

Pru p 7 Predicts Severe Reactions after Ingestion of Peach in Japanese Children and Adolescents

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Keywords

Anaphylaxis · Children · Allergen component · Peach allergy · Pru p 7

Abstract

Introduction: Component-resolved diagnostics is used to diagnose food allergies. However, few reports have evaluated the severity of peach fruit allergy using peach allergen components, including Pru p 7. **Objective:** This study aimed to predict peach fruit allergy severity based on the presence of specific IgE (sIgE) antibodies (Abs) to peach allergenic components. **Methods:** Twenty-seven patients with peach fruit allergy were enrolled and classified into two groups: the local reaction (LR) group, including 12 patients with only oral or throat mucosal symptoms, and the systemic reaction (SR) group, including 15 patients, 10 of whom experienced anaphylaxis. Serum sIgE Abs against crude peach extract – Pru p 1, 2, 3, 4, and 7 – and tree pollen were measured. **Results:** sIgE Ab titers of Pru p 1 and 4 and alder pollen in the LR group were significantly higher than those in the SR group. sIgE against Pru p 7 was significantly higher in the SR group than in the LR group. The frequencies of sIgE Abs against Pru p 1, 4, and 7 in the LR group were 91.7, 66.7, and 16.7%, respec-

tively, while in the SR group these were 80, 20, and 60%. Sensitization to Pru p 2 and 3 was detected but limited in all patients. **Conclusions:** These findings suggest that sensitization to Pru p 1 and Pru p 4 is associated with local symptoms, and sensitization to Pru p 7 is associated with SR and anaphylaxis. To predict the severity of peach fruit allergy, it is useful to assess sIgE Ab reactions combining Pru p 1, 4, and 7.

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Introduction

Peach (*Prunus persica*) fruit allergy is frequently encountered in pediatric outpatient clinics. Peaches are one of the common causes of fruit allergy in Japan and Western countries [1]. Component-resolved diagnostics (CRD) is a diagnostic approach that defines allergen sensitization of patients at the molecular level [2]. Moreover, reports using CRD to assess peach allergies are increasing [2]. In recent years, four types of peach allergies have been reported according to sensitizing allergen components.

Edited by: O. Palomares, Madrid.

One well-known type of peach fruit allergy is pollen-food allergy syndrome (PFAS), which develops due to cross-reactivity and sensitization to Bet v 1, a major allergen from birch pollen. Bet v 1 is one of the pathogenesis-related protein-10 (PR-10) components with cross-reactivity to the peach homolog Pru p 1. PFAS can also develop due to another allergen, fruit profilin (Pru p 4), which has cross-reactivity to profilins from tree, grass, and weed pollen. The third type of reaction is non-pollen-related peach fruit allergy due to sensitization to lipid transfer protein (LTP). Pru p 3 is one LTP homolog found in peaches. This type is frequently reported in the Mediterranean area and is associated with severe clinical symptoms. The fourth type of reaction is a peach fruit allergy caused by the gibberellin-regulated protein (GRP) Pru p 7. Pru p 7 was first reported by Tuppo et al. [3] in 2013 and is related to severe allergic reactions, similar to those of LTP [1, 3]. Therefore, laboratory tests for Pru p 7-specific IgE (sIgE) are important for predicting severe allergic symptoms. Recently, it was reported that GRP from Cupressaceae pollen might be a primary sensitizer for peach fruit allergy [4]. Moreover, in Southern Europe, patients with a cypress pollen allergy frequently have a concomitant peach fruit allergy [4]. Additionally, Pru p 2, a thaumatin-like protein (TLP; PR-5), has been reported to be one of the allergens responsible in PFAS [5]. TLP is also present in Cupressaceae pollens. Pru p 9, PR-1, has recently been identified as an allergen component of peach pollen. Pru p 9 has been reported to exhibit symptoms such as bronchial asthma and rhinitis [6].

However, reports are limited regarding sIgE antibody (Ab) development and reaction to these 5 peach allergen components in children and adolescents with peach fruit allergy. Our aim was to predict the severity of peach fruit allergy by measuring sIgE sensitivity to the peach-allergen components Pru p 1, Pru p 2, Pru p 3, Pru p 4, and Pru p 7 using standard and experimental ImmunoCAP tests, and to investigate the relationship between these components and tree pollen sensitization.

Materials and Methods

Patients

Twenty-seven consecutive patients diagnosed with a peach fruit allergy at the Department of Pediatrics, Dokkyo Medical University Hospital, between October 2012 and September 2017 were enrolled in the present study. Diagnosis was made on the basis of a convincing history of allergic reactions within 2 h after ingesting peach and the presence of sIgE Abs to crude peach extract (>0.1 UA/mL) in the sera of patients. This study was approved by the Ethical Review Board of Dokkyo Medical University.

Patient Groups and Symptoms

The patients were classified into two groups according to their symptoms following the ingestion of peach: the local reaction (LR) only group, and the systemic reaction (SR) group. LRs consisted of only mucosal symptoms, which included oral itching, pharyngeal itching, and/or angioedema of the lips. SRs consisted of itching or urticaria, cough, dyspnea, and/or vomiting [7]. We defined anaphylaxis as 2 or more of the following symptoms that occurred rapidly after the ingestion of peach: involvement of the skin-mucosal tissue (e.g., generalized hives, itching and skin flushing, and angioedema of the lips), respiratory compromise (e.g., coughing, dyspnea, wheezing and bronchospasm, stridor, and reduced peak expiratory flow or hypoxemia), reduced blood pressure or associated symptoms (e.g., hypotonia [collapse], syncope, or incontinence), and persistent gastrointestinal symptoms (e.g., crampy abdominal pain or vomiting) [8].

Serum-Specific IgE Sensitivity Measurements by ImmunoCAP

The sIgE values to commercially available crude peach extract, Pru p 1, Pru p 3, Pru p 4, and Japanese cedar and alder pollen were measured by ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden). For measurement of the sensitivity of sIgE Abs to recombinant Pru p 2 produced by insect cells or native Pru p 7 purified from peach pulp according to the methods developed by Tuppo et al. [3], the allergens were immobilized on an experimental ImmunoCAP. The cut-off value for sensitization was set at >0.35 UA/mL. Since Pru p 9 is an allergenic component of peach pollen, it was not measured because it was not related to this peach fruit allergy.

Statistical Analysis

For the analysis, sIgE Ab levels below the lower limit of quantitation (<0.10 UA/mL) were assigned a value of 0.09 UA/mL for statistical calculations, while sIgE Ab levels over the higher limit of quantitation (>100 UA/mL) were assigned a value of 101 UA/mL. Statistical analysis was performed using SPSS version 25 (IBM Corp., Armonk, NY, USA). Data were compared using Mann-Whitney U tests. Using a receiver operating characteristic (ROC) curve, the cut-off values at which Pru p 1, Pru p 4, and Pru p 7 were classified into the LR and the SR group were calculated. $p < 0.05$ was considered statistically significant.

Results

Patient Groups

Twenty-seven patients were enrolled in this study. The median age at the time of blood sampling was 13 years (range 7–20). All patients had pollinosis. The LR group consisted of 12 patients (age range 7–20 years; median age 13.5; 8 were males). The SR group consisted of 15 patients (age range 9–19 years; median age 13.0; 8 were males). There were no differences in baseline characteristics between the LR and SR groups in terms of blood sampling, age, and sex (Table 1). However, the number of causative plant food allergens in the LR group was significantly higher than that in the SR group.

Table 1. Characteristics of the LR and SR groups

	All patients	LR group	SR group	<i>p</i> value
Patients	27	12	15	
Age, years	13 (7–20)	13.5 (7–20)	13 (9–19)	0.492
Female	16 (59)	8 (67)	8 (53)	0.641
Pollinosis	27 (100)	12 (100)	15 (100)	
Peach allergy reactions				
Oropharyngeal symptoms	18 (63)	12 (100)	6 (40)	
Lip edema	2 (7)	1 (8)	1 (7)	
Facial edema	3 (11)		3 (20)	
Conjunctival injection	3 (11)		3 (20)	
Ear pruritus	1 (4)		1 (7)	
Facial urticaria	1 (4)		1 (7)	
Systemic pruritus	3 (11)		3 (20)	
Systemic urticaria	8 (30)		8 (53)	
Coughing	2 (7)		2 (13)	
Dyspnea	8 (30)		8 (53)	
Vomiting	1 (4)		1 (7)	
Cofactor				
Exercise			8 (53)	

Data are presented as *n* (%) or the mean (range). LR, local reaction; DR, systemic reaction.

Allergy Symptoms

Among the 27 patients, oropharyngeal symptoms were seen most frequently, appearing in 17 patients (17/27, 63%). Systemic urticaria and dyspnea were seen in 8 patients (8/27, 30%), followed by facial edema, conjunctival injection, and systemic pruritus, which were each observed in 3 patients (3/27, 11%; Table 1, 2).

All patients in the LR group experienced oropharyngeal symptoms. Angioedema of the lips was only reported in 1 patient. The symptoms seen in the SR group included systemic urticaria in 8 cases (8/15, 53%), dyspnea in 8 cases (8/15, 53%), and oropharyngeal symptoms in 5 cases (5/15, 33%). Overall, 10 patients (10/15, 67%) developed anaphylactic reactions (Table 2); for these patients, the most common symptom other than skin and mucosal symptoms was dyspnea (8/10, 80%), and 2 patients experienced a cough (2/10, 20%). Only 1 patient experienced vomiting. Exercise was a cofactor in the 8 patients who experienced anaphylaxis (Table 1).

Sensitization Rate to Peach and Tree Pollen Allergens

Sensitization rates to Pru p 1, Pru p 4, and Grey alder in the LR group were significantly higher than those in the SR group, while the sensitization rates to Pru p 7 in the SR group were significantly higher than those in the LR group. There were no differences noted in the sensitization rates of crude peach extract and Japanese cedar between the two groups (Fig. 1, 2). Pru p 3 was positive in

3 cases in the LR group and in 1 case in the SR group. It was low in 14% (4/27) of all cases.

Analysis Using a ROC Curve

Using a ROC curve, the cut-off value for diagnosing the LR and the SR groups was calculated. Pru p 1 (area under the curve; AUC 0.856) and Pru p 4 (AUC 0.794) were useful for diagnosis of the LR group (Fig. 3a). The cut-off value for Pru p 1 was 35.1 IU/mL, the sensitivity was 66.7%, and the specificity was 86.7%. The cut-off value of Pru p 4 was 1.92 IU/mL, the sensitivity was 58.3%, and the specificity was 93.3%. On the other hand, Pru p 7 (AUC 0.894) was useful for diagnosis of the SR group (Fig. 3b). The cut-off value of Pru p 7 was 0.102 IU/mL, the sensitivity was 86.7%, and the specificity was 83.3%.

Combination with Multiple Components

We examined whether allergy severity could be evaluated by combining the peach allergen components of Pru p 1, Pru p 4, and Pru p 7, which resulted in significant differences (Fig. 1) between the LR and SR groups. When Pru p 7 was negative, and either Pru p 1 or Pru p 4 was positive (LR group, 10 patients; SR group, 2 patients), none of the 12 patients experienced anaphylaxis. When Pru p 7 was positive, and either Pru p 1 or Pru p 4 was negative (LR group, none; SR group, 12 patients), there were 9 cases of anaphylaxis out of 12.

Table 2. All patient characteristics and serum-specific IgE sensitization outcomes

Patient No.	Group	Age, years	Sex	Symptoms (peach)	Anaphylaxis	Cofactor	Pollinosis	sIgE, UA/mL									Reported food allergens to other plant foods	
								Peach	Pru p 1	Pru p 2	Pru p 3	Pru p 4	Pru p 7	Japanese cedar	Grey alder			
1	LR	20	M	Os, El	–	None	+	0.82	3.53	<0.1	0.85	2.79	<0.1	18.4	6.71	Cherries, grapefruit, dekopon, watermelon, melon, wheat		
2	LR	7	M	Os	–	None	+	21.2	45.9	<0.1	<0.1	<0.1	<0.1	75.8	43.3	Apple		
3	LR	14	F	Os	–	None	+	2.52	20.1	<0.1	0.30	<0.1	<0.1	≥100	24.6	Orange, kiwi, pineapple, watermelon, melon, corn		
4	LR	15	F	Os	–	None	+	18.8	65.8	<0.1	<0.1	<0.1	<0.1	≥100	≥100	Apple, pear, cherries, strawberry, melon, bean sprouts, soy		
5	LR	13	M	Os	–	None	+	4.10	42.6	<0.1	<0.1	7.31	<0.1	≥100	49.4	Melon		
6	LR	10	M	Os	–	None	+	18.7	44.6	0.87	<0.1	18.8	<0.1	≥100	NT	Pear, banana, melon, bean sprouts, cucumber, nuts, buckwheat		
7	LR	9	M	Os	–	None	+	46.1	>100	<0.1	<0.1	15.5	<0.1	≥100	≥100	Apple, orange, strawberry, banana, kiwi, pineapple, melon, persimmon		
8	LR	15	F	Os	–	None	+	1.44	8.19	<0.1	0.13	<0.1	<0.1	≥100	11.9	Apple, kiwi, pineapple		
9	LR	16	F	Os	–	None	+	0.33	0.14	0.31	<0.1	1.06	<0.1	≥100	2.69	Apple, orange, grapefruit, strawberry, kiwi, pineapple, watermelon, papaya, tomato, bamboo shoots		
10	LR	8	M	Os	–	None	+	71.8	>100	0.85	0.60	7.81	0.92	≥100	≥100	Strawberry, pineapple		
11	LR	16	M	Os	–	None	+	19.7	87.4	0.26	6.99	3.34	0.48	≥100	≥100	Avocado, nuts, buckwheat		
12	LR	13	M	Os	–	None	+	21.6	>100	0.17	0.28	4.00	<0.1	95	≥100	Apple, strawberry, banana, kiwi, watermelon, melon, tomato		
13	SR	14	M	Os, El, Uf	–	None	+	24.8	27.9	0.32	0.16	7.79	<0.1	NT	98.1	Apple, kiwi, watermelon, peanuts, nuts		
14	SR	12	F	Pe, Os	–	None	+	10.9	42.39	<0.1	0.55	<0.1	<0.1	≥100	40.2	Eggplant		
15	SR	14	M	Os, Ps, Ci	–	None	+	5.62	7.88	<0.1	<0.1	<0.1	2.71	88.7	NT	None		
16	SR	13	M	Os, Ps	–	None	+	5.81	16.54	<0.1	<0.1	<0.1	1.79	≥100	60.9	Apple, pear, kiwi		
17	SR	13	F	Us, Ef	–	None	+	0.43	<0.1	<0.1	0.22	<0.1	1.13	≥100	0.41	Apple, orange, kiwi		
18	SR	13	F	Os, Dy	+	None	+	1.31	1.14	<0.1	<0.1	<0.1	6.72	31.9	1.74	Cherries, strawberry, Japanese apricot		
19	SR	14	F	Os, Us, Co, Dy	+	None	+	2.95	<0.1	0.10	0.65	<0.1	0.12	≥100	4.30	Sweet potato		
20	SR	9	M	Ci, Ef, Dy	+	Exercise	+	0.96	<0.1	<0.1	NT	<0.1	8.20	≥100	0.34	Orange, grapefruit, melon		
21	SR	9	F	Ps, Dy	+	Exercise	+	2.02	0.29	0.15	0.13	<0.1	6.44	≥100	1.25	Grapefruit		
22	SR	11	M	Us, Ef, Co	+	Exercise	+	2.34	<0.1	<0.1	<0.1	<0.1	12.2	≥100	0.13	None		
23	SR	12	F	Us, Ci, Vo	+	Exercise	+	17	48.5	<0.1	<0.1	<0.1	19.8	NT	≥100	Pear, cherries, strawberry, banana, kiwi, tomato, soy, spinach		
24	SR	12	M	Us, Dy	+	Exercise	+	8.02	<0.1	<0.1	<0.1	<0.1	12.1	≥100	2.98	None		
25	SR	16	F	Us, Dy	+	Exercise	+	0.42	<0.1	<0.1	<0.1	<0.1	0.76	30.2	<0.1	Apple, cherries, orange, grapefruit, strawberry		
26	SR	19	M	Us, Dy	+	Exercise	+	0.21	<0.1	<0.1	<0.1	<0.1	0.45	15.4	0.19	Orange, grapefruit, watermelon, eggplant		
27	SR	11	M	Us, Dy	+	Exercise	+	20.4	27.2	<0.1	<0.1	<0.1	24.5	≥100	≥100	Loquat, Japanese apricot		
Symptoms are patient reported: Os, oropharyngeal symptoms; El, Lip edema; Ef, facial edema; Ci, conjunctival injection; Pe, ear pruritus; Pf, facial pruritus; Uf, facial urticaria; Ps, systemic pruritus; Us, systemic urticaria; Co, coughing; Dy, dyspnea; Vo, vomiting; NT, not tested.																		

Symptoms are patient reported: Os, oropharyngeal symptoms; El, Lip edema; Ef, facial edema; Ci, conjunctival injection; Pe, ear pruritus; Pf, facial pruritus; Uf, facial urticaria; Ps, systemic pruritus; Us, systemic urticaria; Co, coughing; Dy, dyspnea; Vo, vomiting; NT, not tested.

Discussion

In the present study, sIgE Abs to the allergen components related to peach fruit allergy registered in the WHO/IUIS allergen nomenclature (available at <http://allergen.org/>) were measured in the sera of children and adolescents diagnosed with peach fruit allergy. Pru p 9, present in peach pollen, has been reported. However, this was a study on peach fruit allergy and this component has not

been measured previously. The results were compared to allergic symptoms after the ingestion of peach and the sIgE Ab concentration to major tree pollen allergens in Japan. Sensitization to Pru p 1, Pru p 4, and alder pollen were associated with oral allergy symptoms (the LR group) as has been shown in previous reports [1]. In recent years, the number of children sensitized to alder pollen has been increasing, and we see many children with PFAS in our outpatient clinic. Alder pollen and birch pol-

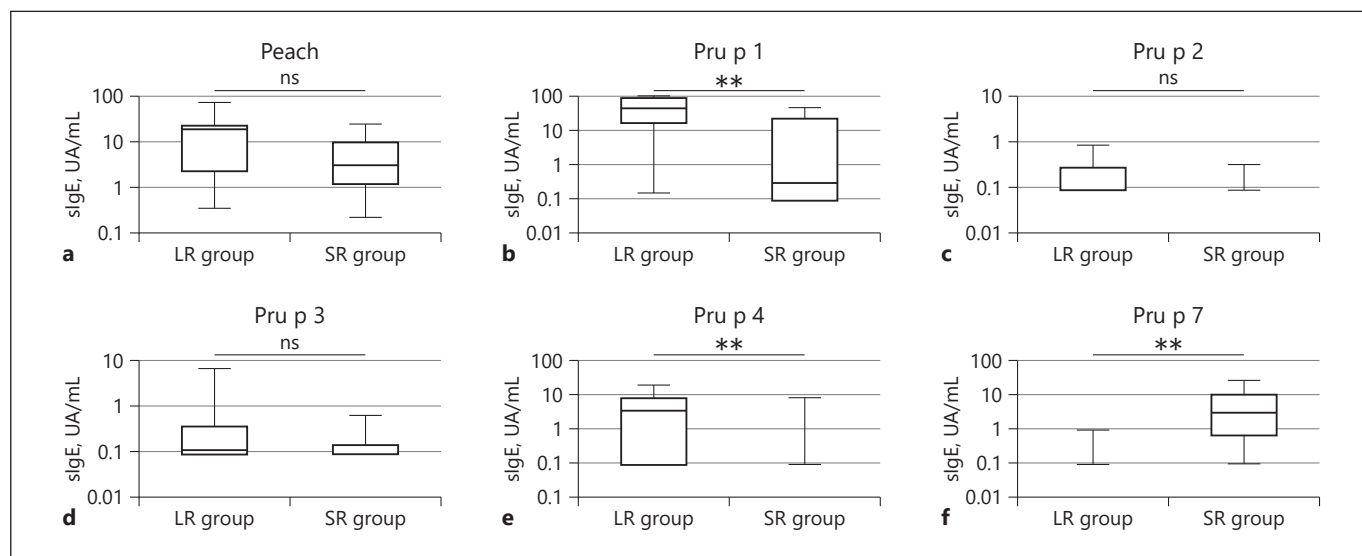


Fig. 1. a–f Box plots comparing sIgE levels between the LR and SR groups. The LR and SR groups were compared for sIgE concentrations to peach and peach-allergen components. All sIgE Ab sensitivities were measured by ImmunoCAP (Thermo Fisher Scientific). Pru p 1 (**b**) showed significantly higher values in the LR group

than in the SR group; Pru p 4 (**e**) showed significantly higher values in the LR group than in the SR group; Pru p 7 (**f**) showed significantly higher values in the SR group than in the LR group. ** $p < 0.01$. ns, not significant; LR, local reaction; SR, systematic reaction; sIgE, specific IgE Abs.

Fig. 2. Box plots comparing pollen sIgE levels between the LR and SR groups. The LR and SR groups were compared for Japanese cedar (**a**) and Grey alder (**b**) pollen sIgE. All sIgE Ab sensitivities were measured by ImmunoCAP (Thermo Fisher Scientific). Grey alder (**b**) showed significantly higher sIgE values in the LR group than in the SR group. * $p < 0.05$. ns, not significant; LR, local reaction; SR, systematic reaction; sIgE, specific IgE Abs.

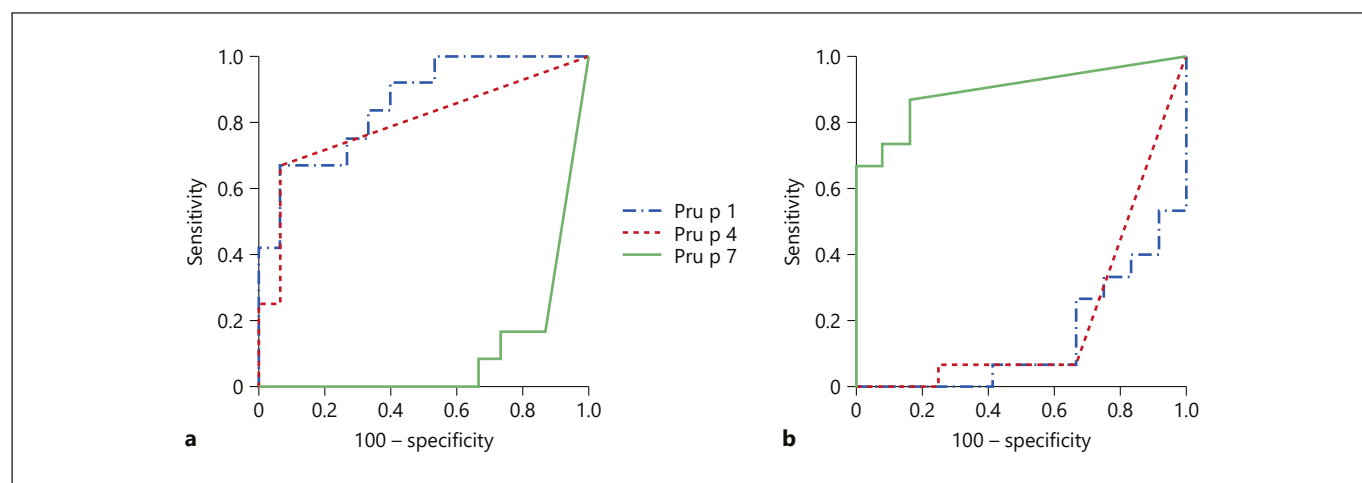
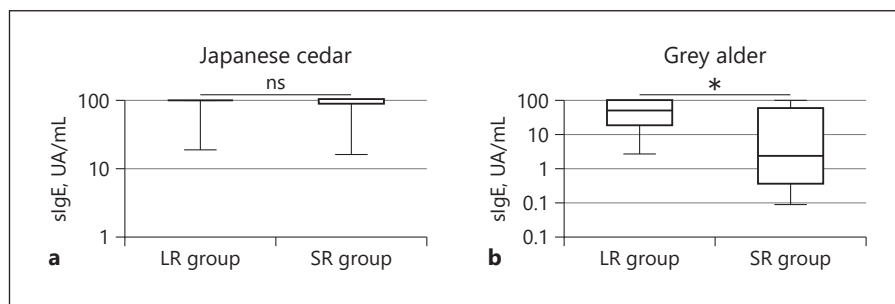


Fig. 3. ROC curve for Pru p 1, Pru p 4, and Pru p 7 sIgE: LR patients only (**a**), SR patients only (**b**).

len sIgE Abs are highly correlated [9]. Patients with birch pollinosis have allergic symptoms due to the Rosaceae family of fruits such as apples and peaches [10]. Alder pollen might be the primary sensitizer to protein-10 and/or profilin in peach fruit allergy patients experiencing oral symptoms.

The cut-off value of Pru p 7 sIgE was very low. If Pru p 7 is detected, it is thought that it can be diagnosed as an SR, so we believe that it is possible to distinguish between local and systemic responses by combining three components to improve diagnostic accuracy. In the SR group, 80% of patients were sensitized to Pru p 7; however, only 2 (17%) were sensitized to this component in the LR group, and these patients had low sIgE Ab titers. Therefore, we suggest that when Pru p 7 is negative and either Pru p 1 or Pru p 4 is positive, there is a high possibility for an LR. We also found that when Pru p 7 was positive and either Pru p 1 or Pru p 4 were positive, there was a high possibility of anaphylaxis. Only 1 patient with Pru p 3 (LTP) developed sensitization in the anaphylaxis group. The reason that LTP was less sensitized as compared to sensitization of Pru p 7 may have been due to a difference in eating habits and the distribution of allergens in peaches rather than differences in peach cultivars [1]. It has been observed that Pru p 7 is distributed in both peach peel and pulp; however, Pru p 3 is localized in the peach peel [1, 3]. Most Japanese individuals eat peeled peaches, and therefore do not ingest the LTP that is found in the peel. However, in Western countries it has been suggested that there is LTP sensitization when peaches are eaten unpeeled [1]. Ebisawa et al. [11] reported the sensitization of Ara h 9, as peanut LTP, which was also less common in Japan. Meanwhile, in China, Ma et al. [12] reported that the sensitization component of peanut allergy patients was mainly Ara h 9. Most of these patients were sensitized to mugwort pollen, and many suffered from peach allergies. This fact is very similar to Mediterranean sensitization [13]. There are mugworts in Japan, but there are many types, and we thought that these had different affects.

Tuppo et al. [3] reported that Peamaclein (Pru p 7) was a new marker in 2013. The following year, Inomata et al. [1] reported that Pru p 7 was related to SRs. In the report by Tuppo et al. [3], 14 patients (mean age 26.0 years; range 5–45) showed a positive response to purified Pru p 7 by skin prick tests. Of the 14 patients, 2 (14.3%) presented with anaphylaxis. One of these had positive sIgE Abs only to Pru p 7, while the other was positive to both Pru p 3 and Pru p 7. Inomata et al. [1, 14] reported that 64.3% of 14 patients with SRs to peach (mean age 32.0 years; range 7–55) had sIgE to purified Pru p 7, and that GRP sensi-

tization was frequently seen in patients with facial edema, laryngeal tightness, and food-dependent exercise-induced anaphylaxis (FDEIA). In our study, laryngeal symptoms (4/15, 27%), FDEIA (8/15, 53%), and anaphylaxis (10/15, 67%) were seen in Pru p 7-sensitized patients.

In southern Europe, patients with a cypress allergy frequently had peach fruit allergy [4]. Recently, it was reported that Cupressaceae (*Cupressus sempervirens*) pollen might be a primary sensitizer of peach and citrus allergies [15]. All patients in our study were strongly sensitized to Japanese cedar pollen. Furthermore, there was no significant difference in the sensitization rate and sIgE Ab titers to Japanese cedar pollen between the LR and SR groups. Therefore, we could not confirm that sensitization to Pru p 7 was caused by Cupressaceae pollen. Studies regarding other types of Cupressaceae pollen (*Chamaecyparis obtusa*, *Juniperus chinensis*) would help supplement the findings of the current research. As Pru p 7 is resistant to heat and digestion, sensitization of Pru p 7 might be via the gastrointestinal tract [16].

Sensitization to Pru p 2 and Pru p 3 was low in both the LR and SR groups. Several reports from Japan have shown a low frequency of LTP sensitization in patients with plant food allergy, and our results confirm this [1]. There is currently limited research on TLP sensitization in Japan. However, TLP from Japanese cedar pollen (Cry j 3) has been characterized, and it was found that 27% of patients with Japanese cedar pollinosis were sensitized to Cry j 3 [17]. Furthermore, the cross-reactivity between Cry j 3 and Pru p 2 might be low, because patients in both the LR and SR groups were strongly sensitized to Japanese cedar pollen. However, further studies on the role of Pru p 2 in peach allergies are needed.

We also found that sIgE Ab levels to Pru p 1, Pru p 4, and Pru p 7 were relatively higher than those to crude peach extract. Two patients had sIgE Abs <0.35 UA/ml to crude extract; however, their sIgE Abs to allergen components were positive with respect to the cut-off for sensitization (Pru p 4, 1.06 UA/mL; Pru p 7, 0.45 UA/mL). Thus, using peach allergen components for measuring sIgE Abs can be more sensitive than using crude peach extract alone.

There is a limitation to this study. Ideally, diagnoses should be confirmed by oral food challenge. However, we performed oral food challenge tests only in some cases. Although it is a verification tool used to assess adult patients, according to the diagnostic algorithm developed by Skypala et al. [18], it is possible to diagnose PFAS using a diagnostic questionnaire. Our patients were children and adolescents; however, it is possible that this algorithm could be applied to the LR group. In the SR group, if the

peach-allergic patients were experiencing severe symptoms such as anaphylaxis, it was difficult to perform oral food challenge tests. Roberts [19] reported that, if a patient has a history of adverse reactions to a particular food, the possibility that the food is the allergen is approximately 50%, and, if a patient has a history of three similar adverse reactions to a particular food, the possibility that the food is the allergen rises to approximately 100%. The number of inductions in the SR group was 1.9 on average, and most patients had a history of two or more allergic symptoms. The number of our cases is small, and we plan to expand this sample and re-examine the current cases.

To conclude, we demonstrated that CRD with Pru p 1, Pru p 4, and Pru p 7 in combination can be useful for predicting the severity of peach fruit allergy in children and adolescents. Sensitization to Pru p 7 might predict severe allergic reactions after the ingestion of peach, especially anaphylaxis, when exercise is a cofactor. There is cross-reactivity within the GRP family among fruits (Rosaceae, Rutaceae) and vegetables. Therefore, patients who are sensitized to Pru p 7 should also consider other fruits and vegetables as potential causative allergens and be aware that exercise and other cofactors may cause anaphylaxis after peach consumption. We suggest, therefore, that this awareness in patients/guardians and medical personal, as well as the extended testing described above, may help to prevent allergic reactions, especially severe reactions such as anaphylaxis.

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Acknowledgements

We appreciate the aid of our colleagues at Dokkyo Medical University, Department Pediatrics. We thank Prof. Nobuyuki Maruyama of the Graduate School of Agriculture, Kyoto University, for providing recombinant Pru p 2, Dr. Jonas Lidholm of Thermo Fisher Scientific for providing the experimental ImmunoCAP tests, and Mr. Akira Tanaka for the helpful discussion.

Statement of Ethics

This study was approved by the Ethical Review Board of Dokkyo Medical University (R-7-22). The study design and risks were fully explained to patients and their guardians, and informed consent was obtained from all participants prior to their enrollment.

Disclosure Statement

We have no conflicts of interest directly relevant to the content of this article. We received no financial support directly relevant to the content of this article.

Author Contributions

Y.A. and S.Y. designed this study. Y.A. performed statistical analyses and drafted the manuscript. S.Y. supervised the project. All authors collected cases, contributed to and approved the final draft for publication.

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