ELSEVIER

Auris, Nasus, Larynx 29 (2002) 261–266

AURIS NASUS LARYNX
INTERNATIONAL JOURNAL OF ORL & HNS

www.elsevier.com/locate/anl

Birch-pollen sensitization in an area without atmospheric birch pollens

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Received 17 September 2001; received in revised form 10 December 2001; accepted 18 January 2002

Abstract

Objective: To clarify the incidence of individuals with a subclinical allergy to birch pollen and the possible allergic association between birch pollen and other allergens in areas without atmospheric birch pollen. *Methods:* Birch-pollen-specific immunoglobulin E concentration in sera, together with those for some other inhaled and ingested allergens, was measured in 409 male and 525 female patients (an average age of 58.6 years, born and raised in an area without atmospheric birch pollen) with suspicious nose and/or throat allergies. Concomitantly, types and concentrations of pollen grains in the regional air were examined. *Results:* Of 934 patients 13.2% showed birch-pollen-specific immunoglobulin E although no birch pollens were observed in the atmospheric air. The rate was relatively low in comparison with those for clinically important inhaled allergens in this area: 35.2% for Japanese cedar pollen, 24.7% for house dust and 23.2% for cypress pollen. Spearman's rank correlation analysis and logistic regression analysis revealed that birch pollen correlated strongly with apple and some foodstuffs commonly ingested by all age groups ($\rho > 0.6000$, odds ratio $>$ 27.191). *Conclusions:* A considerably large number of patients with a subclinical allergy to birch pollen exist in an area without atmospheric birch pollen. Measurement of specific immunoglobulin E to birch pollen is important even in such areas for screening and diagnosing patients with oral allergy syndrome. © 2002 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Birch pollen; Japanese cedar pollen; Cypress pollen; Ingested allergens; Allergic association

1. Introduction

Association can occur between pollen and ingested allergens. Many authors, mainly from Scandinavian countries, have reported that allergy to birch pollen (BP) is often associated with oral allergy syndrome (OAS), characterized by itching and edema when eating fresh fruits such as apple, peach and cherry, and sometimes other fruits and vegetables [1–7]. In Japan, Hokkaido, an island located in the north, is an area where birch trees grow naturally. A recent study revealed that about 26% of habitants in Hokkaido were suspected to be allergic to BP and about 16% of the patients with birch pollinosis developed OAS [8]. However, little is known about the incidence of individuals with an allergy to BP or the possible association between BP and other inhaled and ingested allergens in habitants who were born and raised in areas without atmospheric BP.

The objective of this study was to clarify the incidence of individuals with a subclinical allergy to BP and the possible association between BP and other inhaled and ingested allergens in an area without atmospheric BP by examining local patients with a suspicious nose and/or throat allergy.

We present the results, which indicate that a considerably large number of individuals with BP-specific immunoglobulin E (IgE) exist in an area without atmospheric BP, and those could possibly become allergic to

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PII: S0385-8146(02)00007-X

some unidentified ingested allergens besides those reported.

2. Materials and methods

2.1. Subjects

Subjects were 934 patients, comprising 409 males and 525 females with an average age of 58.6 years (range 4–94 years), who had been suspected of having allergic reactions in the nose and/or throat on clinical history and otolaryngologic examination between April 1996 and November 1998. All patients were born and raised in areas where birch trees do not grow naturally. The majority of patients were from this area, located in the middle of Honshu island, where Japanese cedar pollen (JCP) and cypress pollen (CP) are the dominating seasonal allergens.

2.2. Collection and analysis of atmospheric pollens

Pollens in the regional air were collected by a gravity method between January 1996 and December 1998. The Durham gravity sampler with a thinly greased slide [9] was exposed for 24 h daily on the flat rooftop of a two-storey building. One of the authors (Y.I.) who had continued examining the atmospheric pollens in this area since 1987 collected the pollen-covered slide each day and examined the types and numbers of pollen grains per square centimeter of slide surface under microscope.

2.3. Total and specific IgE determination

Using a liquid-phase test system (AlaSTAT) for the determination of allergen-specific immunoglobulin E (IgE) in sera [10], the total IgE concentration (IU/ml) and allergen-specific IgE concentration (IU/ml) for the following allergens were measured at SRL, Inc. (Tokyo, Japan): BP, JCP, CP, house dust collected inside Japan (HD6), apple and two broad screening panels of common foods (FP7 and FP8). FP7 contained hen's egg white, cow's milk, wheat, rice, peanuts and soybeans, which are often causative for allergic reaction in children. FP8 contained Indian corn, sesame, buckwheat, crab and shrimp, which cause allergic reaction mainly in adults.

Classification for the AlaSTAT allergen-specific IgE values was done as follows: 0 (<0.35 IU/ml, considered to be negative), 1 (≥ 0.35 IU/ml), 2 (≥ 1.50 IU/ml), 3 (≥ 3.00 IU/ml) and 4 (≥ 15.00 IU/ml).

2.4. Statistical analysis

Data were analyzed with the statistical software SAS/STAT Version 6.12 (SAS Institute Inc., 1998). Spearman's rank correlation coefficients (ρ) were calculated to test the degree of linear association between selected variables. We attached much importance to ρ values rather than P values which tend to fall with the increase in the number of subjects. When ρ was larger than 0.6000, the correlation between variables was interpreted to be practically significant in this study. Logistic regression analysis was also used to investigate the relationship between the ingested allergens and a set of possibly explanatory variables. For the analysis, AlaSTAT class values were grouped into binary responses (0 representing class 0 and 1 representing class 1–4). Regression coefficients (RC), P values by Wald χ^2 test and the odds ratios (OR) with their 95% confidence intervals (95%CI) were calculated, and $P<0.05$ was considered statistically significant.

3. Results

3.1. Pollens observed in the regional air

A large amount of tree pollens and a small amount of grass and weed pollens were collected mostly in the tree flowering season between January and June (Table 1). Among the trees, Japanese cedar (*Cryptomeria japonica*) was the major pollen producer in this area. Pollen from birch (*Betulae*) was not detected at all throughout the years. Instead, we observed a small amount of pollens from *Alnus*, *Corylus* and *Carpinus*, all of which are grouped into *Betulaceae* (birch family).

3.2. Appearance of allergen specific IgE

Table 1
Type and concentration of pollens observed between 1996 and 1998

Types of pollen		Annual pollen counts (/cm^2) 1996	1997	1998
Cryptomeria japonica		2524.7	5658.7	2200.0
Cupressaceae		389.1	2586.3	387.2
Pinaceae		932.6	1167.4	735.1
Fagaceae		864.4	1110.3	818.8
Betulaceae as a whole		140.4	282.2	140.9
	Betulae	0.0	0.0	0.0
	Alnus	71.6	166.8	116.7
	Corylus	3.9	3.6	6.9
	Carpinus	64.9	111.8	17.3
Ulmaceae		67.1	168.7	116.7
Other tree pollens		97.2	130.5	133.1
Polygonaceae		27.8	26.6	22.4
Gramineae		149.9	139.8	108.1
Moraceae		24.0	35.4	20.8
Ulticaceae		8.3	11.5	11.4
Compositae		74.8	35.5	10.4
Other grass and weed pollens		354.9	376.0	225.0

Table 2
Demographic characteristics of patients grouped by inhaled antigen-specific IgE assay results

Antigen-specific IgE (+ if AlaSTAT class 1 or higher)				Sex		Mean age	Mean total IgE value	Number
BP	JCP	CP	HD6	M	F	(years old)	(IU/ml)	of patients
+	−	−	−	5	4	69.9	213.0	9
+	+	−	−	5	6	72.2	114.7	11
+	−	+	−	1	1	72.5	75.0	2
+	−	−	+	2	3	62.2	1892.0	5
+	+	+	−	14	19	59.8	199.3	33
+	+	−	+	6	6	48.8	886.5	12
+	−	+	+	0	1	71.0	5.0	1
+	+	+	+	25	25	46.9	868.1	50
−	+	−	−	24	29	52.3	192.5	53
−	+	+	−	18	43	51.1	242.0	61
−	+	−	+	20	22	42.3	425.8	42
−	+	+	+	28	39	40.9	678.3	67
−	−	+	−	3	0	46.3	360.0	3
−	−	+	+					0
−	−	−	+	35	19	57.9	667.5	54
−	−	−	−	223	308	64.3	93.6	531
		Total		409	525	58.6	226.1	934

Abbreviations used: HD, house dust; M, male; F, female.

Table 2 shows the demographic characteristics of patients grouped by inhaled antigen-specific IgE assay results. The ratio of patients with positive IgE (AlaSTAT Classes 1–4) specific to JCP was highest (329/934: 35.2%) followed by those with IgE to HD6 (231/934: 24.7%), CP (217/934: 23.2%) and BP (123/934: 13.2%).

The ratio of patients with positive IgE specific to each ingested allergen was relatively low: those to FP7, FP8 and apple were 12.7, 10.3 and 6.1%, respectively. The majority of patients with IgE specific to any ingested allergens were with IgE specific to BP: namely, BP positive patients accounted for 74.8% (89/119) of FP-7 positive, 79.2% (76/96) of FP8 positive and 94.7% (54/57) of apple positive (Table 3).

3.3. Relationship between ingested allergens and explanatory variables

3.3.1. Spearman's rank correlation analysis

BP correlated strongly with apple, FP7 and FP8, and the correlation coefficients were 0.6319, 0.7083 and 0.6765, respectively. However, the other inhaled allergens (JCP, CP and HD6) did not have such a strong ($\rho > 0.6000$) correlation with ingested allergens. Only CP showed a tendency ($\rho = 0.4178$) to correlate with FP8 (Table 4).

In the group of inhaled allergens, JCP correlated strongly with CP ($\rho = 0.7725$) and tended to correlate with HD6 ($\rho = 0.4979$). On the other hand, the ingested allergens correlated strongly with each other, where ρ values were 0.6049 between apple and FP7, 0.6530 between apple and FP8, and 0.7689 between FP7 and FP8 (Table 4).

Total IgE tended to correlate with HD6 ($\rho = 0.4975$), but not with the remaining allergens. The age of patients did not correlate with the other variables (Table 4).

3.3.2. Logistic regression analysis

Apple was most strongly affected by BP, where RC = 4.6429, $P < 0.0001$ and OR = 103.841 (95%CI: 28.981–372.073). CP also significantly affected apple, where the respective figures were 1.4735, 0.0032 and 4.365 (1.636–11.642) (Table 5).

FP7 was most strongly affected by BP, where RC = 3.7635, $P < 0.0001$ and OR = 43.099 (95%CI: 23.019–80.692) (Table 5).

FP8 was also affected by BP most strongly, where RC = 3.3029, $P < 0.0001$ and OR = 27.191 (95%CI: 14.382–51.408). CP also significantly affected FP8, where the respective figures were 1.4088, 0.0005 and 4.091 (1.857–9.001) (Table 5).

P values were calculated to be less than 0.05 between some variables (age and apple, total IgE and FP7, age and FP8, total IgE and FP8) in the logistic regression analysis (Table 5). However, their OR which had approximated to 1.000 suggested that the correlation was of no clinical relevance.

None of the remaining factors (sex, HD6 and JCP) were shown to significantly affect those ingested allergens (Table 5).

Table 3
AlaSTAT class distribution of ingested allergen-specific IgE in patients grouped by inhaled allergen-specific IgE assay results

Antigen-specific IgE (+ if AlaSTAT class 1 or higher)				AlaSTAT class distribution																		Number of patients
				food panel 7-specific IgE						food panel 8-specific IgE						apple-specific IgE						
BP	JCP	CP	HD6	0	1	2	3	4	1≦	0	1	2	3	4	1≦	0	1	2	3	4	1≦	
+	−	−	−	4	5				5(55.6%)	6	3				3(33.3%)	7	2				2(22.2%)	9
+	+	−	−	3	8				8(72.7%)	4	7				7(63.6%)	8	3				3(27.3%)	11
+	−	+	−		1			1	2(100%)	1	1				1(50.0%)	2					0	2
+	−	−	+	2	2	1			3(60.0%)	5					0	4	1				1(20.0%)	5
+	+	+	−	9	19	5			24(72.7%)	10	18	4	1		23(69.7%)	16	15	1	1		17(51.5%)	33
+	+	−	+	5	6		1		7(58.3%)	8	3	1			4(33.3%)	10	2				2(16.7%)	12
+	−	+	+			1			1(100%)			1			1(100%)			1			1(100%)	1
+	+	+	+	11	18	6	13	2	39(78.0%)	13	17	9	10	1	37(74.0%)	22	18	4	5		1 28(56.0%)	50
−	+	−	−	49	3	1			4(7.5%)	53					0	53					0	53
−	+	+	−	57	3	1			4(6.6%)	56	5				5(8.2%)	61					0	61
−	+	−	+	40	2				2(4.8%)	41			1		1(2.4%)	42					0	42
−	+	+	+	61	4	2			6(9.0%)	61	5		1		6(9.0%)	67					0	67
−	−	+	−	3					0	3					0	3					0	3
−	−	+	+																			0
−	−	−	+	51	2	1			3(5.6%)	48	6				6(11.1%)	54					0	54
−	−	−	−	520	10	1			11(2.1%)	529	2				2(0.4%)	528	3				3(0.6%)	531
Total				815	83	19	14	3	119(12.7%)	838	67	15	13	1	96(10.3%)	877	44	6	6	1	57(6.1%)	934

4. Discussion

We confirmed a considerably large number of individuals with IgE specific to BP in patients with suspicious nose and/or throat allergies in a region where BP had not been collected in the atmospheric air during the study period. Far from that, it has never been reported yet in the past that BP was collected in the air of this and neighboring areas. We also confirmed that BP could correlate strongly with ingested allergens probably in a similar mechanism to that reported by many authors from areas with birch trees [1–8]. The statistical results were not changed after a regrouping of AlaSTAT allergen-specific IgE classes, namely 0–1 into 0 (negative) and 2–4 into 1 (positive). These results suggest that the direct or indirect influence of BP should be taken into account when studying OAS by fruits and vegetables even in an area virtually without atmospheric BP.

Appearance of IgE specific to BP in those patients could most probably be explained by cross-reactivity towards pollens from *Alnus*, *Carpinus* or *Corylus* in birch family and likely to other deciduous trees [11,12], as a small number of which were actually collected in the atmospheric air. However, to make the assumption more understandable, it is important to detect IgEs specific to pollens from trees belonging to families *Betulaceae*, *Corylaceae* and *Fagaceae* in these patients with IgE specific to BP.

BP could correlate with more foodstuffs than those reported. Among the foodstuffs contained in FP7, peanut was listed by Eriksson et al. [6] as obviously related to BP allergy, while the same authors listed hen's egg white and cow's milk as foodstuffs not significantly relating to BP allergy. However, the allergic association between BP and the remaining foodstuffs (wheat, rice and soybean) in FP7 has not yet been described. The present study apparently showed that BP could associ-

Table 4
Spearman's correlation coefficients between selected variables

	total IgE	BP	JCP	CP	HD6	apple	FP7	FP8
age	-0.1059	-0.0415	-0.3965	-0.2895	-0.3206	0.0281	-0.0335	-0.0139
total IgE		0.2215	0.3961	0.3644	0.4975	0.1356	0.2346	0.2442
birch pollen (BP)			0.3691	0.4321	0.2772	0.6319	0.7083	0.6765
Japanese cedar pollen (JCP)				0.7725	0.4979	0.2380	0.3114	0.3265
cypress pollen (CP)					0.3980	0.3346	0.3715	0.4178
house dust (HD) 6						0.1815	0.2410	0.2564
apple							0.6049	0.6530
food panel (FP) 7								0.7689

Correlation between variables was interpreted to be practically significant when $\rho > 0.6000$.

Table 5
Association of selected factors with ingested allergens assessed by logistic regression analysis

	apple			food panel (FP) 7			food panel (FP) 8		
	RC	p value	OR (95%CI)	RC	p value	OR (95%CI)	RC	p value	OR (95%CI)
sex	-0.2582	0.5106	0.772 (0.358-1.667)	0.3097	0.2894	1.363 (0.769-2.417)	-0.2074	0.5123	0.813 (0.437-1.511)
age	0.0291	0.0037	1.030 (1.010-1.050)	0.0052	0.5051	1.005 (0.990-1.021)	0.0207	0.0134	1.021 (1.004-1.038)
total IgE	0.0001	0.6402	1.000 (1.000-1.000)	0.0007	0.0004	1.001 (1.000-1.001)	0.0005	0.0189	1.000 (1.000-1.001)
HD6	0.3555	0.4090	1.427 (0.614-3.318)	-0.1439	0.6786	0.866 (0.438-1.711)	0.3828	0.2820	1.466 (0.358-1.667)
BP	4.6429	<0.0001	103.841 (28.981-372.073)	3.7635	<0.0001	43.099 (23.019-80.692)	3.3029	<0.0001	27.191 (14.382-51.408)
JCP	0.1162	0.8531	1.123 (0.328-3.845)	0.6084	0.1395	1.837 (0.820-4.118)	0.7270	0.1314	2.069 (0.805-5.320)
CP	1.4735	0.0032	4.365 (1.636-11.642)	0.3905	0.3034	1.478 (0.702-3.108)	1.4088	0.0005	4.091 (1.857-9.001)

Abbreviations used in this table besides those on the former tables: RC, regression coefficient; OR, odds ratio; 95%CI, 95% confidence intervals. Association was considered as significant when $P < 0.05$.

ate with one or more foodstuffs (Indian corn, sesame, buckwheat, crab and shrimp) in FP8 which have never been investigated in detail. To avoid OAS and much more severe systemic anaphylaxis, more studies should be carried out in areas where BP is the dominating cause of pollinosis.

Cross reactivity between JCP and CP is well known in Japan. Actually, in the present study 211 (64.1%) of 329 patients with IgE specific to JCP had IgE specific to CP, and only 6 (2.8%) of 217 patients with IgE specific to CP did not show IgE specific to JCP. Little is known about the incidence of OAS in patients with JCP and/or CP. There have not yet been any nation-wide investigations focusing on the incidence in Japan. A questionnaire-study by allergologists in our area revealed that 30 (7.4%) of 404 patients with manifesting cedar pollinosis reported oral allergy symptoms evoked by fruits [13]. The incidence was considerably high. Melon was the most frequently reported cause followed by peach, water melon, kiwi fruit, apple and fig, in that order [13]. However, the study was done without considering the possibly overlapping antigens like BP, a typical OAS inducer, or CP, which may potentially develop OAS as suggested in the present study. There is only a small possibility that JCP induces OAS, because it did not correlate with either apple, FP7, or FP8. Namely, correlation coefficients between JCP and those ingested allergens were low ($0.2380 \leq \rho \leq 0.3265$); moreover, JCP could not be a factor significantly affecting them by logistic regression analysis ($0.1314 \leq P \leq 0.8531$). The same could be said for the relationship between HD6 and those ingested allergens.

On the other hand, OAS might be induced in individuals with IgE specific to CP, because CP seemed to associate weakly with either of apple (OR = 4.365) and FP8 (OR = 4.091) by logistic regression analysis (Table 5). However, we rather doubt the correlation of clinical importance between CP and those ingested allergens, which was not shown by Spearman's rank correlation analysis (Table 4).

5. Conclusion

There exist a considerably large number of patients with IgE specific to BP which can possibly associate with other ingested allergens even in an area without atmospheric BP. Sensitization to BP in those patients could probably be explained by cross-reactivity between BP and pollens from trees in birch family which had been collected in the atmospheric air. Measurement of BP-specific IgE may be equally as useful as that of ingested allergen-specific IgEs for screening patients with OAS.

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