

Sensitization to a nonnative plant without exposure is a marker of panallergen sensitization



Mary Beth Hogan, MD^a,

Gayle L. Allenback, MS, MPH, Gstat^b, Vonita Chawla, MD^a,

Nilima Mehta, MSPH^a, Greg Plunkett, PhD^c, and

Nevin W. Wilson, MD^a

Clinical Implications

- Sensitization to nonnative plants demonstrates cross-reactivity toward panallergens such as profilin. Using nonnative plants as clinical markers for panallergen sensitization may identify children at risk for polysensitization, which could eventually lead to safer, more effective immunotherapy formulation for polysensitized patients.

TO THE EDITOR:

Panallergens are molecules that are highly homologous across plant species and represent potential cross-reacting allergens. Panallergens play a vital role in cellular processes, which explains their conserved occurrence throughout the plant kingdom.¹ Profilin, a cellular actin-binding protein, and polcalcin, a calcium-binding protein, have been identified among other panallergens. We performed a case series analysis of 126 patients (2-66 years; mean age, 14 years; 60.3% males) who attended the University of Nevada, Reno Allergy Clinic (see Table 1 for summary of patient characteristics). Our study aimed at identifying sensitization to a nonnative tree—*Syagrus romanzoffiana* (Queen Palm)—among a native population not exposed to Queen Palm because geographical and climatic conditions do not support its growth in the Great Basin region.² Therefore, theoretically, in our stable and predominantly pediatric population, defined as not previously living outside the Great Basin, Queen Palm would not elicit sensitization.

Patients with allergic rhinitis were skin tested (DermaPik) to regional pollens, with saline and histamine controls. Positive skin test results were defined as a wheal and flare of at least one-half the size of the histamine control and larger than the saline control.² Our patients tend to have continuous symptoms throughout the pollen season, likely from daily exposure to high winds without rain to remove seasonal pollen from the desert floor. Queen Palm extract (ALK-Abelló, Round Rock, Texas) was also included, with profilin quantity determined by ELISA inhibition assay, because it has not been previously characterized. *Polysensitization* was defined as sensitization to 3 or more aeroallergens, to be consistent with our previous study and with the allergy literature.^{2,3} Institutional review board exemption was obtained (no. E12-074).

The major allergen in palm tree pollens is profilin, Phod 2, with the most studied species being Date Palm, *Phoenix dactylifera*,⁴ so this was used as the profilin source in the ELISA inhibition assay. Minor palm allergens previously identified

include a 40kD protein of unknown function and a 90kD protein (galactosidase).⁵ Profilin (Coc p 2) quantity in the Queen Palm, *Syagrus romanzoffiana* (also called *Cocos plumosa*), extract used in this study was determined to be 10 µg/mL. Analyses of the skin test reactivity of patients showing sensitization to Queen Palm are presented in Table II. Sensitization to Queen Palm was noted in children 7 years or younger, who were likely sensitized to profilin. This recognition of a nonnative tree species increased greatly with the age of the child (Table II), with a significant increase in sensitization to Queen Palm from the 7 year or younger age group to the 8- to 18-year-old age group ($P < .001$). However, the percentage of adults (age range, 19-66 years) likely sensitized to profilin (Queen Palm) was less than that seen in the older children (Table II), suggesting possible age differences in the population presenting for rhinitis evaluation.

We also found that sensitization to Queen Palm was significantly associated with sensitization to each of the other 36 aeroallergens tested ($P < .001$), including allergenic weeds, grasses, and trees common to the Nevada Great Basin region² (for list of aeroallergens included, see Table E1 in this article's Online Repository at www.jaci-inpractice.org). Increasing profilin sensitization with age was also "linked" to increasing aeroallergen polysensitization. Seventy percent of our patients were polysensitized to a mean number of 16.2 aeroallergens (Table II). When classified by type of aeroallergen, 61.6% of patients were polysensitized to weeds, 60.3% were polysensitized to grasses, and 57.9% were polysensitized to trees. However, the subset of patients positive for Queen Palm (and likely profilin) was sensitized to a mean number of 29.5 aeroallergens. In contrast, patients who did not show sensitization to Queen Palm were only sensitized to an average of 7.4 aeroallergens. This demonstrates that patients with this possible profilin sensitization were polysensitized to a significantly higher number of aeroallergens than those who were not sensitized to Queen Palm ($P < .001$). Children 7 years or younger were less polysensitized, compared with children aged 8 to 18 years (45.7% vs. 81.8%, respectively; $P < .001$). Older children aged 8 to 18 years also had a significantly higher mean number of positive aeroallergens than did younger children aged 7 years or less (21.0 vs. 8.1 years, respectively; $P < .001$). A significant association was found between the presence of allergic rhinitis and polysensitization ($P < .001$), but no association was found between the presence of asthma or oral allergy syndrome and polysensitization.

Fasce et al⁶ previously reported early pollen sensitization, with 88% of children ($n = 340$) polysensitized at the age of 11 years, and 59% of these sensitized as early as 3 years of age. In our previous study,² more than 50% of children aged 2 to 3 years were sensitized to at least 1 aeroallergen, which increased with age up to 75% in children aged 6 to 7 years. In our present study, potential profilin sensitization was associated both with increasing age and with aeroallergen polysensitization.

We have shown that Queen Palm contains a significant amount of profilin, a known panallergen. Second, our patients, who were native to the Great Basin region, were found to be sensitized to a nonnative tree (containing profilin) that cannot grow in the high desert of Nevada. Similarly, Plunkett et al⁷ studied Queen Palm sensitization (along with 14 regional

TABLE I. Demographic characteristics and atopic conditions in our patient population

Characteristic	n (%) of patients
Age (y)	
0-7	35 (29.4)
8-18	66 (55.5)
19-66	18 (15.1)
Sex	
Male	76 (60.3)
Female	47 (37.3)
Atopic conditions	
Asthma	51 (40.5)
Allergic rhinitis	100 (79.4)
Oral allergy syndrome	14 (11.1)
Anaphylaxis	1 (0.8)

TABLE II. Queen of Palm sensitization, polysensitization, and mean number of aeroallergens, by age group and atopic condition

Patient Characteristic	Queen of Palm sensitization (%)	Polysensitization (≥3 aeroallergens) (%)	Mean no. of positive aeroallergens
By age group (y)			
0-7 (n = 35)	17.1	45.7	8.1 ± 11.4
8-18 (n = 66)	53.0	81.8	21.0 ± 14.3
19-66 (n = 18)	33.3	66.7	14.3 ± 12.8
By atopic condition			
Asthma	39.2	66.7	15.8 ± 14.7
Allergic rhinitis	50.0	88.0	20.4 ± 13.1
Oral allergy syndrome	42.9	78.6	19.9 ± 14.9
Total sample (n = 126)	39.7	69.8	16.2 ± 14.3

pollens) and antiprofilin IgE via ISAC microarray testing in 65 patients. More than 30% of patients were sensitized to Queen Palm and demonstrated antiprofilin IgE. Seventy-three percent of patients with Queen Palm skin test sensitization and antiprofilin IgE were sensitized to 8 other pollens, compared with only 22% of those patients negative to Queen Palm by skin test and IgE microarray. Both studies suggest that polysensitization to other pollens is closely linked with a probable sensitization to profilin. A highly conserved conformational structure among pollen profilins may contribute to these similar findings.

This pattern of sensitization to a nonnative profilin-containing tree demonstrates cross-reactivity to panallergen-like molecules. The major panallergen component of palm extract is profilin, and the large quantity of this panallergen noted in Queen Palm extract suggests that this was the most likely source of panallergen cross-reactivity. It is possible that polcalcin or PR-10 like proteins could be minor components of our findings and also contribute to cross-reactive skin test results of nonnative species. However, a

large number of the pollens to which the patients were skin tested are known profilin-containing pollens (eg, birch, timothy, sagebrush, and ragweed).² Thus, we have shown that using a nonnative tree that contains a panallergen may be useful as a clinical marker of polysensitization associated with that particular panallergen.

In-depth investigation into panallergens and polysensitization may have future treatment implications, especially in populations at risk of acquiring sensitization at an early age.⁷ For polysensitized patients, new studies that examine the total quantity of profilin required for an immune response to immunotherapy, without overdosing profilin components, may further help to improve safety while retaining efficacy. Our study has shown that a nonnative plant may be a clinically useful marker for potential profilin sensitization and polysensitization. This finding poses exciting possibilities for future clinical studies to evaluate panallergen identification, formulation, and utility in immunotherapy treatment of polysensitized patients.

^aDepartment of Pediatrics, University of Nevada School of Medicine – Las Vegas, Las Vegas, Nev

^bOffice of Medical Research, University of Nevada School of Medicine – Las Vegas, Las Vegas, Nev

^cALK-Abello, Inc, Round Rock, Texas

Conflicts of interest: G. Plunkett is employed by ALK, Inc. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication September 23, 2015; revised February 24, 2016; accepted for publication February 29, 2016.

Available online April 7, 2016.

Corresponding author: Mary Beth Hogan, MD, Department of Pediatrics, University of Nevada School of Medicine, 1524 Pinto Lane, Third Floor, Las Vegas, NV 89106. E-mail: mbhogan@medicine.nevada.edu.

2213-2198

© 2016 American Academy of Allergy, Asthma & Immunology

<http://dx.doi.org/10.1016/j.jaip.2016.02.017>

REFERENCES

- Hauser M, Roulias A, Ferreira F, Egger M. Panallergens and their impact on the allergic patient. *Allergy Asthma Clin Immunol* 2010;6:1.
- Wong V, Wilson NW, Peele K, Hogan MB. Early pollen sensitization in children is dependent upon regional aeroallergen exposure. *J Allergy (Cairo)* 2012;2012: 583765.
- Miguera M, Davila I, Frati F, Azpeitia A, Jeanpetit Y, Lheritier-Barrand M, et al. Types of sensitization to aeroallergens: definitions, prevalences and impact on the diagnosis and treatment of allergic respiratory disease. *Clin Translational Allergy* 2014;4:1-8.
- Radauer C, Willeroider M, Fuchs H, Hoffmann-Sommergruber K, Thalhammer J, Ferreira F, et al. Cross-reactive and species-specific immunoglobulin E epitopes of plant profilins: an experimental and structure-based analysis. *Clin Exp Allergy* 2006;36:920-9.
- Postigo I, Guisantes JA, Negro JM, Rodriguez-Pacheco R, David-Garcia D, Martinez J. Identification of 2 new allergens of *Phoenix dactylifera* using an immunoproteomics approach. *J Investig Allergol Clin Immunol* 2009;19:504-7.
- Fasce L, Tosca MA, Olcese R, Milanese M, Erba D, Ciprandi G. The natural history of allergy: the development of new sensitizations in asthmatic children. *Immunol Lett* 2004;93:45-50.
- Plunkett G, Barber D, Villalobos EM, Jacobs JS, Hallett JS, Mostofi T, et al. Skin prick tests to multiple pollens and prevalence of IgE specific to profilin. *Allergy Asthma Clin Immunol* 2014;10:A12.

TABLE E1. Great Basin aeroallergens available in skin test panel

Weeds	Grasses	Trees	
Dock	Timothy	Privet	Birch
Pigweed	Brome	Mountain cedar	Olive
Russian thistle	Bermuda	Sycamore	Ash
Saltbush	Saltgrass	Pine	Aspen
Sagebrush	Johnson	Elm	Willow
Western ragweed	Alfalfa	Ailanthus	Cottonwood
Tall and short ragweed		Locust	Pecan
Rabbitbush		Maple	Walnut
Marsh elder		Sweet gum	Alder
Plantain		Mulberry	Oak

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.