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Letter to the Editor

Occupational food allergy due to parvalbumin and phaseolin induced by epicutaneous sensitization



Dear Editor

Sensitization in food allergy is traditionally thought to occur via the intestinal tract. In recent years, it has been proposed that the primary mechanism for the development of food allergies is epicutaneous sensitization.^{1,2} In Japan, numerous cases of wheat allergy that developed from epicutaneous sensitization to hydrolyzed wheat protein (Glupearl 19S) in soap (sold by Yuuka Co., Ltd., Fukuoka, Japan) have been reported; this finding suggests that food allergies may be caused by epicutaneous sensitization.³

A 25-year-old man with atopic dermatitis (LDH: 321 U/L, TARC level: 2208 pg/ml, SCORAD index: 24) and pollinosis visited our hospital for investigation of food allergy and hand eczema. He had worked as a sushi chef and handled raw fish with his bare hands. After one year, he experienced itchiness in his hands after touching multiple types of fish, and intraoral itchiness, respiratory difficulty, diarrhea and abdominal pain occurred after consuming them. Consequently, he changed his job and became a Japanese sweets maker. He touches white bean paste (white kidney beans) with his bare hands for making Japanese sweets in daily work. After 6 months in this job, he felt itchy on his hands after touching white bean paste, and the hand eczema had worsened. When he consumed white bean paste, he began to experience the same symptoms as consuming fish. He had no history of food allergy before working in the aforementioned occupations. We considered the possibility that his food allergies were induced by epicutaneous sensitization. The total IgE level was 841 IU/mL. The levels of specific IgE antibodies by ImmunoCAP (Phadia Inc., Tokyo, Japan) were: class 2 for codfish, flatfish, salmon, mackerel, sardine and horse mackerel, class 3 for soybeans and class 4 for kidney beans. On the other hand, specific IgE antibodies for wheat, gluten, ω -5 gliadin, latex and anisakis were not detected. In skin prick test, he showed positive reactions for several kinds of fish (raw, as is) such as young yellowtail, horse mackerel, salmon roe, flatfish, sardine and white kidney bean.⁴ The tests for prawns, octopus, spiral shellfish, anisakis and black bean paste with azuki beans were negative. The positive control (1% of histamine dihydrochloride, Wako Pure Chemical Industries, Ltd., Osaka, Japan) exhibited a reaction of 3 × 3 mm. The negative control (physiological saline) exhibited no reaction. The skin prick test reaction was considered positive if a wheal ≥ 3 mm diameter appeared after 15–20 min of application. The fluorescence intensities of specific IgE antibodies to

parvalbumin and Gly m 5 in microarray immunoassay analysis (immune solid phase allergen chip; The microarray ISAC[®] (ThermoFisher, Uppsala, Sweden) were 19.3 ISAC Standardized Units; ISU(class 3), 25.4 ISU(class 3).⁵ Then, we performed two-dimensional electrophoresis and western blot (2D-western blot) to identify antigens of white kidney beans. Reactions were observed at 20–25-kDa and 48-kDa for white kidney beans (Fig. 1). In mass spectrometric analysis, the protein spots to react with the patient's serum in the white kidney bean were found to be “phaseolin” which included phaseolin, precursor, alpha-type, beta-type (Table 1).

As a mechanism underlying the development of food allergies, Lack proposed the concept that oral antigen exposure promoted immune tolerance rather than sensitization and that epicutaneous exposure affected sensitization in 2008.¹ In an experiment on mice, it was reported that specific IgE antibodies were produced when scratched skin was exposed to peanuts.² Our patient exhibited positive reactions in the skin prick test with multiple types of fish, and the microarray assay demonstrated high fluorescence intensity for specific IgE antibodies to parvalbumin and Gly m 5. We therefore considered that parvalbumin, a panallergen common to fish, was the causative fish antigen in the present patient. Onesimo *et al.* reported a case of contact urticaria involving specific IgE antibodies to parvalbumin.⁶ C. Hilger *et al.* reported a case of near-fatal IgE-mediated anaphylactic reaction that developed within minutes of eating fried frog legs in an adult. Although they defined parvalbumin as the causative antigen, they did not mention about mechanism of pathogenesis (e.g. epicutaneous sensitization).⁷ On the other hand, we used immunoblotting to serologically investigate the causative antigens about white kidney beans in the present case. Results of 2D-western blot analysis indicated the main antigens were phaseolin, a 7S class trimeric glycoprotein that is highly homologous to beta-conglycinin (Glym5) (Fig. 1, Table 1). Rouge P *et al.* performed immunoblotting analysis in a case of severe anaphylaxis induced by white kidney beans, with phaseolin (vicilin) and PHA (lectin) as the suspected causative antigens.⁸ Kasera *et al.* showed that the main sensitizing antigen in beans found among patients with asthma and rhinitis in India was also present in kidney beans.⁹ They also identified eight main types of antigens with immunoblotting and demonstrated cross-reactivity with other beans. However, they did not perform antigenic analysis. The history of present case and our findings indicate the possibility of epicutaneous sensitization through occupational exposure to parvalbumin and phaseolin, leading to food allergy. We considered that directly touch with bare hands to fish and white

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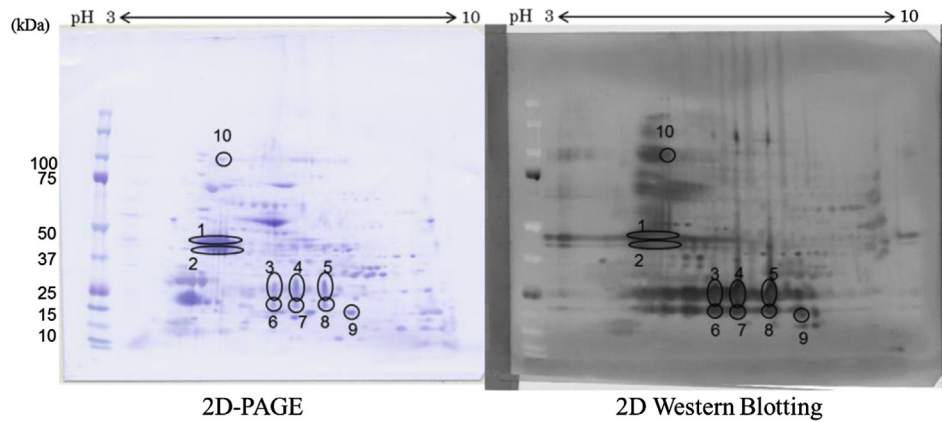


Fig. 1. Results of 2D-PAGE and western blot assay of white kidney beans using the patient's serum. Two-dimensional electrophoresis was performed to separate proteins of white kidney beans, which were then allowed to react with the patient's serum. Reactions indicated IgE antibody binding to white kidney beans were observed at 20–25-kDa and 48-kDa.

Table 1

Results of mass spectrometric analysis.

Protein	Spot no.	Accession no.	Sequence coverage (%)	Score
RecName: Full = Phaseolin, alpha-type; Flags: Precursor	1	gi 130169	11	237
RecName: Full = Phaseolin, alpha-type; Flags: Precursor	2	gi 130169	5	105
phaseolin [<i>Phaseolus vulgaris</i>]	3	gi 403594	9	154
albumin-2 [<i>Phaseolus vulgaris</i>]	3	gi 312982408	5	81
phaseolin [<i>Phaseolus vulgaris</i>]	4	gi 403594	5	61
alpha-amylase inhibitor [<i>Phaseolus vulgaris</i>]	4	gi 501106	9	149
RecName: Full = Phaseolin, beta-type; Flags: Precursor	5	gi 130170	6	91
unnamed protein product [<i>Phaseolus vulgaris</i>]	6	gi 21040	8	94
RecName: Full = Phaseolin, beta-type; Flags: Precursor	7	gi 130170	6	100
alpha-phaseolin [<i>Phaseolus vulgaris</i>]	8	gi 295832	12	172
legumin [<i>Phaseolus vulgaris</i>]	9	gi 312982406	5	127
RecName: Full = Cell division cycle protein 48 homolog	10	gi 2492504	4	88
PREDICTED: cell division cycle protein 48 homolog [<i>Glycine max</i>]	10	gi 356533213	4	86

We performed mass spectrometric analysis using 3200 QTRAP[®] mass spectrometer (AB Sciex, MA, USA) with Prominence[®] LC system (Shimadzu, Kyoto, Japan). The MS/MS spectra were searched against entries in the NCBI database using the Mascot[®] search program (Matrix Science, London, UK). The protein spots of 2D western blot assay in the white kidney bean analysis were found to be phaseolin, a 7S class trimeric glycoprotein that is highly homologous to beta-conglycinin (Gly m5).

kidney beans in daily work might facilitate the sensitization to these foods in our patient who were impaired skin barrier function from atopic dermatitis.

In the present study, we reported a patient with food allergies to fish and white kidney bean that were possibly induced by epicutaneous sensitization to parvalbumin and phaseolin occupationally. Further examination of additional cases is needed to elucidate the mechanisms of food allergy related to epicutaneous sensitization.

Conflicts of interests

KH is an employee of Hoyo Co., Ltd. The rest of the authors have no conflict of interest.

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