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1. Bjorksten F, Halmepuro L, Hanuksela M, Lahti A. Extraction and properties of apple allergens. *Allergy*. 1980;35:671–677.
2. Bradford MM. A rapid and sensitive method for the quantification of microgram quantities of protein utilizing the principle of protein-dye binding. *Anal Biochem*. 1976;72:248–254.
3. Kauppinen K, Kousa M, Reunala T. Aromatic plants: a cause of severe attacks of angio-edema and urticaria. *Contact Dermatitis*. 1980;6:251–254.
4. Cordobés-Durán C, García-Menaya JM, Lombardero M, Ledesma A, Bobadilla P. Detection of a 12-kilodalton lipid transfer protein allergen in parsley. *J Invest Allergol Clin Immunol*. 2007;17:282–283.
5. Pigatto PD, Bigardi A, Fumagalli M, Legori A, Altomare GF. Ig-E-mediated contact and generalized urticaria from *Eruca sativa*. *Contact Dermatitis*. 1991;25:191–192.
6. Liccardi G, Salzillo A, Mistrello G, Roncarolo D, D'Amato M, D'Amato G. Intraoral and respiratory allergy to *Eruca sativa* (Cruciferae family) in a subject with sensitization to pollen allergens. *J Allergy Clin Immunol*. 1998;101:559–560.
7. Asero R, Monsalve R, Barber D. Profilin sensitization detected in the office by skin prick test: a study of prevalence and clinical relevance of profilin as a plant food allergen. *Clin Exp Allergy*. 2008;38:1033–1037.

SEASONAL EOSINOPHILIC BRONCHITIS DUE TO ALLERGY TO CUPRESSUS ARIZONICA POLLEN

Nonasthmatic eosinophilic bronchitis (NAEB) is characterized by chronic cough and sputum eosinophil counts higher than 2.5% of total cells in the absence of reversible airflow limitation and airway hyperresponsiveness.¹ Sporadic cases of work-related NAEB have been reported,² the diagnosis being confirmed when significant increases in eosinophils counts in induced sputum are found after exposure to the offending agent (either in the workplace or after specific inhalation challenge [SIC]) compared with baseline.² However, detailed profiles of sensitizing allergens have not been reported, and the cause usually remains unknown.

Two nonsmoking patients (a 34-year-old woman and a 27-year-old man) who live in the suburbs of Madrid, Spain, were referred to our institution for sneezing, nasal congestion, rhinorrhea, and persistent, dry cough, without dyspnea or wheezing. The symptoms had been present within the last 3 to 4 years, from late December until March (pollination period for *Cupressus arizonica* in Spain), and the patients remained asymptomatic the rest of the year.

Both patients had normal chest radiograph results and negative Mantoux test results. Other common causes of chronic cough, such as gastroesophageal reflux, were ruled out. Skin prick tests with common aeroallergens (ALK-Abelló, Madrid, Spain) and total and specific IgE measurements (Phadia, Uppsala, Sweden) were performed. Spirometry, methacholine challenges, fraction of exhaled nitric oxide (FeNO) measurements (NioxMino; Aero-

crine AB, Solna, Sweden), and sputum induction were performed both during and outside the pollination period.

Both patients were monosensitized (positive skin prick test result and positive specific IgE determinations) to *C arizonica* pollen (2.19 and 1.76 kU/L, respectively). Total serum IgE measurements were 87 and 25 kU/L, respectively. Spirometric parameters were always normal (patient 1: forced vital capacity [FVC], 3.15 L [105%]; forced expiratory volume in 1 second [FEV₁], 3.1 L [119%]; FEV₁/FVC, 98%; patient 2: FVC, 6.15 L [115%]; FEV₁, 4.91 L [115%]; FEV₁/FVC, 79%), and no changes were observed after inhalation of salbutamol, 400 µg (administered via metered-dose inhaler), either during or outside the pollination season. Methacholine challenges, performed using the dosimeter method, produced negative results in February and September (provocative concentration inducing a 20% decrease in FEV₁, >16 mg/mL). Cough frequency score, which was obtained using a visual analog scale (0 = never cough, 10 = cough all day), was correlated with the Cupressaceae pollen load in 2009 (0 score out of season in both patients and 6 and 5 score in patient 1 and patient 2, respectively, during the 2009 *C arizonica* pollen season). The Cupressaceae annual total pollen count during 2009 was 4,500 grains/mm³.

Sputum samples were collected after inhalation of hypertonic saline and then processed following European Respiratory Society recommendations³ within 2 hours after induction, as previously described.⁴

In the second patient, the sputum induction performed in February was unsuccessful, so we performed SIC with *C arizonica* pollen extract (ALK-Abelló) out of its pollination season. A sputum sample was obtained and processed the previous day, as the baseline reference. Twenty-four hours after the SIC, a methacholine test was repeated, followed by a new sputum induction. FeNO measurements were performed before and 24 hours after the SIC, previous to pulmonary function and airway hyperresponsiveness testing. The patient developed dry cough at the end of the challenge, but neither asthmatic response nor change in airway responsiveness to methacholine was observed within the 24 hours after the SIC. The FeNO measurements and the percentage of eosinophils in induced sputum during and outside the *C arizonica* season (patient 1) and before and after the SIC with *C arizonica* extract (patient 2) are summarized in Table 1.

SIC with *C arizonica* pollen extract produced negative results in 2 control nonatopic subjects and in 2 patients with rhinoconjunctivitis who were sensitized to *C arizonica* pollen.

To our knowledge, this is the first report of sensitization to a common pollen (*C arizonica*) as a causative agent of NAEB. The cough totally subsided in both patients after treatment with inhaled corticosteroids (budesonide, 400 µg twice daily) during *C arizonica* pollination season the following year.

Table 1. Comparison of FeNO and Eosinophils in Sputum With or Without Exposure to *Cupressus arizonica* Pollen

	FeNO, ppb		Eosinophils in induced sputum, %	
	Out of season	Exposure to pollen	Out of season	Exposure to pollen
Patient 1	24	68	2.3	33 (season)
Patient 2	14	41	1	8.3 (SIC)

Abbreviations: FeNO, fraction of exhaled nitric oxide; SIC, specific inhalation challenge.

Genera of the Cupressaceae family (*Cupressus*, *Juniperus*, and *Cryptomeria*) are an important cause of allergic disorders in various geographical areas, including North America, Mediterranean countries such as France,⁵ Italy, Israel,⁶ and Spain,⁷ or Japan.⁸ A study performed by Sato et al⁸ found that levels of specific IgE to cedar pollen (*Cryptomeria japonica*) was significantly higher in patients with NAEB than in those with bronchial asthma, suggesting the implication of cedar pollen in the etiopathogenesis of NAEB, but an etiologic relationship was not demonstrated. Moreover, the allergenic load has recently increased, given the extensive use of Cupressaceae plants as hedges in residential areas or for ornamental purposes.⁵

Therefore, in geographical areas where this pollen is predominant, NAEB should be considered in the differential diagnosis of persistent cough during wintertime.

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1. Gibson PG, Dolovich J, Denburg J, Ramsdale EH, Hargreave FE. Chronic cough: eosinophilic bronchitis without asthma. *Lancet*. 1989;1:1346–1348.
2. Quirce S. Eosinophilic bronchitis in the workplace. *Curr Opin Allergy Clin Immunol*. 2004;4:87–91.
3. Efthimiadis A, Spanevello A, Hamid Q, et al. Methods of sputum processing for cell counts, immunocytochemistry and in situ hybridisation. *Eur Respir J*. 2002;20(suppl 37):S19–S23.
4. Sastre B, Fernández-Nieto M, Mollá R, et al. Increased prostaglandin E2 levels in the airway of patients with eosinophilic bronchitis. *Allergy*. 2008;63:58–66.
5. Charpin D, Hughes B, Mallea M, et al. Seasonal allergic symptoms and their relation to pollen exposure in south-east France. *Clin Exp Allergy*. 1993;23:435–439.
6. Bousquet J, Knani J, Hejjaoui A, et al. Heterogeneity of atopy I: clinical and immunological characteristics of patients allergic to cypress pollen. *Allergy*. 1993;48:183–188.
7. Subiza J, Jerez M, Jimenez JA, et al. Allergenic pollen pollinosis in Madrid. *J Allergy Clin Immunol*. 1995;96:15–23.
8. Sato S, Saito J, Sato Y, et al. Clinical usefulness of fractional exhaled nitric oxide for diagnosing prolonged cough. *Respir Med*. 2008;102:1452–1459.