

Short communication

Allergy to foods in patients monosensitized to *Artemisia* pollen

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It is known that patients with pollinosis may display clinical characteristics caused by allergy to certain fruits and vegetables, but subjects allergic to *Artemisia* seem to show particularly peculiar characteristics. The clinical features of 84 patients with rhinitis, asthma, urticaria, and/or anaphylaxis whose inhalant allergy was exclusively to *Artemisia vulgaris* were studied and compared with a control group of 50 patients monosensitized to grass pollen. The mean age for the beginning of symptoms was 30.2 years, and this was higher than in the control group ($P < 0.05$). We found the main incidence to be in women (70.2%). Some 42.3% had family history of atopia, lower than in the control group ($P < 0.05$), while the prevalence of asthma and urticaria was significantly higher ($P < 0.05$). Food hypersensitivity was reported by 23 patients (27.3%) allergic to *Artemisia*. The foods responsible (with respective numbers of cases) were honey (14), sunflower seeds (11), camomile (four), pistachio (three), hazelnut (two), lettuce (two), pollen (two), beer (two), almond (one), peanut (one), other nuts (one), carrot (one), and apple (one). None of the patients monosensitized to grass had food allergy. CAP inhibition experiments were carried out on a single patient. Results showed the existence of common antigenic epitopes in pistachio and *Artemisia* pollen for this patient. We concluded that mugwort hay fever can be associated with the Compositae family of foods, but that it is not normally associated with other foods.

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Botanic species included in the Compositae family such as *Artemisia vulgaris* (mugwort) and *Ambrosia* (ragweed) are a known cause of pollinosis. Some cases of allergy to *Helianthus annuus* (sunflower) (1) and *Chrysanthemum* (chrysanthemum) (2) have also been published. Other allergenic species include *Taraxacum officinale* (dandelion) and *Anthemis nobilis* (camomile). There is cross-reactivity among the pollens of these species, but this aspect has not been sufficiently studied (3, 4).

Some patients sensitized to Compositae pollen may develop allergic symptoms after touching or ingesting Compositae food or tea such as camomile (5–7) or sunflower seed (8), or even unrelated foods, such as honey (9), celery, carrot, and spices (10–13). It is known that patients with pollinosis may have oral and systemic manifestations because

of allergy to certain vegetables, but subjects allergic to *Artemisia* seem to show peculiar characteristics.

The aim of this study was to analyze the clinical features of patients monosensitized to *Artemisia* and the relationship that exists with the allergy to certain foods.

Material and methods

Patients

A total of 84 patients was included in the study. All of them had attended our hospital for 3 consecutive years and had a clinical history of rhinoconjunctivitis, asthma, urticaria, and/or anaphylaxis, shown by skin test inhalant allergen sensitivity exclusive to *A. vulgaris*. In these patients, food histories were considered to be positive only if the patient had

experienced the same symptoms on at least two occasions and if the symptoms began less than 1 h after food ingestion. Only consistent clinical histories were considered. Fifty patients who were monosensitized to grass pollen, and who also attended consecutively, constituted the control group.

Skin test for aeroallergens

In all the patients, the tested allergens by prick test included pollen from grass, weeds (*Parietaria judaica*, *A. vulgaris*, *Rumex acetosella*, *Plantago lanceolata*, and *Chenopodium album*), and trees (*Olea europeae*); mites (*Dermatophagoides pteronyssinus* and *D. farinae*); molds (*Alternaria*, *Cladosporium*, and *Aspergillus*); and cat and dog epithelia (Abelló SA, Spain). We did not test with birch pollen because birch is not a common tree in our area. Positive (histamine 10 mg/ml) and negative (saline solution) controls were included. The reactions were read after 15 min and were considered to be positive if there was a wheal that measured over 3 mm in diameter.

Skin tests for food allergens

Skin testing was carried out by the prick method for natural fruit or vegetables, according to the method of Dreborg & Foucard (14), in all patients with symptoms related to these foods. We did not carry out skin tests with honey, which frequently contains Compositae pollen (15, 16), or with camomile, since cross-reactivity with *Artemisia* has already been established (6, 16).

Total and specific IgE determination

Total IgE levels and levels of specific IgE to *Artemisia* and foods involved in the clinical history were measured by the Pharmacia CAP System. The results were expressed in kU/l. Levels ≥ 0.35 kU/l were considered to be positive.

Statistical analysis

The chi-square test was used for differences between proportions of both groups (monosensitized to *Artemisia* and grass). Differences in age were analyzed by Student's *t*-test. A *P* value of 0.05 was taken as the limit of significance.

Results

Epidemiologic and clinical data

Table 1 shows the main clinical data on patients with allergy to *Artemisia* and grass pollen and their

Table 1. Clinical characteristics of patients monosensitized to grass and *Artemisia* pollen

Clinical data	Grass (n=50)	<i>Artemisia</i> (n=84)	P
Sex			
F	25 (50%)	59 (70.3%)	<0.01
M	25 (50%)	25 (29.7%)	<0.01
Age at beginning (years)	18.3	30.5	<0.001
Family history of allergy	34 (73.9%)	38 (42.2%)	<0.01
Period of symptoms			
Seasonal	50 (100%)	27 (32.2%)	<0.001
Perennial	0	57 (67.8%)	<0.001
Symptoms			
Rhinoconjunctivitis	50 (100%)	75 (89.2%)	<0.05
Asthma	18 (36%)	46 (54.7%)	<0.05
Oral allergy syndrome	0	8 (9.5%)	<0.05
Urticaria/angioedema	1 (2%)	36 (42.8%)	<0.001
Gastrointestinal	0	3 (3.5%)	ND
Anaphylaxis	0	4 (4.7%)	ND
Food allergy	0	23 (27.3%)	<0.001
Intolerance of NSAIDs	1 (2%)	4 (4.7%)	ND

NSAIDs: nonsteroidal anti-inflammatory drugs; ND = not determined.

differences. Differences can be seen both in the frequency of positive family history of atopy (42.2% and 73.9%, respectively) (*P* < 0.01) and in the age at onset of symptoms (mean ages 30.2 and 18.3 years, respectively) (*P* < 0.001). A significantly higher frequency of asthma and urticaria was also reported in patients with allergy to *Artemisia*. Furthermore, in 67.8% of these patients, the symptoms were perennial.

Food hypersensitivity was reported by 23/84 patients (27.3%) allergic to *Artemisia*, with an outstandingly high frequency of allergy to honey (16.6%), followed by sunflower seed (13%) and camomile (5.9%). Some 3.5% (3/84) of patients were allergic to pistachio. Other foods involved were lettuce, hazelnut, beer, pollen, almond, peanut, other nuts, apple, and carrot (Table 2). In contrast, none of the patients sensitized to grass presented food allergy. Urticaria was the most common symptom of food allergy (Table 3).

Skin test to foods

The positivity of the prick test with natural foods changed depending on the food tested, although generally it showed good correlation to CAP (Table 2). In the case of sunflower seeds, the test was positive in 5/11 (45.4%) patients and for pistachio in 1/3. In 10 patients monosensitized to grass, the skin test for these foods was negative.

Table 2. Patients monosensitized to *Artemisia* with food allergy. Skin test (ST) and CAP (kU/l)

Patient no.	<i>Artemisia</i> (kU/l)	Honey (kU/l) (n=14)	Sunflower seed		Camomile (kU/l) (n=5)	Pistachio		Lettuce		Hazelnut		Other foods and pollen	Total IgE (kU/l)
			ST (n=11)	(kU/l)		ST (n=3)	(kU/l)	ST (n=2)	(kU/l)	ST (n=2)	(kU/l)		
1	0.36	0.36	Negative	<0.35	—	—	—	—	—	—	—	—	18
2	0.36	—	Positive	0.49	—	—	—	—	—	—	—	Beer	22
3	3	—	Positive	1.12	—	—	—	—	—	Negative	<0.35	—	57
4	6	—	Positive	<0.35	—	—	—	—	—	—	—	—	80
5	2.47	1.25	Negative	<0.35	2	Negative	<0.35	—	—	—	—	—	180
6	0.40	—	—	—	—	—	—	Positive	0.91	—	—	—	187
7	19.5	1.85	Positive	0.85	—	—	—	—	—	—	—	Beer, pollen	274
8	11.7	—	Negative	<0.35	6.25	—	—	—	—	—	—	—	36.5
9	1.32	1.15	—	—	—	—	—	—	—	—	—	—	543
10	5.97	—	—	—	3.32	—	—	—	—	—	—	—	116
11	3.2	1.68	Positive	2.71	—	—	—	—	—	—	—	Apple	20.4
12	6.71	2.72	—	—	—	—	—	—	—	—	—	—	115
13	14	4.82	—	—	—	—	—	—	—	—	—	—	274
14	0.51	<0.35	—	—	0.38	—	—	—	—	—	—	—	130
15	18.2	3.69	Negative	<0.35	—	—	—	Positive	1.12	—	—	Pollen	44
16	13.3	0.36	—	—	—	Positive	5.85	—	—	—	—	—	150
17	2.87	—	—	—	—	—	—	—	—	Positive	2.15	*	300
18	0.7	0.36	—	—	—	—	—	—	—	—	—	—	31
19	<0.35	—	—	—	—	—	—	—	—	—	—	Carrot	180
20	0.55	<0.35	Negative	<0.35	—	—	—	—	—	—	—	—	4.5
21	6.85	0.36	—	—	—	—	—	—	—	—	—	—	115
22	15	1.78	—	—	—	—	—	—	—	—	—	—	220
23	1.36	—	Negative	<0.35	1.30	Negative	<0.35	—	—	—	—	—	54

* Almond, peanut, other nuts.

Table 3. Manifestations of food allergy in patients monosensitized to *Artemisia* (no. of cases)

Urticaria				
Sunflower seed	8	Almond		1
Honey	6	Peanut		1
Camomile	5	Other nuts		1
Pistachio	3	Carrot		1
Pollen	2	Apple		1
Lettuce	2	Beer		2
Hazelnut	2			
Oral allergy syndrome				
Honey	5	Lettuce		1
Sunflower seed	4	Pistachio		1
Camomile	3			
Gastrointestinal symptoms				
Honey	2			
Edema of glottis				
Honey	1	Pollen		1
Sunflower seed	1			
Anaphylaxis				
Honey	4	Pollen		2
Sunflower seed	2			

Total and specific IgE levels

Table 2 shows the value of CAP for foods. Some 85.7% of patients (12/14) with clinical reactions to honey and 100% (5/5) to camomile gave positive

CAP results. Positivity for sunflower seed CAP was observed in 4/5 (80%) patients with positive skin tests to sunflower seed, and in 1/3 of those with allergy to pistachio (concurring with the skin test). In five patients monosensitized to grass, the CAP for these foods was negative.

Positive specific IgE to *Artemisia* was observed in 48/54 (88.8%) patients (range 0.36–21.4 kU/l, mean 3.94 kU/l). The IgE was determined in 44 cases: range 11–1339 kU/l, mean 157 kU/l.

CAP inhibition studies

We carried out immunoinhibition in liquid phase in the CAP system, as previously described (17), to prove partial identity between pistachio and *Artemisia* pollen. We used the serum of patient 16, which was positive to *Artemisia* (13.3 kU/l) and pistachio (5.85 kU/l). We used extract of *Artemisia* pollen (Abelló SA, Madrid, Spain) as an allergen in liquid phase, and pistachio as an allergen in solid phase (ImmunoCAP, Pharmacia). The *Artemisia* extract inhibited the binding of pistachio-positive serum to solid-phase pistachio in a dose-dependent manner, obtaining an inhibition of 82% with 100 BU, 61% with 10 BU, 35% with 1 BU, and 19% with 0.1 BU. The inhibition shows that in this

patient the allergenic relation between pistachio and *Artemisia* is one of partial identity.

Discussion

A. vulgaris, an important member of the Compositae family, causes some cases of pollinosis (varying between 3 and 48%) (17–19). Nevertheless, patients usually exhibit sensitivity to other pollens; thus, it is unusual to find patients monosensitized.

In this study, we analyzed the clinical features of 84 patients monosensitized to *Artemisia*, and found some features which coincide with those previously described by May (20), such as the late age of the beginning of symptoms, lower frequency of positive family history of atopy, and persistence of respiratory symptoms in seasons of the year which do not coincide with the pollination of *Artemisia*. According to these findings, the development of sensitivity to *Artemisia* probably requires more years of exposure to its antigens than sensitivity to grass pollen. This could be the result of a lower intensity of exposure to *Artemisia* pollen. Although *Artemisia* pollinates in our area from late July to November (21), 67.8% of the patients had perennial symptoms, and in our series this could not be explained by sensitivity to other pneumoallergens. Perhaps it is explicable by the persistence of a nonspecific hyperactivity in the respiratory tract. Moreover, as far as grasses are concerned, sensitivity to *Artemisia* increases the probability of suffering from asthma ($P < 0.05$).

In our survey, 27.3% of the patients with allergy to *Artemisia* presented acute episodes of food allergy. In contrast, it is surprising not to find in the group of patients monosensitized to grasses any cases of food allergy, although previous studies have related grasses to allergies to peanut, tomato, and melon (17, 22). However, in both groups, some potential sensitization to other foods may not have been reported in the history, and therefore not tested in this experimental approach.

The study of the foods involved allows us to distinguish two groups. The first is composed of products of the Compositae family such as sunflower seeds, camomile, and lettuce. We can also include honey within this group, because it contains pollen from insect-pollinated Compositae (9, 15), and beer because it contains *Artemisia* species for flavoring (23). Twenty-one patients (25%) monosensitized to *Artemisia* presented symptoms to this group. Honey, sunflower seeds, and pollen appear to be the most important because they were involved in all cases of systemic anaphylaxis.

In particular, honey was the food which caused most allergy (16.6%), showing CAP specific IgE in

85.7% of patients with a positive history. However, it is not possible to reach any conclusions about the specificity of CAP or skin tests in food allergy since we have not studied the rate of latent sensitizations to foods in *Artemisia* pollen-allergic patients without food hypersensitivity. Clinical response varies with each variety of honey, and the amount and species of pollens it contains (15). An important number of patients (13%) had symptoms from sunflower seeds. It has been found that sunflower and *Artemisia* allergens (pollen) produce antigenic cross-reaction, but whether or not this affects the allergenic epitopes is not known (24).

Cases of anaphylaxis have been described after ingestion of camomile (5, 6) or conjunctivitis after camomile tea eyewash (7). In our series, five patients (5.9%) suffered urticaria after ingestion of camomile, with positive CAP in all of them. Upon microscopic examination, large quantities of *A. nobilis* pollen have been observed in all commercially available camomile teas tested so far (6). Cross-reactivity between *Matricaria* and *Artemisia* pollen could explain these reactions.

Lettuce also belongs to the Compositae family, and we found two patients (2.38%) sensitized to this food. Moreover, two patients had urticaria after ingestion of beer. In a sample of patients, most of whom were sensitized to *Artemisia*, several cases of allergy to beer have been described (18). On the other hand, seven patients (8.3%) presented acute episodes of facial angioedema after contact with chrysanthemums. Studies have shown cross-reactivity of this flower with *Artemisia* (3).

The second group of foods involved is not botanically related to the Compositae. A significantly lower number of patients (9.5%) were allergic to pistachio, hazelnut, almond, peanut, and other nuts. An association of allergy to dried fruits with *Artemisia* has been suggested by other authors (18), but monosensitized patients were not studied. The existence of vegetable panallergens such as profilins (25) or other common antigens could explain these reactions. In this respect, an 18-kDa protein from hazelnut shares allergenic epitopes with *Bet v* I (26). Our CAP inhibition experiments with *Artemisia* pollen and pistachio suggest the presence of at least some epitopes to both allergens. Since only one patient was studied, general conclusions cannot be drawn.

Several studies relate allergy to *Artemisia* with hypersensitivity to celery, carrot, and spices belonging to the Umbeliferae family (10, 11, 13). In our series, only one patient was sensitized to carrot (CAP 8.16 kU/l), and none to celery or spices. Consequently, we do not think that associations in patients sensitized to *Artemisia* are common.

The relationships described above allow us to predict that the Compositae group will be easily distinguishable from other associations between fruits and vegetables and different pollen types (17, 27–29). The relationship with pistachio is less clear, and our results must be regarded as preliminary.

In conclusion, we found that associations between mugwort hay fever and fruits and vegetables are important for foods belonging to the Compositae family and foods which contain pollen from these plants, but that such an association is infrequent in other foods. Although some authors have found a relationship between *Artemisia* and carrot, celery, and spices, there is little clinical relevance in patients monosensitized to *Artemisia*.

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