The seasonality of eosinophilic esophagitis flares in children and adolescents in Arizona

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Abstract

Background: Eosinophilic esophagitis (EoE) is a clinicopathologic disorder with upper gastrointestinal symptoms and esophageal eosinophilia. The pathogenesis is multifactorial. While not as prominently as food allergens, aeroallergens have been implicated in the pathogenesis of EoE. The objective of this study is to determine the seasonality of EoE flares in Arizona.

Methods: We performed a retrospective analysis of data from patients aged 5 to 18 years with EoE seen at PCH between June 2010- 2011. Data including flares, atopies, and patient demographics was collected. A Chi-square analysis was used to analyze incidence and season of EoE flares.

Results: Records from 148 patients and 361 clinical visits were reviewed. Ninety four patients (63.5%) experienced a flare during the study period. One hundred and six patients (71.6%) had environmental allergies, of whom 70 (66%) had EoE flares in the fall. Food allergy testing was positive in 85.8% of patients. Of those with food allergy, 65% had EoE flares. Fall EoE flares are the most clinically symptomatic.

Conclusions: EoE flares in children in Arizona are significantly increased in the fall season. This suggests a role for seasonal environmental allergens in the pathogenesis of EoE. Prospective studies looking at desert specific environmental testing and EoE flares are needed.

Disclosures: None

Objectives

1. To determine the incidence of seasonal flares of eosinophilic esophagitis.
2. To characterize patients that experience disease flares of EoE.

Background

Eosinophilic esophagitis (EoE) is a clinicopathologic disorder of the esophagus characterized by upper gastrointestinal symptoms in association with esophageal eosinophilia. EoE is now known to be a separate entity with diagnosis now requiring exclusion of PPI-responsive esophageal eosinophilia. Updated consensus recommendations in 2011 describe EoE as a "chronic, immune/antigen-mediated, esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation" [1].

The pathogenesis of EoE is likely multi-factorial, with contribution from both genetic and environmental factors. Accumulating evidence suggests an extracellular immune-mediated response, specifically TH2-mediated, with demonstrations of overexpressed interleukin-13 and induced eotaxin-3[2,3]. An allergic component to the pathogenesis of EoE is also supported by the presence of co-atopic conditions in the majority of patients[4,5].

Food allergy is well established in the literature as a known component of EoE based both on antigen testing and resolution of clinical and histologic abnormalities with dietary removal of food antigens[6-9]. Less is known, however, about the role of environmental allergens in EoE disease.

Studies have characterized the seasonal distribution of new diagnoses of EoE, demonstrating a correlation between time of new diagnosis and pollen count[10,11]. No relationship between environmental allergens and disease relapses has been documented to date, however. There is also no published work from the southwestern United States, an area distinguishable from other regions by its unique desert allergen profile.

Of the five most common allergen categories (food, common ragweed, mold, house dust mites, and cats/dogs) Phoenix ranks second of thirty major U.S. cities in allergen sensitization based on quantitative measurement of circulating IgE to specific allergens[12]. Phoenix Children's Hospital Gastroenterology Department is a large division with thriteen providers. The department serves a large population of patients with EoE and observes recurrence of disease in the pediatric population. Characterization of the allergy profile, patient demographics, and seasonality of disease recurrence may provide an understanding of the pathogenesis of eosinophilic esophagitis in the pediatric population.

Methods

- Retrospective review of Phoenix Children Hospital's billing database MedAptus is performed
- Outpatient gastroenterology visits coded with ICD-9 Code 530.13 for eosinophilic esophagitis are identified after IRB approval by the PCH Institutional Review Board (IRB 12-015)
- Exclusion criteria are set and identify valid visits to be included in study. A chart was excluded if:
  - Patient shows lack of remission for >= 8 weeks prior to study OR is newly diagnosed with EoE
  - Incorrectly coded as EoE, defined as symptoms of esophageal dysfunction *and* histology demonstrating >= 15 eosinophils per HPF on esophageal biopsy
  - Visit is unrelated to EoE diagnosis
  - Records are incomplete or unobtainable
- Flares are defined as recurrence of the following:
  - Clinical symptoms of dysphagia, regurgitation, globus, odynophagia, heart burn AND/OR
  - Histology demonstrating >=15 eosinophils per HPF on esophageal biopsy

  In an otherwise asymptomatic individual with a previous diagnosis of EoE
- Arizona seasons were defined as: spring from Feb 15 to June 15, and fall from Sept 1 to Nov 30, according to the typical pattern of allergen pollination[13,14]
- For the univariate influence of risk factors on flares a chi-square or exact Fisher's test test was used. The multivariate impact of risk factors on outcome was assessed with a logistic regression model. The incidence rates were compared with a binominal test. Pairwise comparisons were corrected using the Bonferroni method.

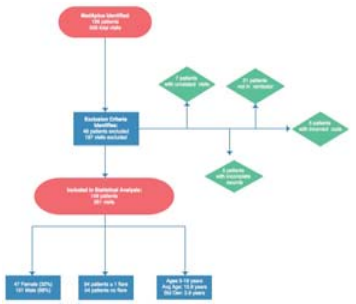

Figure 1

Results

Table 1:	Characteristics of Patient Population (n, %)
Gender	
Male	101 (68%)
Female	47 (32%)
Environmental Allergy	106 (72%)
Food Allergy	127 (86%)
Environmental and Food Allergy	98 (66%)
GERD	37 (25%)
Autism	13 (9%)
Irritable Bowel Disease	2 (1%)

Table 2:	Control vs. EoE Flare Populations		
	Control Group (n, % of control)	EoE Flares (n, % of flares)	p value
Total	54 (36% of population)	94 (64% of population)	
Gender			
Male	39 (72%)	62 (66%)	
Female	15 (28%)	32 (34%)	
Environmental Allergies	36 (67%)	70 (74%)	0.31
Food Allergies	44 (81%)	83 (88%)	0.25
Environmental and Food Allergies	32 (59%)	66 (70%)	0.56

Table 3	Seasonal Distribution Odds Ratios	
	Odds Ratio	p-Value
Fall vs.Other Months (spring excluded)	1.856	0.08
Spring vs. Other Months (fall excluded)	0.819	0.155

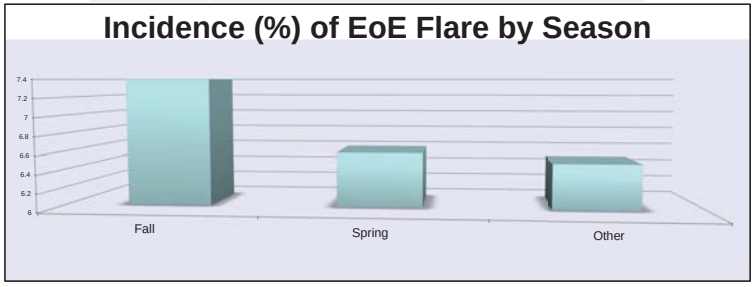

Figure 2 Increased incidence of flares in the Fall season (7.4%), which was statistically significant (p=0.041). The odds ratio of Fall season flares vs. other seasons was 1.856 (p=0.08). When examined by month, October had a very high incidence of visits characterized as EoE flare, with 18 of 28 visits by pediatric patients previously in remission experiencing new or worsening symptoms.

Discussion

The unique allergen profile of the southwest region may provide clues about this distribution of our findings. The peak of the fall allergen season occurs in October when bermuda grass is scalped, rye grass is planted, and ragweed pollinates. In April all spring-time trees, rye grass and ragweed pollinate.

Patients may be more likely to seek their providers for flares during these times for two reasons. First, they are being exposed to the peak level of aeroallergens during the peak season. Second, a known priming affect exists in allergy processes. The introduction of pollens in September for the fall and February for the spring season primes the immune response, resulting in significant symptoms 2-4 weeks later.

The characterization of the presence or absence of atopic symptoms in patients also showed differences between the control and flare groups, although this was not statistically significant. A greater percentage of the flare group had environmental allergies and/or food allergies than those who did not flare during the study period (p=0.31 and 0.25, respectively). These findings may suggest that pediatric EoE patients in Arizona with environmental allergies may be at an increased risk for disease recurrence.

Demographics of the patient population were found to be consistent with what has been described in the literature, including a higher prevalence in males and an obvious association with environmental and food allergy.

No literature to date has described patterns of disease recurrence and the characteristics of those who flare.

Limitations:
- retrospective study
- confounders: arbitrary provider referral practices,
- unknown variables that may skew the data

Conclusions

- Aeroallergens may play a role in the recurrence of EoE in pediatric patients living in Arizona.
- Flares of EoE peaked during fall season.
- Prospective studies are needed that further describe the pediatric population that experiences disease recurrence and examine desert-specific environmental allergen testing in relation to EoE flares.

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