



Letter

Association of eosinophilic esophagitis and food pollen allergy syndrome

Eosinophilic esophagitis (EoE), an inflammatory condition of the esophagus, is an important cause of dysphagia. The fibroinflammatory response, if not addressed, may result in advanced disease.¹ Initially thought to be rare, the incidence of EoE is increasing, currently ranging from 1.3 to 9.5 per 100,000 in various series.^{1,2} Despite the increased incidence, the pathophysiology of this disease is not well understood.³ EoE is associated with a high sensitization rate to both foods and aeroallergens,⁴ although the role sensitization plays is not completely clear.

Profilin and PR-10 are allergens that have a high level of homology between pollens and food proteins.⁵ Recently, patients with EoE were found to have a high prevalence of sensitization to common food pollen allergens, including profilin and PR-10,⁶ yet the clinical relevance of these sensitizations is unknown. Sensitization to these shared allergens is the underlying mechanism of pollen food allergy syndrome (PFAS), also known as oral allergy syndrome.⁷ In this study, we have, for the first time, evaluated the prevalence of symptomatic PFAS in a large cohort of patients with EoE.

Records of adult patients (18 years and older) diagnosed with EoE at Rush University and Northwestern Medicine Allergy-Immunology clinics between January 2005 and December 2014 were reviewed. The diagnosis of EoE was based on clinical symptoms related to esophageal dysfunction plus a minimum of 15 eosinophils per high-power field on esophageal biopsy (performed after at least 8 weeks of treatment with a proton pump inhibitor), in the absence of eosinophilic infiltration in the rest of the gastrointestinal tract and other organs, and a lack of other causes for eosinophilic inflammation.³ All patients were tested for aeroallergen sensitivity (a common group of trees, grasses, and weeds local to Illinois, house dust mite, molds, cockroach, cat, and dog). The control group consisted of age- and sex-matched patients without a diagnosis of gastrointestinal reflux disease or symptoms of dysphagia who presented with symptoms of allergic rhinitis and tested positive for any of the same aeroallergens. Both groups were also questioned about PFAS symptoms as part of the designed clinic template used for these patients, which was consistent between the 2 institutes. The questions included presence of itching or burning sensation with eating any fresh fruit, vegetable, or nut followed by specific questions about how long the symptoms last,

how the patients respond to antihistamines, and whether there is a seasonality to these symptoms. They were also asked if they have ever had other symptoms (cutaneous, respiratory, and cardiovascular) along with these oral symptoms to rule out food allergy. PFAS was defined as having the aforementioned oral symptoms and a positive skin test result for the associated plant pollen. The prevalence of PFAS and other factors in the patients with EoE was compared with that of the control group by unpaired *t* tests and χ^2 tests. Statistical analyses were performed using SPSS statistical software, version 21.0 (IBM Inc, Armonk, New York). *P* < .05 was considered significant. The study was approved by the Northwestern University and Rush University institutional review boards.

We studied 186 adults with EoE: 121 from Northwestern and 65 from Rush University. The control group consisted of 209 adults with allergic rhinitis (AR) (defined by aeroallergen sensitivity on a skin prick test with correlating rhinitis symptoms: 149 from Northwestern and 60 from Rush University). There were no significant differences in age, sex, body mass index, and race distribution of the groups from the 2 centers (neither in AR nor in EoE cases).

The demographics and atopic characteristics of the EoE and AR control groups are compared in Table 1. Among the EoE cases, 168 (90.4%) were sensitized to at least 1 aeroallergen; however, only 106 (56.4%) of the EoE cases had rhinitis symptoms. PFAS prevalence was significantly higher in patients with EoE than AR controls (Table 1). The prevalence of sensitization to pollen allergens (tree, grass, and/or weed) was significantly higher in EoE cases than in AR controls. The high prevalence of PFAS was not explained by the high rate of sensitization to pollen; in the subgroup of patients with EoE and AR controls who were sensitized to the pollen aeroallergens, symptomatic PFAS was present in 50.9% of EoE cases and 10.2% of AR cases (χ^2 test, *P* < .001) (Table 1).

Close to half of patients with EoE from 2 referral institutions had PFAS. This incidence is significantly higher than what was found in our control AR patients (7.2%), consistent with another study from the United States reporting the prevalence of symptomatic PFAS in adults with AR to be approximately 8%.⁸

Thus, we demonstrate, for the first time, that adults with EoE have a high prevalence of PFAS and plant pollen sensitization. In the mouse model of EoE, the intranasal exposure of aeroallergen can lead to esophageal eosinophilia.⁹ We propose that in adults, EoE may begin with sensitization to pollen aeroallergens, leading to cross-reactive food protein sensitization. The uncontrolled nasal inflammation attributable to pollen exposure, along with exposure to cross-reactive foods in the mouth and potentially the esophagus (before those foods are degraded in the stomach), may play a role in

Disclosures: Authors have nothing to disclose.

Funding Sources: Dr Mahdavinia reported receiving support from a Cohn Scholarship from the Rush University mentoring office. Dr Bishehsari reported receiving support from Rush Translational Sciences Consortium/Swim Across America and Rush University, Department of Medicine, Academic Mentoring Program Research Track Award.

Table 1
Demographic and Clinical Characteristics of 186 Patients With Eosinophilic Esophagitis and 209 Patients With Allergic Rhinitis Visited at Northwestern Medicine or Rush University Medical Center Between 2005 and 2014^a

Variable	Patients with eosinophilic esophagitis (n = 186)	Patients with allergic rhinitis (n = 209)	P value
Male	104 (55.3)	109 (52.1)	.93 (χ^2 test)
Age, mean (SD), y	38.08 (11.9)	37.65 (14.5)	.74 (t test)
Asthma	57 (30.3)	62 (29.7)	.46 (χ^2 test)
Symptomatic allergic rhinitis	106 (56.4)	209 (100)	<.001 (χ^2 test)
Sensitization to at least 1 aeroallergen	168 (90.4)	209 (100)	<.001 (χ^2 test)
Sensitization to at least 1 pollen (tree, grass, and/or weed)	155 (82.4)	146 (69.9)	<.001 (χ^2 test)
Symptomatic PFAS among all cases	79 (42)	15 (7.2)	<.001 (χ^2 test)
Symptomatic PFAS among pollen-sensitized cases	79/155 (50.9)	15/146 (10.2)	<.001 (χ^2 test)

Abbreviation: PFAS, pollen food allergy syndrome.

^aData are presented as number (percentage) of patients unless otherwise indicated.

esophageal allergic inflammation. Pollen sensitization is seen in a proportion of pediatric EoE cases, in which it is linked to seasonal exacerbation of eosinophilic inflammation.¹⁰ The reactivity to aeroallergens in EoE increases with age.⁴ Therefore, the observed association of PFAS with EoE might be restricted to adults and possibly the small proportion of older pediatric EoE cases who are aeroallergen sensitized.

Another explanation is that the increased sensitization to aeroallergens is an epiphenomenon and occurs because of epithelial barrier disruption in EoE,³ resulting in sensitization to food proteins, specifically profilins and PR-10 proteins, with subsequent sensitization to aeroallergens as noted on skin testing caused by cross-reactivity. Finally, patients with EoE may be sensitized to the pollen food allergens, not to the major allergens, and thus symptoms and disease are limited to the gastrointestinal tract and not the nose.

Our results for the 2 institutions (Rush and Northwestern) remained unchanged when patients from each center were analyzed separately, strengthening our findings. The scope of the study is restricted by its retrospective nature and may have resulted in underreporting of some of the findings. However, this would have affected both case and control groups equally and is less likely to account for the remarkable differences present between the groups. Because of the retrospective nature of this report, we could not investigate the temporality of EoE and PFAS. Another limitation of the study is that the PFAS diagnosis was based on symptoms and positive skin test results to the associated pollen and was not confirmed by skin prick testing to culprit fresh fruits or vegetables or in vitro component testing for the common pollen food allergen. A future prospective study using these preferred methods for diagnosis of PFAS while investigating the timing of PFAS in relation to EoE symptoms is needed to shed light into the mechanism of this observation.

In conclusion, to our knowledge, this is the first study to find that adults with EoE have a high prevalence of PFAS and pollen sensitization. This finding, in accordance with a previous report of high sensitization to profilins and PR-10 in EoE,⁶ suggests that common pollen aeroallergens may play a role in the pathogenesis of EoE. Subclinical untreated inflammation in the absence of active nasal symptoms could lead to an impaired esophageal barrier function with an increased susceptibility to food allergen sensitization—a sort of atopic march. Future studies are needed to elucidate the underlying mechanism of this association.

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