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Letter to the Editor

A case of anaphylaxis due to fish collagen in a gummy candy

Dear Editor,

Fish collagen peptides have recently been used as an ingredient in various foods and supplements for their putative benefits for beauty and health. We present herein a rare case of anaphylaxis due to fish collagen in a gummy candy.

An otherwise healthy, 25-year-old Japanese female had recurrent episodes of anaphylaxis shock after eating a gummy candy containing artificial fruit flavor and fish collagen. After treatment at the emergency room in a hospital, she visited our hospital to determine the cause of her allergy. Her medical history did not

have atopic dermatitis and hand eczema but her past-history, she experienced anaphylaxis after eating grilled fish but not after eating raw fish before. Total IgE was 153 IU/ml and specific IgE values were

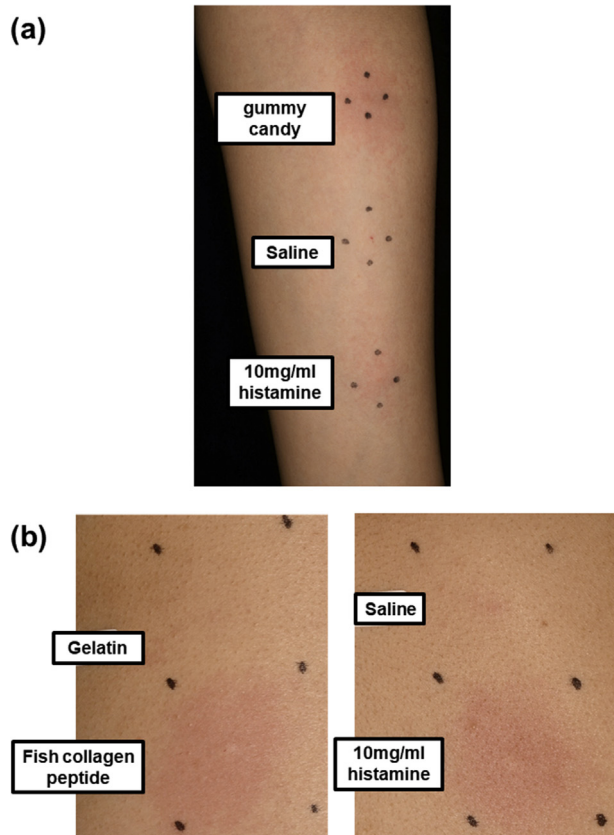


Fig. 1. (a) Prick-to-prick test with gummy candy after 15 min. (b) Prick-to-prick test of gelatin and fish collagen peptide after 15 min.

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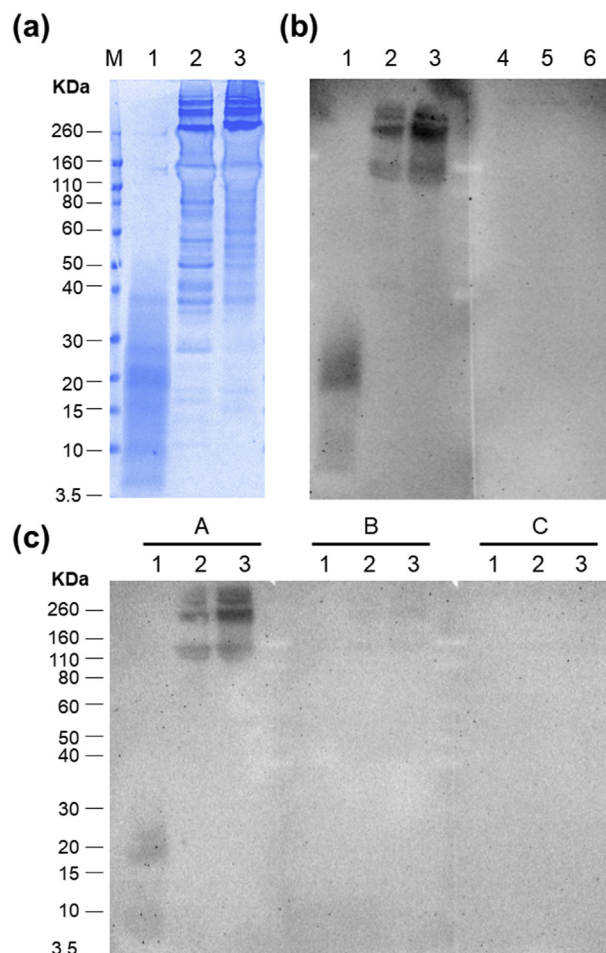


Fig. 2. (a) SDS-polyacrylamide gel electrophoresis (SDS-PAGE). Gel stained with Colloidal Blue Coomassie. Lane 1: fish collagen peptide, Lane 2: raw salmon skin, Lane 3: heated salmon skin. M, marker. (b) Immunoglobulin E (IgE) immunoblotting. Lane 1 and 4: fish collagen peptide, Lane 2 and 5: raw salmon skin, Lane 3 and 6: heated salmon skin. Lane 1, 2 and 3: reacted with 10% patient's serum, Lane 4, 5 and 6: reacted with 10% serum from a healthy control. (c) Inhibition assay of immunoglobulin E immunoblotting. Transferred fish collagen peptide and salmon skin protein were reacted with 10% serum from the patient containing each extract as inhibitors. Lane 1 = fish collagen peptide, Lane 2 = raw salmon skin, Lane 3 = heated salmon skin. Group A: serum + phosphate-buffered saline; group B: serum + 100 ug/ml fish collagen peptide; group C: serum + 1000 ug/ml fish collagen peptide.

as follows: gelatin (0 Ua/mL, class 0), tuna (2.23 Ua/mL, class 2), cod (0.55 Ua/mL, class 1), turbot (0.40 Ua/mL, class 1), anisakis (0 Ua/mL, class 0), pork (0 Ua/mL, class 0) and beef (0 Ua/mL, class 0). A prick-to-prick test was performed as previously reported using 10 mg/ml of histamine as a positive control and saline as a negative control.¹ The candy was soaked in distilled water for 1 h to prepare a 10 w/v% extract. The prick-to-prick test showed a positive reaction to gummy candy (3+) after 15 min (Fig. 1a). A further test using ingredients of the candy were negative for 10 and 1 w/v% gelatin but positive for 0.1 w/v% fish collagen peptide (3+) (Fig. 1b). Two healthy volunteers showed negative for all the tests. Raw and heated (100 °C for 10 min) salmon skin, as an example of fish collagen, and collagen peptide at 200 mg/ml was reacted in phosphate-buffered saline (pH 8) at 37 °C for 2 h. The extracted protein concentration in the supernatant was determined and treated by NuPAGE[®] LDS sample buffer and NuPAGE[®] reducing agent (Life Science[®], Zurich, Switzerland). SDS-polyacrylamide gel electrophoresis (SDS-PAGE) was performed with 4–12% NuPAGE[®] Bis-Tris Precast Gel (Life Technologies[®] Carlsbad, CA, USA), and fractionated protein bands, weighing variously from 5 kDa to 280 kDa, were visualized using Colloidal Blue Coomassie (Sigma–Aldrich) (Fig. 2a). For IgE immunodetection, the proteins, transferred to a nitrocellulose membrane, were incubated for 24 h in a 10% serum solution of the patient or a healthy control. Alkaline phosphatase-conjugated mouse monoclonal B3102E8 anti-human IgE mAbs (Abcam[®], Cambridge, UK) was then added after 1/500 dilution. Finally, Noverx[™] AP chemiluminescent Substrate (CDP-Star[™], invitrogen) was used to visualize the molecules. Immunoblotting with the patient's serum showed various bands from 5 kDa to 30 kDa for fish collagen peptides, and two major bands at 130–160 kDa and 260–280 kDa for raw and heated salmon skin (Fig. 2b). None of the target proteins were detected in the serum from a healthy control subject (Fig. 2b). Pre-treated 10% patient's serum with 0.1 mg of fish collagen peptides overnight suppressed expression level of specific bands in 130–160 kDa and 260–280 kDa bands of salmon skin protein (Fig. 2c). Based on these findings, we diagnosed this case as a fish collagen allergy.

Anisakis and parvalbumin have recently been known as allergens in fish allergy. In 2000, fish collagen was reported to be an allergen in fish allergy as well.^{2,3} Interestingly, heated fish muscle showed IgE reactivity to fish collagen, indicating that heating

increased the reactivity against fish collagen.⁴ Similarly, in the present case, the heated salmon skin sample showed strong IgE reactivity for fish collagen. We expect that the patient has been sensitized to fish collagen by oral sensitization. Because she had no customs of cooking herself and she had many chances to eat grilled fish at childhood. We extracted collagen peptides from various species of edible fish but were unable to identify a specific species with allergenic properties.

The present report is the first to document anaphylaxis due to fish collagen in a gummy candy. As consumers are unaware of allergy caused by fish collagen peptide in food, physicians are advised to inform their patients about the risk.

Conflict of interest

The authors have no conflict of interest to declare.

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