protein in this case.

Report of a case

A 32-year-old Japanese female developed wheals and an oral stinging sensation 30 min after she ate salt-preserved jellyfish as a supper. These symptoms diminished in approximately 15 min. Then, 90 min after the intake of jellyfish,

an asthma-like attack, hypotension, nausea, vomiting and abdominal pain developed, when she was hula dancing. Then, she lost consciousness and was taken to a nearby hospital and admitted. First, she was treated with a drip infusion of pentazocine hydrochloride for abdominal pain and then with a drip infusion of corticosteroids and antihistamines. Her symptoms cleared 2 days after the treatment. Five days after the initial admission, she was referred to our hospital for evaluation of the possible causative material for the anaphylaxis.

She was a surfer and had a history of frequent stings by *Portuguese man-of war*, a common large stinging jellyfish around Japan, as well as other unidentified jellyfish. She always noticed toxic lesions including erythemas, bullae and a burning sensation, when she was stung by jellyfish. In Yanagawa city, on Kyushu island where she lived, people traditionally eat uncooked jellyfish, which is preserved by treatment with salt. However, this was the first time she had eaten uncooked jellyfish.

The physical examination of the skin showed several small pigmented nodular lesions with a linear arrangement on the right lower leg, which were scars left after severe dermatitis due to stings by *Portuguese man-of war* (figure 1A). A radioallergosorbent test (RAST) for jellyfish was not available in Japan. Therefore, we performed prick-to-prick test for the salted jellyfish, which the patient ate before the anaphylactic attack. The salted jellyfish is made using *Rhopilema esculentum*, which is a common jellyfish in the Kyushu area and is called Bizen jellyfish or Aka (red) jellyfish in Japanese (figure 1B). This test showed a positive reaction as strong as that produced by histamine (figure 1C).



Figure 1. A) Clinical appearance of the patient. Linearly arranged small scars on the right lower leg. B) The salted jellyfish (*Rhopilema esculentum*) material, which were used for both prick-to-prick test and immunoblotting. C) The result of the prick-to-prick test. The positive reaction to jellyfish was stronger than that induced by histamine.

Three healthy volunteers as negative controls showed no reaction to this jellyfish. According to these results, we diagnosed her condition as immediate allergy to the salted jellyfish.

Materials and methods

We performed immunoblot analysis for IgE antibodies in the patient serum using extracts from various jellyfish materials. We used the salted jellyfish material, which was the same as that used for the prick-to-prick test (figure 1B). For the salted jellyfish, we could not separate umbrella and tentacle parts. As the most native protein materials, we used both umbrella and tentacle parts of living *Aurelia aurita* (moon jelly). This jellyfish was obtained from an aquarium in our neighborhood, because the living *Rhopilema esculentum*, which is the same as salted jellyfish, was not available. Furthermore, we also tried to extract proteins from cooked jellyfish obtained from a Chinese restaurant. As control sera for the immunoblot study, we collected 6 sera from normal healthy volunteers. Three volunteers had been stung by jellyfish several times, while the other 3 volunteers had had no episodes.

For preparation of extracts from *Aurelia aurita*, either umbrella or tentacle parts of the jellyfish were homogenized with $2 \times$ SDS-sample buffer and then the tissues were lysed by sonication. For preparation of extracts from salted jellyfish and cooked jellyfish, tissues were cut into small pieces and were homogenized with SDS-sample buffer and then the tissues were lysed by sonication. After centrifugation, the supernatants were used for immunoblotting.

For immunoblotting, the proteins in the prepared jellyfish extracts were separated by an SDS-PAGE and transferred

onto polyvinylidene difluoride membrane. After blocking with buffer containing skim milk, the membranes were incubated with sera from the patient and normal controls with or without past history of jellyfish dermatitis and then reacted with anti-human IgE mouse monoclonal antibody. After being washed, the membranes were reacted with horseradish peroxidase-conjugated anti-mouse IgG goat polyclonal antibody. Protein bands were visualized using Ez-West Blue (ATTO).

Results

First, using Coomassie brilliant blue (CBB) staining and silver staining of SDS-PAGE gel, we confirmed protein extractability from the 4 materials. Judging from the results of CBB or silver stained lanes, a higher amount of protein was extracted from the living jellyfish, less protein from the salted jellyfish but almost no proteins from the cooked jellyfish (figure 2A; CBB, figure 2B; silver).

We did not examine the cooked jellyfish material by immunoblotting because the proteins in the cooked jellyfish were denatured and could not be extracted. Because the protein concentration was different in extracts between living jellyfish and salted jellyfish, the three extracts were adjusted to $2 \mu\text{g}$ for application.

By this immunoblot study, IgE antibodies in the patient serum specifically reacted with two proteins, approximately 200 kDa protein, in all extracts from tentacle and umbrella of the living jellyfish and the salted jellyfish and an approximately 25 kDa protein in extracts from umbrella and tentacle of the living jellyfish but not in extracts from the salted jellyfish (figure 2C). None of the 6 control sera showed positive reactivity with either protein. Other protein

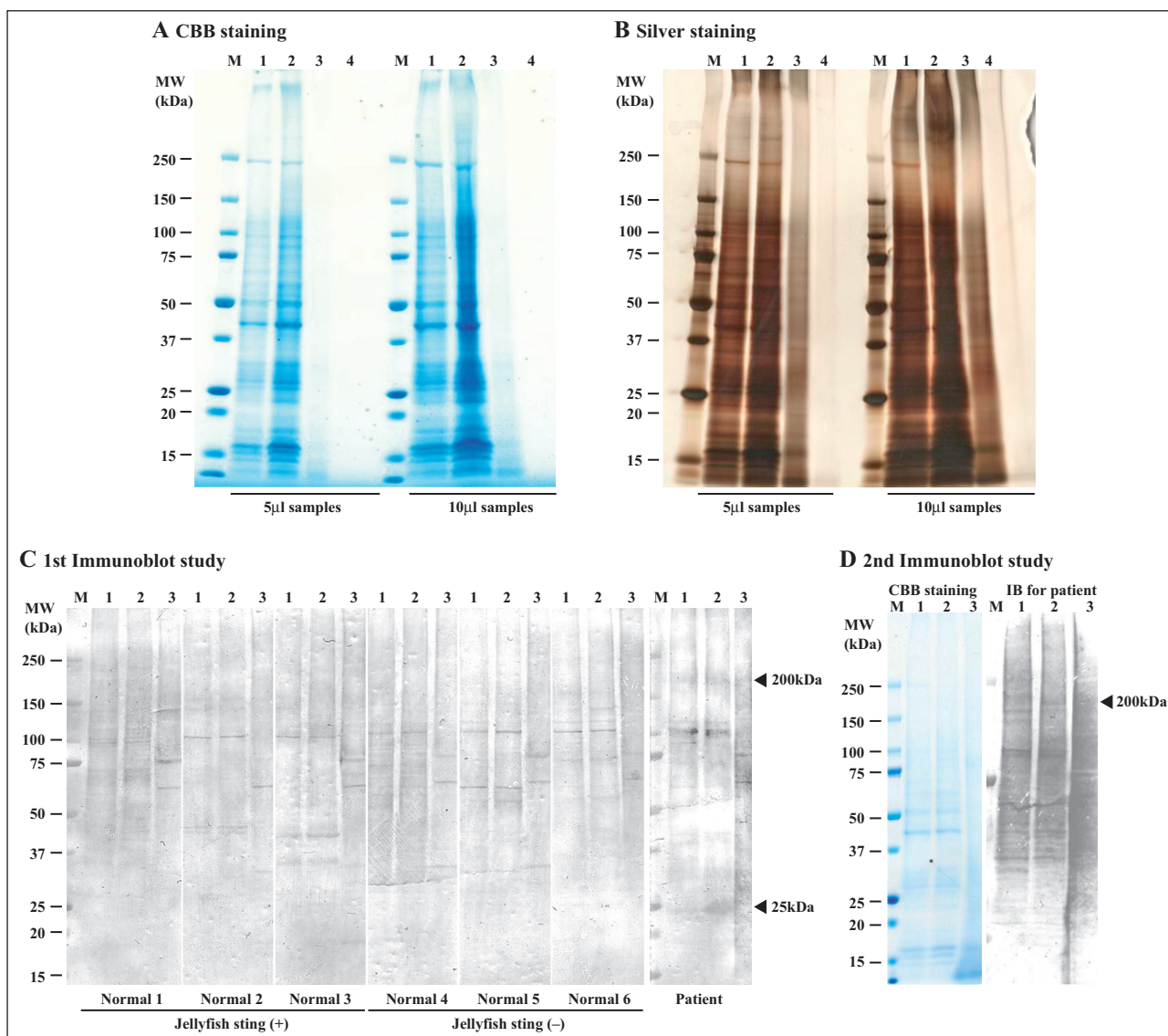


Figure 2. The results of SDS-PAGE and immunoblot studies. **A)** CBB stained gel. The extracts of umbrella part (lanes 1) and tentacle part (lanes 2) of living jellyfish, whole salted jellyfish (lanes 3) and cooked jellyfish (lanes 4) were applied on the wells of the 5-20% gradient gel. Five µl (left panel) and 10 µL (right panel) of the original extract samples were applied on the wells. **B)** Gel stained with silver staining. The wells of the gel were applied by the same serum samples as those for the gel for CBB staining. **C)** The results of the first IgE immunoblot experiment for all the 6 normal control sera and the patient serum. Lanes 1 are for extract from umbrella part of living jellyfish, lanes 2 are for extract from tentacle part of living jellyfish, and lanes 3 are for extract from salted jellyfish. Sera from three normal controls without jellyfish dermatitis, three normal controls with jellyfish dermatitis and the patient were examined IgE antibodies in the patient serum (most right panel) reacted with an approximately 200 kDa protein (shown by an arrowhead in the right) in all lanes, and with an approximately 25 kDa protein (shown by an arrowhead in the right) only in lanes 1 and 2. **D)** The results of the secondly repeated IgE immunoblot experiment only for the patient serum. In this experiment, the same reactivity with the 200 kDa protein was detected, while the reactivity with the 25 kDa protein was unclear. The positions of molecular weight markers are shown in lanes “M”, and the molecular weights (kDa) are indicated in the left of the panels for all studies.

bands reacting with the patient IgE antibodies were also detected in lanes for most control sera with and without a history of jellyfish sting, indicating that they were a non-specific reactivity. This reactivity with the 200 kDa and the 25 kDa proteins by IgE antibodies in patient serum was repeatedly confirmed by three additional experiments performed separately (*figure 2D*).

Discussion

It may be possible to consider that immediate systemic reaction in our case was caused by skin contact with the salted jellyfish. However, this is unlikely in our case, because the patient ate the salted jellyfish without touching it.

Nevertheless, although most skin conditions caused by skin contact with jellyfish are due to a direct toxic effect, it may be hypothesized that some part of the skin response is allergic in nature.

The skin is one of the major routes of sensitization and allergen sensitization through the skin can induce systemic allergic responses [8, 9]. Food allergy induced by cutaneous sensitization is considered to be rare. However, it has recently been shown that allergen sensitization through the skin or respiratory organs can later develop systemic food allergy [8, 9]. The patient in this study was a surfer and had frequently been stung by jellyfish. Therefore, we speculate that this case was primarily sensitized to jellyfish through the contact with jellyfish tentacles, and, later, anaphylaxis was induced by the intake of whole jellyfish. The duration between ingestion of jellyfish and development of anaphylaxis was rather long in the present patient. Intriguingly, the patient showed anaphylaxis after hula dance exercise. Therefore, anaphylaxis in the present patient might be caused or developed by exercise.

IgE antibodies in the patient serum reacted with two proteins with molecular weights of approximately 200 kDa and 25 kDa, although the antigen molecules for these bands have not yet been identified. Interestingly, the 200 kDa protein was found in both living jellyfish and salted jellyfish, while the 25 kDa protein was detected only in living jellyfish. Therefore, the 200 kDa protein, but not the 25 kDa protein, is likely to cause anaphylaxis in our patient.

Finally, we tried to obtain a protein sample from the cooked jellyfish which was served as a standard Chinese dish. However, we could not extract visible amount of proteins in two standard protein staining procedures. We speculated that the cooking process might denature proteins in the cooked jellyfish and only a small amount of extractable proteins remained. This may explain why there have been no reported cases of generalized anaphylaxis caused by eating cooked jellyfish in Chinese restaurants. ■

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