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Food and aeroallergen sensitization in adult eosinophilic esophagitis

Eosinophilic esophagitis (EoE) is a disorder that has increased in prevalence and causes significant morbidity in children and adults.¹ The diagnosis of EoE requires endoscopic demonstration of greater than 15 eosinophils per high-power field in at least 1 esophageal biopsy specimen.

Although numerous studies have been published describing the clinicopathologic features of pediatric patients with EoE, fewer have reported findings in adult EoE patients. The objective of this study is to report the baseline clinical characteristics, endoscopic evaluation, and sensitization profile of adult patients with EoE.

Patients were retrospectively selected based on the following study criteria: (1) Demonstration of a clinical history suggestive of EoE, (2) presence of 15 or more eosinophils/high-power field on esophageal biopsy, (3) age 18 years or older. All patients had been evaluated by a gastroenterologist and referred to the Allergy department with a diagnosis of EoE. Sixty-six eligible patients evaluated between January 2008 and December 2012 were included. Not all patients had baseline proton-pump inhibitor treatment data available. The protocol was approved by the Institutional Review Board of the Ohio State University Medical Center.

Allergy evaluation included atopic and diet histories. Food allergy was defined by a clinical history of IgE-mediated symptoms (e.g., hives, angioedema, anaphylaxis) and positive allergy testing. No oral food challenges were performed. Immediate hypersensitivity was evaluated by skin prick testing (SPT) to a panel of food and environmental allergens using a Greer pick with commercially available extracts (Greer Laboratories, Inc, Lenoir, North Carolina). The standard food panel included egg, milk, wheat, soy, peanuts, tree nuts, fish, and shellfish. In select patients, when guided by clinical history, other foods were tested to include other legumes, grains, meats, vegetables, and fruits. A standard panel of environmental allergens included pollens, molds, dust mite, cat, and dog. Skin prick responses with wheal sizes 3 mm or larger than the negative control were considered positive.

Fisher's exact method was used to test differences in categorical variables, and the Wilcoxon rank-sum procedure was used in continuous variables. Exact logistic regression was used to estimate odds ratios.

The median duration of symptoms before endoscopy was 2 months (range, 0–62). The most frequently reported atopic diseases were allergic rhinitis (92%), asthma (38%), and food allergy (21%). Dysphagia was the most common symptom reported (92%), followed by oral symptoms (17%). Reported disease complications included food impaction (48%) and the need for esophageal dilation (27%). Common endoscopic findings included esophageal rings (36%), Schatzki's ring (23%), and longitudinal furrows (30%).

Most of the patients had positive SPT to aeroallergens (89%). Younger patients (age <40 years) had a higher likelihood of having

positive SPT to both food allergens and environmental allergens ($P = .015$ and $.001$, respectively; Table 1). Patients younger than age 40 years were more likely to have sensitivity to soy ($P = .04$), milk ($P = .04$), shellfish ($P = .04$), dust mite ($P = .01$), and animal dander ($P = .04$) as compared with those who were 40 years of age or older.

Eighteen patients (27%) had a total of 66 esophageal dilations. Although we found no significant associations with age, the proportion of patients having dilation increased among those in their third and fourth decades of life and peaked in the fifth decade.

This study highlights some of the differences between our adult population and pediatric EoE populations. In our group of adult patients, the most commonly identified food sensitizations were to tree nut, peanut, and other legumes. These data contrast reported findings in the pediatric population, where milk, egg, and wheat are the most commonly identified sensitizing foods.^{2,3} When divided by age, our adult patients younger than 40 years were most commonly positive to milk, soy, and shellfish, which more closely resembles pediatric sensitivities. Although milk and soy may be more frequently implicated in pediatric EoE data, the increased milk sensitivity observed in children has been identified through serum-specific immunoglobulin E (IgE) testing in pediatric studies, whereas it was identified by skin prick testing in our adult population.⁴ Additionally, some centers have found that milk protein allergy can be relevant in pediatric patients even in the face of negative serum milk-specific IgE testing, which adds confounding features to this observation.⁵

Complications of EoE, including food impaction and need for esophageal dilation, have been widely described.¹ The rate of food impaction in our group (48%) was higher than that reported in children (7%–36%). The rate of esophageal dilations in studies looking only at adult EoE patients has been reported to be as high as 28% to 30%, which is consistent with the 27% found in our study.^{6–8} This contrasts with studies that have followed pediatric EoE cohorts into adulthood, which have found rates to be closer to 15%.^{9,10} We found that the peak age of esophageal dilation was in the age group of 41 to 50 years, with a decline as the patient age increased. This trend may suggest that the risk of esophageal dilations may peak in middle-aged adults with EoE, perhaps signifying a need for more aggressive management and monitoring in this group of patients.

A major limitation is that this study is a retrospective review; therefore, aside from the standard 8 foods, the remainder of the food skin prick tests performed varied by ordering provider, and specific IgE testing and total IgE levels were not performed on all patients. This study does not address the effect of dietary interventions. Additionally, we could not determine whether food sensitization was clinically relevant, because post-food avoidance endoscopy was not standardly performed. Although the updated 2011

Table 1

Odds ratios based on exact logistic regression where the variable is regressed on age

Outcome variable	<40 years N (%)	≥40 years N (%)	OR ^a	95% CI	
Total, N	40	26			
Male	28 (70)	13 (50)	0.43	0.14	1.35
Duration of symptoms median (range), months	2 (0–62)	2.5 (0–57)			
Clinical findings					
Esophageal dilations	9 (23)	9 (35)	1.81	0.52	6.28
Dysphagia	38 (95)	23 (88)	0.61	0.04	8.95
Chest pain	5 (13)	1 (4)	0.28	0.01	2.77
Food impaction	17 (43)	15 (58)	1.83	0.61	5.66
Abdominal pain	7 (18)	4 (15)	0.86	0.16	3.87
OAS	7 (18)	4 (15)	0.90	0.17	4.07
Endoscopic findings					
Longitudinal furrows	14 (35)	6 (23)	0.65	0.17	2.28
White plaques	4 (10)	1 (4)	0.41	0.01	4.52
Irregular Z-line	3 (8)	3 (12)	1.82	0.22	15.0
Ringed esophagus	16 (40)	8 (31)	0.79	0.23	2.61
Schatzki's ring	6 (15)	9 (35)	3.60	0.93	15.1
Feline appearance	5 (13)	4 (15)	1.46	0.26	7.75
Circumferential folds	8 (20)	1 (4)	0.19	0.00	1.62
Skin prick test findings					
Any food	32 (80)	13 (50)	0.26 ^b	0.07	0.85
Egg	5 (13)	0 (0)	0.21	0.00	1.64
Milk	10 (25)	1 (4)	0.12 ^b	0.00	0.94
Wheat	6 (15)	2 (8)	0.48	0.04	3.02
Soy	10 (25)	1 (4)	0.12 ^b	0.00	0.97
Peanut	20 (50)	7 (27)	0.37	0.11	1.19
Tree nut	13 (33)	4 (15)	0.47	0.08	2.34
Fish	4 (10)	2 (8)	0.74	0.06	5.68
Shellfish	7 (18)	0 (0)	0.14 ^b	0.00	0.97
Any environmental	40 (100)	19 (73)	0.05 ^b	0.00	0.38
Tree	26 (65)	13 (50)	0.59	0.19	1.83
Grass	26 (65)	15 (58)	0.75	0.24	2.43
Weeds	29 (73)	15 (58)	0.52	0.16	1.67
Mold	18 (45)	8 (31)	0.55	0.17	1.75
Dust mite	25 (63)	8 (31)	0.25 ^b	0.07	0.80
Animal dander	20 (50)	6 (23)	0.29 ^b	0.08	0.96

Abbreviation: OAS, oral allergy syndrome.

^aOdds ratios based on exact logistic regression because of the small number of observations.^bIndicates statistical significance as the 95% confidence interval does not cross 1.0.

International Gastrointestinal Eosinophil Researchers Consensus Guidelines recommend that proton-pump inhibitor-responsive eosinophilic esophagitis be excluded, many patients were evaluated before the publication of these guidelines.¹

Overall, our results suggest a heterogeneity in the adult population of EoE patients such that the younger adult EoE populations (age <40 years) resemble the known SPT sensitivities and clinical course of pediatric EoE patients, whereas the older population (age >40 years) may be a phenotypically different subpopulation of this disorder.

Future prospective studies looking at causality, phenotypes, and rates of complications may ultimately lead to more directed evaluation and treatment based on age and other associated factors.

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