

Clinical, Anamnestic and Serological Features of Peach Allergy in Portugal

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Key Words

Peach allergy • Pollinosis • Portugal • Recombinant allergen • rPru p 3

Abstract

Background: Peach is a common food allergen source throughout Europe. The aim of this study was to characterize peach allergy in a Portuguese patient population. **Methods:** Thirty peach-allergic patients confirmed by double-blind placebo-controlled food challenges and 29 controls were included. All subjects completed a standardized questionnaire regarding symptoms and epidemiologic characteristics, skin prick tests with inhalant allergens and foods as well as specific IgE antibodies to peach, recombinant peach allergens rPru p 1, rPru p 3, rPru p 4 and cross-reactive carbohydrate determinants. **Results:** Thirty-seven percent of patients reported only oral allergy syndrome, while 37% reported generalized urticaria and/or angioedema, 17% localized contact urticaria and 10% anaphylaxis with peach. Sensitization to other *Rosaceae* fruits and tree nuts was present in 90 and 77% of the patients, respectively. Respiratory allergy history was associated with less severe symptoms (oral allergy syndrome or contact urticaria; $p < 0.01$) and positive skin prick test to peach peel or plum with more

severe symptoms (urticaria and/or angioedema or anaphylaxis; $p < 0.05$). Ninety-seven percent were sensitized to Pru p 3, 13% to Pru p 4, 3% to Pru p 1 and 10% to cross-reactive carbohydrate determinants. Pru p 3 specific IgE was associated with *Artemisia vulgaris* sensitization and tree nut allergy ($p < 0.05$) but not with clinical severity. **Conclusions:** Half the patients reported systemic reactions to peach. Peach allergy appeared predominantly mediated by Pru p 3 but some patients were sensitized to Pru p 4. Applying a 0.10 kU_A/l cutoff level, the diagnostic value of combining the 3 recombinant allergens was noteworthy, with 100% sensitivity and 90% specificity.

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Background

Peach is the fruit of the peach tree (*Prunus persica* or *Prunus vulgaris*), a member of the botanical *Rosaceae* family. Its origins are attributed to China, where it was known as 'tree of life'. It was brought to Europe by Romans. After America's discovery it was taken there by Spanish colonists [1].

Portugal is a country with considerable production and consumption of *Rosaceae* fruits. Peach, with an an-

nual production of 49,000 tons/year and a per capita consumption of 7.2 kg/year, represents the third most consumed *Rosaceae* fruit, after apple and pear [2].

Peach allergy is the most frequent type of food allergy in the adult population in southern Europe [3, 4]. In a Spanish study, allergic reactions were 4 times more frequent to peaches than to apples, despite greater apple consumption [5]. Peach is a common cause of food allergy in Italy [6, 7], Spain [8] and Portugal, probably related to its large production and consumption, to the south European pollen load and sensitization rates and, as recently suggested, increased contact with peach fuzz [9].

Clinical presentation includes both mild and severe symptoms. Local reactions such as localized contact urticaria (CU) and oral allergy syndrome (OAS) are observed in >50% of patients [6, 10–13]. Systemic reactions (generalized urticaria/angioedema or anaphylaxis) are frequently observed (18–44%), even in the absence of OAS [6, 10–13].

Several allergens have been identified in peach. Sensitization to Pru p 3, the peach lipid transfer protein (LTP), has been detected in >90% of peach-allergic patients in Spain [14, 15], being the only allergen identified thus far in peach-allergic patients without associated pollen allergy [11, 16].

Pru p 1 is a structural homolog to the birch pollen major allergen Bet v 1, which belongs to class 10 of pathogenesis-related proteins. Sensitization to this protein, although very frequent in northern European peach-allergic patients, is less frequently responsible for peach allergy in the Mediterranean area [13, 17].

Pru p 4, the peach profilin, is very similar to other allergenic profilins from plant foods and pollens. A high correlation between reactivity to rPru p 4 and rBet v 2, the birch profilin, has been found in sera from peach-allergic patients [18], but its clinical relevance is not consensual [1, 5].

The aim of this study was to characterize the clinical and sensitization profile of Portuguese peach-allergic patients and to establish whether these aspects have an influence in symptom severity, as well as to validate the diagnostic potential of the recombinant peach allergens available.

Material and Methods

Patients

We studied 30 consecutive patients (8 men, 22 women, age 30.4 ± 15.1 years) referred to the Immunoallergology Department of Santa Maria Hospital reporting more than 2 very suggestive and

reproducible episodes of immediate adverse reactions after the ingestion and/or contact with peach. Patients with previous history of latex allergy were excluded.

Twenty-nine age-matched control subjects observed in our department on the same day as the index patient, were also selected. All controls (12 men, 17 women, age 31.2 ± 15.7 years) were peach tolerant, 13 were sensitized to mites and 16 to pollens.

The study was performed with the approval of the local ethics committee and subjects provided informed consent.

Clinical Evaluation

The clinical evaluation included a standardized questionnaire (age; sex; type of reaction with peach; allergy to other foods or latex; past medical and familiar history) and a complete medical history to fully characterize the reported peach-induced reactions. Clinical reactivity to peach was assessed by double-blind placebo-controlled food challenge (DBPCFC), performed according to the European Academy of Allergy and Clinical Immunology (EAACI) guidelines [19], except in those patients who had positive skin prick tests (SPT), positive specific IgE to peach and a convincing history of anaphylaxis immediately after peach ingestion, in the previous year ($n = 3$). For the DBPCFC a total of 150 g of fresh peach (peel and pulp) was masked in a vehicle that consisted of orange and pineapple juices (130 ml), coconut yogurt (125 g), soluble coffee (1 small spoon), dried coconut (1 spoon) and soluble cereals (20 g). A total of 7 doses (1, 4, 10, 20, 20, 20 and 25%) were administered at 20-min intervals. Treatment and placebo were randomly administered on separate days. If the DBPCFC was negative, the patient was subsequently submitted to an open food challenge with fresh peach.

Rub tests with peach were performed in those patients who reported CU when handling peaches. The forearm was rubbed with peach peel for 30 s and examined 15 min later. Reactions were considered positive if local erythema and at least one wheal presented.

Patients were classified into 4 groups, according to the most severe reaction to peach ever experienced: OAS, localized CU, generalized urticaria and/or angioedema and anaphylaxis. For the severity analysis, the first 2 groups were classified as local symptoms and the last 2 as systemic symptoms.

Reactivity or tolerance to other foods was carefully reviewed in the medical history, but was not systematically assessed by oral challenges.

In control subjects, peach tolerance was assessed by questionnaire and negative open oral challenge test.

Skin Prick Tests

All patients underwent SPT with extracts of peach pulp, peach peel, apple pulp, apple peel, pear, plum, cherry, apricot, strawberry, almond, kiwi, banana, avocado, mango, orange, peanut, hazelnut, walnut, chestnut, pine nut, celery, melon, pea, carrot, pineapple, tomato, soy, latex, house dust mites (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Euroglyphus maynei*, *Blomia tropicalis*), storage mite (*Lepidoglyphus destructor*), and pollens of *Lolium perenne*, *Dactylis glomerata*, *Parietaria judaica*, *Artemisia vulgaris*, *Olea europea*, *Plantago lanceolata*, *Betula verrucosa*, *Platanus acerifolia* and *Chenopodium album*. Commercial extracts (BIAL-ARISTEGUI, Bilbao, Spain) were used. Tests were performed according to EAACI guidelines [20]. Saline was used as a negative control and 10 mg/ml histamine

phosphate as a positive control. Results were read after 15 min. Reactions were considered positive if the largest diameter of the wheal was 3 mm greater than the negative control.

Specific IgE Antibody Measurements

A 3-ml sample of peripheral blood was collected from all subjects. Concentrations of specific IgE antibodies to peach, rPru p 1, rPru p 3, rPru p 4 and cross-reactive carbohydrate determinants (CCD; MUXF3 glycopeptide of bromelain) were determined in all subjects by ImmunoCAP 100™ immunoassay system (Phadia, Uppsala, Sweden), according to the manufacturer's instructions. With the calibration curve now supplied with the assay system, a reliable detection of specific IgE can be made down to a concentration of 0.10 kU_A/l. The frequently used 0.35 kU_A/l cutoff was established as a limit of detection in a previous assay generation but might now be abandoned as it no longer represents a technical limitation of the assay. The 0–100 kU_A/l measuring range was used. Since measurements in the 0.10–0.35 kU_A/l interval represent true IgE sensitization and due to the external parameter of positive DBPCFC to peach in our patients, the results of the assay were considered positive if specific IgE was 0.10 kU_A/l or greater.

Statistical Analysis

Statistical analysis was performed using SPSS 13.0 for Windows software (SPSS Inc., Chicago, Ill., USA). Descriptive statistics included for qualitative variables the frequency of positive results (as percentage) and for quantitative variables means $\pm$ SD or medians and 25th–75th percentiles. Comparisons of qualitative variables were carried out by means of the χ^2 or Fisher's exact test. Comparisons of quantitative variables between allergic and nonallergic subgroups were performed by the Mann-Whitney U test. Paired correlations were calculated by the Spearman test (*r*). To compare the age at onset of pollen and food allergies in individual subjects, a Wilcoxon test for paired data was used.

To study factors associated with an IgE response to Pru p 3 (categorized by its median), a logistic regression analysis was used. For the logistic regression analysis, age and SPT mean wheal diameter values were categorized by their median and the adjusted odds ratio (OR) with its 95% confidence interval (CI) was calculated. Values were considered significant at $p < 0.05$.

Results

Clinical Presentation

Most frequently symptoms were local. OAS was reported by 36.7% of the patients and localized CU by 16.7%. Systemic symptoms were mainly generalized urticaria and/or angioedema (36.7% of the patients); nevertheless, 10.0% reported anaphylaxis after peach ingestion.

Regarding respiratory symptoms, 73.3% of peach-allergic patients and 75.9% of control subjects had rhinitis symptoms in the last 12 months ($p > 0.05$), while 53.3% of the patients and just 27.6% of the controls mentioned asthma symptoms in the last 12 months ($p < 0.05$).

Table 1. Frequency of sensitization to different pollens in peach-allergic patients with pollinosis ($n = 17$) and in control subjects with pollen allergy ($n = 16$)

Pollen type	Patients with peach allergy		Control patients (no peach allergy)		p
	n	%	n	%	
<i>Artemisia</i>	12	70.6	4	25.0	<0.01
<i>Betula</i>	2	11.8	0	0	NS
<i>Chenopodium</i>	6	35.3	1	6.3	<0.05
Grass pollen	13	76.5	14	87.5	NS
<i>Olea</i>	7	41.2	6	37.5	NS
<i>Parietaria</i>	8	47.1	2	12.5	<0.05
<i>Plantago</i>	5	29.4	1	6.3	NS
<i>Platanus</i>	1	5.9	0	0	NS

NS = Nonsignificant differences.

Nevertheless, rhinitis and/or asthma symptoms in the last 12 months were associated with less severe peach-related reactions. Respiratory symptoms were present in 87.5% of patients with local symptoms versus 50.0% of patients with systemic symptoms ($p < 0.05$) and in none of the patients with anaphylaxis ($p < 0.05$).

Pollen allergy was present in 56.7% of the patients and in 55.2% of the control subjects ($p > 0.05$). The frequency of sensitization to the tested pollens in the peach-allergic patients is presented in table 1. Polysensitization to several pollen species was present in 94% of peach-allergic patients and in 59% of control patients with pollinosis ($p < 0.05$). Additionally, peach-allergic patients had significantly more sensitizations to *Artemisia*, *Chenopodium* and *Parietaria*.

In addition to peach allergy, 70.0% of the patients reported other food allergies, most commonly to other fresh fruits (66.7%). In this group, apple allergy was the most common (56.7%), followed by cherry (13.3%) and plum (13.3%). Additionally, 20.0% of the patients reported walnut and 16.7% peanut allergy.

Peach allergy onset age was 25.3 ± 11.6 years. Pollen allergy started considerably sooner (14.9 ± 12.8 years; $p < 0.001$) but there was a significant correlation between these 2 dates ($p < 0.01$; $r = 0.62$). The onset age of other fresh fruits allergies (24.8 ± 10.5 years; $p > 0.05$) was similar and significantly correlated to peach allergy onset age ($p < 0.001$; $r = 0.92$).

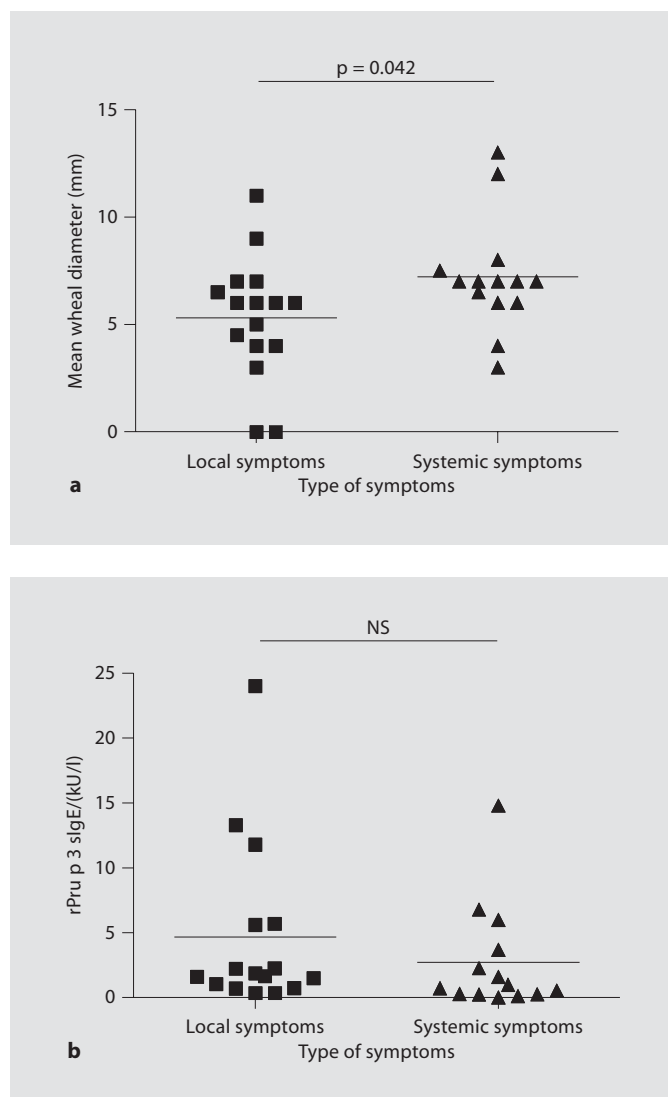


Fig. 1. a Skin prick tests to peach peel in patients with local symptoms ($n = 16$) and in patients with systemic symptoms ($n = 14$). **b** Specific IgE to rPru p 3 in patients with local symptoms ($n = 16$) and in patients with systemic symptoms ($n = 14$). Differences between groups were compared using the Mann-Whitney U test. NS = Statistically not significant; sIgE = specific IgE.

Challenge Tests

DBPCFC were performed in 27 (90%) patients, excluding the 3 patients with anaphylactic reactions. Challenges were considered positive in 22 patients and were negative in the 5 patients that referred only localized CU with peach. In these 5 patients the rub test was positive, confirming the diagnosis.

Table 2. Food SPT results in peach-allergic patients ($n = 30$)

Extract	n	%	Mean wheal diameter, mm ¹
Peach peel	28	93.3	6.3 (4.6–7.0)
Peach pulp	9	30.0	3.5 (3.0–5.3)
Apple peel	18	60.0	4.0 (3.0–5.0)
Apple pulp	3	10.0	4.0 (3.0–5.0)
Pear	2	6.7	3.5 (3.0–4.0)
Plum	14	46.7	4.0 (3.4–5.3)
Cherry	11	36.7	3.0 (3.0–4.0)
Apricot	13	43.3	3.0 (3.0–4.3)
Strawberry	5	16.7	3.0 (3.0–4.0)
Almond	13	43.3	4.0 (3.0–4.3)
Peanut	20	66.7	5.0 (4.0–6.5)
Walnut	13	43.3	4.0 (3.0–6.5)
Hazelnut	12	40.0	4.0 (3.8–5.5)
Pine nut	5	16.7	4.0 (3.0–5.5)
Chestnut	11	36.7	4.0 (3.0–7.0)
Kiwi	2	6.7	3.0 (3.0–3.0)
Banana	3	10.0	4.0 (3.0–5.0)
Avocado	4	13.3	4.3 (4.0–4.9)
Mango	1	3.3	3.0 (3.0–3.0)
Orange	2	6.7	4.5 (4.0–5.0)
Melon	3	10.0	4.3 (3.0–5.5)
Pineapple	0		
Celery	3	10.0	3.0 (3.0–3.0)
Pea	4	13.3	4.5 (3.3–5.8)
Carrot	3	10.0	4.0 (3.0–5.0)
Tomato	3	10.0	6.0 (3.0–7.0)
Soy	3	10.0	4.0 (3.0–4.0)

Extracts were obtained from BIAL-ARISTEGUI.

¹ Excluding patients with negative SPT. Figures are medians with 25th to 75th percentiles in parentheses.

Skin Prick Tests

SPT results are summarized in table 2. Twenty-eight patients (93.3%) were sensitized to peach peel and 9 (30%) to peach pulp. Peach peel sensitization was associated with more severe symptoms: 71.4% of the patients with a positive SPT to peach peel had systemic symptoms versus none of those with a negative SPT ($p < 0.05$). Moreover, peach peel SPT mean wheal diameter was correlated with severity of symptoms (7.2 ± 2.7 mm for patients with systemic symptoms versus 5.2 ± 2.8 mm for patients with local symptoms; $p < 0.05$; fig. 1a). There was also a correlation between peach peel SPT mean wheal diameter and SPT responses to apple peel ($p < 0.05$; $r = 0.554$), plum ($p < 0.05$; $r = 0.428$), apricot ($p < 0.01$; $r = 0.499$) and *Plantago* pollen ($p < 0.05$; $r = 0.416$).

Sensitization to other *Rosaceae* fruits was documented in 90.0% of patients, most frequently to plum (46.3%),

Table 3. Clinical symptoms, demographic characteristic and specific IgE results to peach and recombinant peach allergens in peach-allergic patients (n = 30) and control subjects (n = 29)

Patient	Symptoms	Sex	Age	Specific IgE, kU _A /l				
				peach	rPru p 1	rPru p 3	rPru p 4	CCD
1	CU	F	36	6.14	<0.10	5.69	<0.10	0.10
2	CU	F	13	3.54	<0.10	2.27	4.26	<0.10
3	CU	F	21	0.86	<0.10	1.06	<0.10	<0.10
4	CU	F	20	1.60	<0.10	1.66	<0.10	<0.10
5	CU	F	24	9.51	<0.10	11.80	<0.10	<0.10
CU group: % positive results (≥ 0.10 kU _A /l); n = 5				100%	0	100%	20%	20%
6	OAS	F	51	3.16	<0.10	5.61	<0.10	<0.10
7	OAS	F	18	0.74	<0.10	0.70	<0.10	<0.10
8	OAS	M	17	0.68	<0.10	0.73	<0.10	<0.10
9	OAS	M	19	3.81	<0.10	1.61	6.41	0.58
10	OAS	F	26	14.60	<0.10	13.30	<0.10	<0.10
11	OAS	F	29	3.11	<0.10	1.50	9.69	<0.10
12	OAS	F	25	2.02	<0.10	2.23	<0.10	<0.10
13	OAS	M	45	0.47	<0.10	0.37	<0.10	0.18
14	OAS	F	24	<0.10	0.12	24.00	<0.10	<0.10
15	OAS	F	81	0.29	<0.10	0.34	<0.10	<0.10
16	OAS	M	22	2.04	<0.10	1.87	<0.10	<0.10
OAS group: % positive results (≥ 0.10 kU _A /l); n = 11				91%	9%	100%	10%	18%
17	U/AE	F	27	0.20	<0.10	0.29	<0.10	<0.10
18	U/AE	M	64	0.20	<0.10	<0.10	1.08	<0.10
19	U/AE	M	24	2.83	<0.10	3.67	<0.10	<0.10
20	U/AE	M	20	0.25	<0.10	0.12	<0.10	<0.10
21	U/AE	F	47	7.41	<0.10	14.80	<0.10	<0.10
22	U/AE	M	18	1.95	<0.10	1.59	<0.10	<0.10
23	U/AE	F	24	1.56	<0.10	2.25	<0.10	<0.10
24	U/AE	F	34	0.59	<0.10	0.71	<0.10	<0.10
25	U/AE	F	19	0.27	<0.10	0.56	<0.10	<0.10
26	U/AE	F	36	5.13	<0.10	5.99	<0.10	<0.10
27	U/AE	F	22	4.65	<0.10	6.79	<0.10	<0.10
U/AE group: % positive results (≥ 0.10 kU _A /l); n = 11				100%	0	91%	9%	0
28	AN	F	36	0.71	<0.10	0.99	<0.10	<0.10
29	AN	F	29	<0.10	<0.10	0.24	<0.10	<0.10
30	AN	F	35	0.30	<0.10	0.26	<0.10	<0.10
AN group: % positive results (≥ 0.10 kU _A /l); n = 3				67%	0	100%	0	0
Total patients: % positive results (≥ 0.10 kU _A /l); n = 30				93%	3%	97%	13%	10%
Controls: % positive results (≥ 0.10 kU _A /l); n = 29				3%	0	3%	7%	3%

Specific IgE was measured with the ImmunoCAP 100 immunoassay system (Phadia). U/AE = Generalized urticaria and/or angioedema; AN = anaphylaxis.

apricot (43.3%) and almond (43.3%). Additionally, sensitization to plum was associated with more severe reactions to peach (35.7% of sensitization to plum in patients with local reactions to peach versus 64.3% in patients with systemic reactions; $p < 0.05$).

Sensitizations to peanut and tree nuts were documented in 66.7 and 76.7% of patients, respectively, but these sensitizations were not correlated to severity of clinical reactions to peach.

Specific IgE to Peach and Recombinant Peach Allergens

Specific IgE measurements for peach extract, rPru p 1, rPru p 3, rPru p 4 and CCD are summarized in table 3, both for peach-allergic and control subjects.

Applying 0.35 kU_A/l as cutoff level, 22 peach-allergic patients and none of the control subjects had positive peach-specific IgE (73% sensitivity, 100% specificity). Using a lower cutoff value of 0.10 kU_A/l, the number of positive observations increased to 28 among the peach allergics and 1 among the control subjects (93% sensitivity, 97% specificity).

Pru p 3 was found to be the major peach allergen in the population studied. Using 0.35 kU_A/l as cutoff, 24 of the peach-allergic patients and none of the control subjects had positive specific IgE to rPru p 3 (80% sensitivity, 100% specificity). When the 0.10 kU_A/l cutoff level was used, 29 peach allergics and 1 control subject had positive specific IgE (97% sensitivity, 97% specificity).

No correlation between specific IgE levels to rPru p 3 and clinical severity was observed (fig. 1b). Nevertheless, there was a significant correlation between specific IgE to rPru p 3 and peach ($p < 0.001$; $r = 0.54$). Additionally, there was a correlation between specific IgE to rPru p 3 and SPT (mean wheal diameter) to peanut ($p < 0.001$; $r = 0.622$), chestnut ($p < 0.05$; $r = 0.450$) and *Artemisia* ($p < 0.05$; $r = 0.439$).

In the logistic regression analysis, only cutaneous sensitization to apple peel (OR 4.6; 95% CI 1.0–23.1; $p < 0.05$), peanut (OR 7.3; 95% CI 1.4–38.9; $p < 0.05$) and *Artemisia* (OR 6.0; 95% CI 1.2–30.7; $p < 0.05$) were significantly associated with rPru p 3 sensitization.

Only 1 patient (3.3%) had specific IgE to rPru p 1, whereas none of the control subjects showed specific IgE to this allergen belonging to class 10 of pathogenesis-related proteins.

Four patients (13.3%) displayed specific IgE to rPru p 4, while 2 control subjects, both pollen allergic, had specific IgE to this profilin.

Only 3 patients (10.0%) and 1 control subject were sensitized to CCD.

Combining the results with the 3 recombinant allergens (rPru p 1 and/or rPru p 3 and/or rPru p 4), all patients and 3 control subjects had positive specific IgE (>0.10 kU_A/l), corresponding to 100% sensitivity and 90% specificity.

Discussion

This study characterizes clinical profile and individual allergens involved in peach allergy in Portugal. The observed peach allergy clinical manifestations were variable, with almost half the patients displaying systemic symptoms.

Two clearly different clinical response patterns have been described in *Rosaceae* fruits allergy. In central Europe, OAS prevails [21], whereas in southern Europe these foods frequently trigger more severe, even life-threatening reactions [22]. Our observed reaction pattern is more similar to the one observed in other Mediterranean countries although with a discrete increase in the prevalence of OAS [6, 10–13, 17].

The peach-allergic population studied here displayed a high prevalence of pollen allergy. Additionally, asthma and rhinitis symptoms during the past 12 months were quite above national estimates [23, 24]. The elevated prevalence of rhinitis/asthma symptoms in our patient population could in part result from an atopic selection bias. The selection criteria for the control patients (mite or pollen sensitization) explains the high prevalence of pollen allergy and rhinitis in the control group. Nevertheless, asthma was significantly more frequent in the peach-allergic group than in control subjects. In a previous study performed in Spain, more than 80% of peach-allergic patients were sensitized to pollen and developed asthma more frequently when compared to a control group [12]. Thus, the presence of peach allergy in association with pollinosis might be considered a risk factor for bronchial involvement.

Previous studies found an association between peach allergy and sensitization to pollens of several taxonomically unrelated species, namely *Betula*, *Fraxinus*, *Populus*, *Ulmus*, *Ambrosia*, *Artemisia*, *Chenopodium*, *Plantago*, *Salsola*, *Taraxacum* and *Platanus* [1, 25, 26]. In our peach-allergic patients, we documented significantly more frequent sensitization to *Artemisia*, *Chenopodium* and *Parietaria* than in the control subjects. *Parietaria* pollen is one of the most important allergenic sources in Mediterranean countries and its main allergens are LTP and profilins [27]. Nevertheless, clinically relevant cross-reactivity with peach LTP or profilins has never been demonstrated [28]. Conversely, OAS after peach ingestion in patients with *Chenopodium* allergy has been reported and cross-reactivity between peach and mugwort is well documented [15, 29].

The observed high prevalence of cutaneous sensitization and self-reported food allergy to fresh fruits and tree

nuts has been previously reported [13, 30] and could be explained by an already demonstrated high structural homology between LTP from these different foods [13, 31–34]. On the other hand, as far as we know, this is the first report of an association between sensitization to plum and clinical severity in peach-allergic patients. Nevertheless, since we have used commercial extracts and there is published evidence that certain food allergens are not stable in such preparations, this finding needs to be verified using prick to prick technique with fresh fruit.

Peach and other food allergy onset age were strongly correlated, suggesting a common culprit allergen. Additionally, pollen and peach allergy onset age were significantly correlated. However, pollen allergy typically started earlier, which could suggest that pollen may act as a primary sensitizer and contribute to the immune deviation underlying the development of peach allergy later in life.

Pru p 3 was found to be the major allergen in our peach-allergic population, with a sensitization prevalence of more than 90%. In fact, Pru p 3 has already been recognized as a crucial allergen in Spanish patients with positive DBPCFC to peach [22]. There was a significant correlation between Pru p 3 and peach specific IgE, but the diagnostic value of Pru p 3 specific IgE was slightly better. These values probably reflect the fact that this is the major allergen in our population but also support the clinical utility of this diagnostic tool.

Sensitization to Pru p 3 was also found to be significantly correlated to the magnitude of SPT reactions to peanut, chestnut and *Artemisia*, which may reflect the presence of structurally related lipid transfer proteins in these extracts. Consistent with this notion, Pastorello et al. [35] demonstrated that sensitization to mugwort in patients with peach allergy was due to a common LTP, often without clinical expression. On the other hand, other authors have documented cross-reactivity between Pru p 3 and Art v 3, resulting from primary sensitization either to peach or to mugwort pollen [15, 29].

Fernandez-Rivas et al. [36] reported that the sensitization to Mal d 3, the apple's LTP, was positively associated with presence of IgE responses to *Artemisia* and *Platanus* pollens and negatively associated with the sensitization to Bet v 1. Interestingly, in our study, the logistic regression analysis documented that cutaneous sensitization to apple peel, peanut and *Artemisia* was significantly associated with sensitization to rPru p 3.

Patients with IgE antibodies against LTP have been reported to have severe food anaphylaxis [22] and some

authors reported that LTP carries an intrinsic capacity to induce more severe food allergy [36]. In our population, although the vast majority of patients was only sensitized to LTP, the prevalence of systemic reactions was less than 50%, suggesting that sensitization to Pru p 3 alone may not be sufficient to induce severe symptoms and that other factors may contribute to the association between sensitization profile and clinical severity. In fact, patients monosensitized to LTP, but with only local or mild reactions to *Rosaceae* fruits, have already been reported both in central European [37] and in Spanish populations [17]. Nevertheless, it has been previously documented that Pru p 3 concentration is approximately 7 times higher in peel than in peach pulp [38] and in our study SPT mean wheal diameter to peach peel showed significant correlations with symptom severity.

In the peach-allergic patients studied here, we documented less than 5% of sensitization to rPru p 1, which is comparable to findings in other Mediterranean countries [22] and consistent with the low prevalence of birch pollen sensitization found in this study. Similarly, previous studies performed in Portugal documented that *Betula-ceae* family pollens represent less than 1% of Lisbon total pollen counts [39] and birch pollen affect only 4% of pollen-sensitized patients in this region [40].

In our study, sensitization to CCD and rPru p 4 was also infrequent. According to other studies, approximately 10–20% of all pollen-allergic patients are sensitized to CCD but the clinical relevance of this sensitization is controversial [41, 42]. Similarly, a complete correlation between reactivity to rPru p 4 and rBet v 2 has been found in sera from peach-allergic patients [18], but its clinical relevance is not consensual [1, 5, 22]. Of note, the profilin sensitization prevalence observed is slightly below the one reported in other southern European countries, despite the fact that more than half of our patients were sensitized to pollens and multiple plant foods [17, 22].

Overall, our results establish that Pru p 3 is the major allergen in peach allergy in Portugal and confirm the diagnostic utility of recombinant peach allergens presently at our disposal. In particular, the diagnostic value of combining the 3 recombinant allergens (rPru p 1, rPru p 3 or rPru p 4) was noteworthy, with 100% sensitivity and 90% specificity. Since peach allergy can frequently elicit systemic reactions and is a relatively simple allergen to avoid, it is of utmost importance to rapidly establish the diagnosis, conceivably with the help of these recombinant allergens.

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