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ORIGINAL ARTICLE

Cross-reactive Carbohydrate Determinant Contributes to the False Positive IgE Antibody to Peanut

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ABSTRACT

Background: The importance of peanut allergy has not been well recognized in Japanese society. IgE antibody to peanut can be, however, detected in patients without clinical peanut allergy.

Methods: Clinical characteristics of 14 patients (aged 1–8 years) with peanut allergy were evaluated. IgE antibodies to peanut from patients with and without clinical peanut allergy were compared with those to soybean and other nuts. To examine the role of cross-reactive carbohydrate determinant (CCD) on the clinically false positive detection of peanut IgE, horseradish peroxidase (HRP) and bromelain specific IgE were measured by Uni CAP IgE kit. Inhibition of peanut IgE by HRP was also examined.

Results: The patients repeatedly experienced potentially life-threatening symptoms, including anaphylaxis. Sera from patients with peanut allergy had negative or relatively low IgE antibodies to other nuts. However, clinically false positive peanut IgE showed significant correlation-coefficients with soybean, almond, chestnut, pistachio, macadamia and cashew ($r = 0.61–1.00$). Anti-HRP and anti-bromelain IgE antibodies were detected in the clinically false positive sera, but not in the sera from patients with peanut allergy. Two out of four clinically false positive peanut IgE antibodies were significantly inhibited by HRP.

Conclusions: Social education about the features of peanut allergy is needed in Japan. Anti-CCD IgE antibody was suggested to be one of the mechanisms contributing to the false positive detection of peanut IgE. Detection of anti-HRP or anti-bromelain IgE can be a useful tool to recognize the presence of anti-CCD antibodies.

KEY WORDS

anaphylaxis, cross-reactive carbohydrate determinant, food hypersensitivity, immunoglobulin E, peanut hypersensitivity

INTRODUCTION

Allergies to peanut account for the majority of fatal and near-fatal anaphylactic reactions to foods.[1] In the United States, 3 million people are allergic to peanut or tree nuts, and peanut-induced anaphylaxis causes 50 to 100 deaths per year.[2] In Japan, peanut contributes to 2.4% of immediate type allergic reactions to food.[3] According to the results from this nation-wide study, and because of the severity of allergic symptoms to peanut reported overseas, the Japanese National Ministry of Health, Labor and Welfare designated peanut as one of the five major food allergens required to be specified on the label of food products. However, peanut allergy is not well understood in the community, partially because of the lack of precise information about the prevalence or clinical importance of peanut allergy among the Japanese population.

The first aim of this paper is to report the clinical importance of peanut allergy in Japanese children, and allergic cross-reactivity of peanut to soybean and other nuts.

Measurement of IgE antibody to peanut is a screening test for diagnosis of peanut allergy. However, positive IgE antibody does not always indicate a definitive diagnosis of peanut allergy.[4] The presence of IgE antibody to the carbohydrate (oligosaccharide) moieties in the plant antigen is one of the well-known

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Table 1 Clinical features of peanut allergy

No	Peanut IgE (UA/ml)	Age (Years)	First episode (Years)	Symptoms	Other food allergies	Total IgE (IU/ml)
1	100	6.7	3	Anaphylaxis x2, asthma *	milk, soybean (itch)	689
2	49.6	4.2	2	Anaphylaxis, urticaria	milk	812
3	45.6	3.6		Anaphylaxis x2	milk, walnut (urticaria)	741
4	10.3	6.1		Anaphylaxis	—	1180
5	2.7	4.8	1	Anaphylaxis	milk, eggs	608
6	100	5.6		Urticaria	—	1918
7	85.6	5.0	2	Urticaria, vomiting, diarrhea	—	8316
8	16.1	2.8	3	Urticaria	—	307
9	8.17	2.1	1	Urticaria	eggs, wheat, soybean (urticaria)	215
10	1	2.8		Urticaria, abdominal pain	—	26
11	15.4	1.3	1	Erythema	eggs	583
12	2.01	3.0	2	Erythema, itchy skin	—	217
13	1.08	8.2	3	Erythema	eggs, gelatin, soybean (eczema)	203
14	100	2.3		Eczema after 2 days	milk, eggs, shrimp, chocolate (eczema)	11270

* Induced by prick-to-prick test with peanut butter

Table 2 Clinical features of nut allergy.

No	Age (Years)	Nuts	Symptoms	Walnut IgE (UA/ml)	Peanut IgE (UA/ml)	Peanut allergy
1	3	Walnut	Urticaria	0.35	45.6	+
2	5	Walnut, pine nut	Anaphylaxis	5.52	0.8	-
3	2	Walnut	Cough	0.65	2.2	-
4	3	Walnut	Anaphylaxis	3.36	0.5	-
5	6	Walnut	Urticaria	4.17	14.1	-
6	5	Mixed nuts †	Erythema	4.21	3.4	-

† Almond, cashew, walnut

mechanisms contributing to the clinically false positive detection of IgE antibodies.[5] The common structures of N-linked glycan in plants (fruits, vegetables and pollens) have been well characterized and designated as cross-reactive carbohydrate determinant (CCD).[6] Natural Ara h 1, the major peanut allergen, has a single N-glycosylation site bearing five glycan species in a one to one ratio.[7]

The second aim of this paper is to investigate the role of anti-CCD IgE antibodies in the clinically false positive IgE antibodies to peanut, soybean and other nuts.

METHODS

Fourteen patients (aged 1−8 years, mean ± SD : 4.17 ± 2.0 years) with apparent history of immediate type peanut allergy were recruited to reveal the clinical characteristics of peanut allergy. Six patients with tree nut allergy (aged 2−6 years, 4.63 ± 1.69 years) were also analyzed. Oral challenge tests were not always performed to confirm the diagnosis, because severe anaphylaxis might occur in those with peanut and tree nut allergy.[1]

Sera from the 14 patients with peanut allergy and 8 patients without clinical peanut allergy despite the detection of IgE to peanut (designated as clinically false positive sera) were served for measurement of IgE antibodies to other nuts by UniCAP specific IgE kit (Pharmacia Diagnostics AB, Sweden). The nuts examined were soybean, walnut, almond, cashew nut, chestnut, pistachio, macadamia and pine nut, although some data were lacking due to the limitations of the sera obtained.

Four representative sera from patients with peanut allergy and four clinically false positive sera were examined for IgE antibodies to horseradish peroxidase (HRP)[8] and bromelain (from pineapple stem)[9] by UniCAP specific IgE kit. The UniCAP inhibition test was also performed using peanut ImmunoCAP and HRP (Sigma P6782, St. Louis, MO, USA) as an inhibitor. HRP contains 6 N-linked glycans and bromelain carries only one IgE-binding glycan.[10]

Informed consent was obtained from parents of the subjects to donate their sera for this study.