Cypress Pollen Allergy in a Mediterranean Area

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The prevalence of *Cupressaceae-Taxodiaceae* pollen allergy has increased in the Mediterranean area in recent years [1,2]. In order to assess the impact of this allergy in our area, we carried out a prospective, cross-sectional study at Terrassa Hospital, Vallés Occidental, Barcelona, Spain. The hospital is located in an urban district with more than 800 000 inhabitants. The objectives of this study were as follows: (*1*) to determine the annual incidence of sensitization to *Cupressaceae* pollen in the catchment population; (*2*) to describe the clinical characteristics and the molecular profile of sensitization; (*3*) to test the diagnostic performance of pollen extracts in skin prick testing (SPT), serum sIgE testing, and nasal provocation testing (NPT) for the diagnosis of cypress allergy.

After signing the informed consent document, patients with symptoms suggestive of respiratory allergy and a positive SPT result to ≥1 of the 3 extracts of cypress pollen tested (*Cupressus sempervirens*, *Cupressus arizonica*, and *Juniperus ashei* [Stallergenes]) were included in the study between February 1, 2010 and January 31, 2011. Demographic and clinical data were collected. Serum sIgE to the same 3 species (ImmunoCAP) and to molecular allergens (ImmunoCAP ISAC) was measured. NPT was performed with a *J ashei* extract (Stallergenes).

Symptoms and medication use were recorded in a diary, and cypress pollen concentrations were provided by Xarxa Aerobiologica de Catalunya (Aerobiology Network of Catalonia). A positive SPT result with *Cupressaceae* pollen and concordant respiratory symptoms were considered the gold standard. The statistical analysis was performed using SAS 9.4 and SAS Enterprise 6.1.

A total of 1278 new patients were evaluated. The incidence of sensitization to *Cupressaceae* pollen assessed by SPT was 15.1%, which decreased to 13.7% and 11% when the assessment was based on positive sIgE to complete extract and individual allergens, respectively.

The characteristics of *Cupressaceae* pollen–sensitized patients and the control group (sensitized to other aeroallergens) are shown in the Table, which highlights statistically significant

Table. Characteristics of *Cupressaceae* Pollen–Sensitized Patients and Control Group[a]

			Cupressaceae Pollen–Sensitized (n=122) With Symptoms n=26	Control group (n=530) With Symptoms n=503
Mean (range) age, y	Total		31.1 (7-67)	27.3 (7-73)
	Adults		36.3 (16-67)	34 (16-73)
	Children		11.2 (7-15)	10.8 (7-15)
Sex	Female	Adult	43.4% (46)	37.3% (198)
		Children[a]	13.2% (7)	11.6% (64)
	Male	Adult	56.5% (51)	31.3% (166)
		Children[a]	26% (18)	19.6% (102)
			P=.04	
Atopy	Total		44.2% (54)	45.2% (240)
	Adult		40.6% (39)	42.3% (140)
	Children		42.3% (15)	70.7% (100)
				P<.0001
Mean (range) age at onset of symptoms, y			22 (1-66)	18.4
Symptoms	Rhinitis		30.7% (8)	49.7% (250)
	Rhinoconjunctivitis		57.6% (15)	13.7% (69)
	Asthma		3.8% (1)	24.2% (122)
	Rhinitis or rhinoconjunctivitis + asthma		3.8% (1)	11.5% (58)
	Rhinitis or rhinoconjunctivitis + spasmodic cough		3.8% (1)	0.79% (4)
Sensitization to foods			18% (22) *P*=.0005	7.3% (39)
Median duration of allergic disease, y	Adults		7	ND
	Children		2	ND
Monosensitization			2.4% (3)	36.4% (193) *P*<.0001
Median total IgE			5.3	5.1

Abbreviation: ND, no data.
[a]Statistically significant *P* values are shown.

differences between the groups, as follows: (*1*) male gender was more frequent in the *Cupressaceae* pollen–sensitized children (*P*=.04); (*2*) a family history of atopy was significantly more common in children than in adults in the control group (*P*<.0001); (*3*) sensitization to foods was significantly more frequent in the *Cupressaceae* pollen–sensitized patients (*P*=.0005), especially those sensitized to peach (9/122, 7.3%); and (*4*) monosensitization was more frequent in the control group (*P*<.0001). *Cupressaceae* pollen–sensitized patients were predominantly residents in urban areas (88.5%), where they had lived for an average of 22.1 years (range, 1-63 years).

Most patients were polysensitized (97.6%), and the most frequently detected concurrent sensitizations were to grass and olive pollen.

Wheals and sIgE values induced by *C arizonica* and *J ashei* were wider than those induced by *C sempervirens*.

Most of the patients were asymptomatic (72%), and the most frequent symptoms were rhinoconjunctivitis (16%) and rhinitis (9%).

The molecular profiles of *Cupressaceae* pollen–sensitized patients revealed the following: (1) sensitization to cross-reactive food allergens (lipid transfer protein, 29%; seed storage proteins, 16%) and low sensitization to profilin (9%), thaumatin (7%), and polcalcin (2%); and (2) a high percentage of sensitization to CCD-bearing proteins (Cup a 1, 91.4%; Cry j 1, 67%; Cyn d 1, 51%; Ole e 1 [known as nOle e 1 in ISAC112 in 2013; nowadays known as rOle e 1], 46.8%; Phl p 4, 30.8%; Pla a 2, 28.7%; Jug r 2, 11.7%; and MUFX3, 6.3%). Positivity to Ole e 1 (*P*=.025) and Jug r 2 (*P*=.04) was significantly associated with asymptomatic sensitization to *Cupressaceae*.

A total of 71 specific NPTs were carried out: 47 were positive (13 were allergic), 9 were negative, and 15 were positive to saline serum (nasal hyperreactivity). NPT was highly sensitive (100%) but not very specific (15%), except for the concentration of 1 IR (69%).

The incidence of sensitization to *Cupressaceae* and to the individual allergenic components in SPT was lower than

published for other geographical areas, probably owing to the greater presence of cypress trees in these areas [3].

Sensitization to *Cupressaceae* pollen seems to develop at older ages than with other pollens and is always more common in adults (around 30 years [4]).

Sensitization to peach in this study was similar to that described in patients sensitized to cypress pollen from southern France [5]. An important association was recently reported between cypress pollinosis, levels of pollen exposure, and peach allergy due to sensitization to peamaclein (Pru p 7) in a French population. The authors reported that cypress pollen extract completely outcompeted IgE binding to Pru p 7 [6]. In accordance with previous studies, monosensitization to cypress pollen was exceptional in our population [7].

All patients sensitized to nCry j 1 were also sensitized to nCup a 1, which is consistent with the high cross-reactivity reported between both allergens [8]. Sensitization to polygalacturonase from plane tree pollen, nPla a 2, was higher than that described in a Central European population with pollinosis (15.5%) [9] and may be attributable to genuine sensitization to *Platanus* pollen in a region with high exposure, as well as to cross-reactivity either with *Cupressaceae* polygalacturonase or with CCD-bearing proteins.

In our study, sensitization to lipid transfer protein was almost double that detected among patients with pollen allergy (26.6% vs 12.3%) [10], but similar in patients with food allergy in Madrid (24% vs 37%) [10].

The lack of symptoms observed in our study could be attributed to a diagnosis in a preclinical phase (patients complain of symptoms related to their sensitization to other pollens before symptoms related to *Cupressaceae* pollen develop) or to a genuinely innocent sensitization.

The performance and interpretation of NPTs were affected by the number of patients who underwent the test, which was small, and by the fact that the allergenic extract used (purified *J ashei*, predominantly monomeric) may not represent the native allergen and may induce different types of clinical reactivity.

In summary, in the present study, the incidence of sensitization to *Cupressaceae* pollen was 15%, even though most of the sensitized patients were asymptomatic and polysensitized. *C arizonica* pollen extract proved to be the most useful for diagnosis of sensitization. Most patients were sensitized to nCup a 1, lipid transfer protein, and CCD-bearing proteins, with a low prevalence of sensitization to profilins and polcalcins. Given that NPT showed high sensitivity with low specificity, it may help in the diagnosis of pollinosis to *Cupressaceae* in selected cases. Differences with other geographical regions highlight the need for more local studies.

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Conflicts of Interest

Dr. Castillo received a grant from the Foundation of the Spanish Society of Clinical Allergy and Immunology (SEAIC) during the conduct of the study. The allergenic extract used (purified *Juniperus ashei* standardized by Jun a 1) for the nasal provocation tests was provided free by Stallergenes SA.

Dr. Olga Luengo has no conflict of interests to disclose.

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