Prevalence of Eosinophilic Esophagitis in Children With Refractory Aerodigestive Symptoms

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IMPORTANCE Eosinophilic esophagitis (EoE) is an increasingly important diagnosis for children; it has a remarkable impact on their quality of life and can present with aerodigestive symptoms commonly evaluated by otolaryngologists.

OBJECTIVES To evaluate the prevalence of EoE in children presenting to a pediatric aerodigestive clinic, to describe their presentation, and to review the role of subsequent food allergy evaluation and treatment.

DESIGN Review of a prospective database.

SETTING Tertiary pediatric multispecialty aerodigestive center.

PATIENTS Children with aerodigestive symptoms refractory to medical treatment who underwent direct laryngoscopy with rigid or flexible bronchoscopy and esophagoscopy with or without pH probe study.

MAIN OUTCOMES AND MEASURES Diagnosis of EoE.

RESULTS Between 2003 and 2012, 376 of 1540 children seen in the center (mean [range] age, 4.54 [0-18.6] years; male to female ratio, 1.72:1) remained symptomatic despite medical therapy and thus underwent triple endoscopic evaluation. Of the 376 children, 14 (3.7%) were eventually diagnosed as having EoE, as defined by 15 or more eosinophils per high-power field on esophageal biopsy and either a negative pH study result or nonresponse to a trial of high-dose proton pump inhibitors. The subpopulation with EoE presented with airway symptoms and diagnoses, most commonly cough (n = 6; 42.9%). Inflammatory subglottic stenosis due to EoE was identified in 1 patient. Of the 14 children with EoE, 6 presented with gastrointestinal symptomatology, most commonly choking or gagging. Subsequent treatment including food allergy challenge and elimination diet resulted in a clinical improvement in half of the cases identified.

CONCLUSIONS AND RELEVANCE This represents the largest multispecialty clinic epidemiologic study evaluating the prevalence of EoE in children presenting not strictly with gastrointestinal symptoms but rather with aerodigestive symptoms that are frequently evaluated by pediatric otolaryngologists. Although the prevalence is low, EoE should be considered for children with appropriate symptoms in whom other medical therapies fail.


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Eosinophilic esophagitis (EoE) is a relatively new and increasingly common diagnosis for patients who present with symptoms similar to those with gastroesophageal reflux disease (GERD) but who do not respond to targeted therapy. According to the 2007 American Gastroenterological Association consensus report, EoE is a clinicopathologic diagnosis and requires the exclusion of other causes of esophagitis, namely GERD.1 Eosinophilic esophagitis is an increasingly important diagnosis for children; it has a remarkable prevalence over 4 years from 0.991 to 4.296 per 10 000 children, with a constant incidence of approximately 1 in 10 000 children per year. There tends to be a male predilection.1 The most common presenting symptoms in children are heartburn and regurgitation with other very common presentations including emesis, abdominal pain, food impaction, and dysphagia.1 Less often, children present with failure to thrive, chest pain, and diarrhea.1

Noel et al3 demonstrated an increase in disease prevalence over 4 years from 0.991 to 4.296 per 10 000 children, with a constant incidence of approximately 1 in 10 000 children per year. There tends to be a male predilection.1 The most common presenting symptoms in children are heartburn and regurgitation with other very common presentations including emesis, abdominal pain, food impaction, and dysphagia.1 Less often, children present with failure to thrive, chest pain, and diarrhea.1

Eosinophilic esophagitis can also present with extra esophageal manifestations, as Hartnick et al4 reported in their case of a child with subglottic stenosis complicated by EoE. This raises the question of the incidence of EoE in children with continued airway symptoms that do not respond to targeted medical treatment for initial diagnoses prior to triple endoscopic evaluation. The goals of this study were to assess the prevalence of EoE in a pediatric population with such symptoms and to evaluate the treatment response in those diagnosed as having EoE.

### Methods

Institutional review board approval was obtained from the Massachusetts Eye and Ear Infirmary (MEEI) and was jointly approved by the Massachusetts General Hospital. Children who were seen at the MEEI aerodigestive center were evaluated by a pediatric otolaryngologist, pulmonologist, and gastroenterologist and underwent medical treatment for initial diagnoses. Those in whom therapy failed underwent further investigation with direct laryngoscopy with rigid or flexible bronchoscopy and esophagoscopy, with or without pH probe study. Data pertaining to presentation, diagnoses, endoscopic findings, and treatment outcomes were collected prospectively and stored in a password-encrypted program on a password-encrypted server; informed consent was not deemed necessary for this study. Children through the age 18 years who presented between 2003 and 2012 were included in this review of prospective database of patients with airway symptoms refractory to a trial of medical management.

The diagnosis of EoE was determined by the presence of 15 or more eosinophils per high-power field (HPF) on esophageal biopsy and either a negative pH study result, when not undergoing GERD medical therapy, or nonresponse to a trial of high-dose proton pump inhibitors. Patients with EoE were treated primarily with an elemental or 6-food elimination diet. For patients who partially responded to treatment or in whom treatment failed, a food elimination diet was implemented to determine inflammatory triggers. For children with persistent symptoms despite these measures, alternative treatment such as swallowed steroids were used. With successes in the algorithm, the patients were reintroduced to one food at a time with objective monitoring of sensitivity and inflammation.

Outcomes of children treated with medical management only were measured as improvement, resolution, or failure to improve. As such, treatment outcomes were based on subjective symptomatology as reported by the patients and their families.

### Results

Of 1540 children evaluated between 2003 and 2012 at the aerodigestive center, 376 underwent endoscopic evaluation for symptoms that persisted after initial medical therapy; these were most commonly cough, choking, or vomiting (Table 1). These children were on average 4.54 years old at the time of triple endoscopy, and 63.3% (238 of 376) were male.

After triple endoscopy, more than half of the patients were diagnosed as having GERD or GERD and tracheomalacia. Only 14 of 376 children with refractory aerodigestive symptoms (3.7%) were eventually diagnosed as having EoE; 11 of the 14 were male.

A review of the subpopulation of children with EoE revealed that cough (n = 6, 42.9%) was the most common airway presentation, while others presented with cough, asthma, and hoarseness. One male patient who presented with cough and no gastrointestinal (GI) symptoms was identified as having inflammatory subglottic stenosis secondary to EoE. Of the 14 children with EoE, 6 (42.9%) presented originally with GI complaints in addition to airway symptoms, with choking and vomiting being the most common.

Subsequent medical treatment either improved or resolved airway symptoms in at least half of the patients for each

### Table 1. Refractory Symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Children, No. (%)</th>
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<tbody>
<tr>
<td>Upper airway</td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>166 (44.1)</td>
</tr>
<tr>
<td>Croup</td>
<td>31 (8.2)</td>
</tr>
<tr>
<td>Stridor</td>
<td>31 (8.2)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>29 (7.7)</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>9 (2.4)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td></td>
</tr>
<tr>
<td>Choking</td>
<td>54 (14.4)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>36 (9.6)</td>
</tr>
<tr>
<td>Feeding difficulty or food refusal</td>
<td>23 (6.1)</td>
</tr>
<tr>
<td>Gagging</td>
<td>19 (5.1)</td>
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diagnosis, with the exception of the single patient diagnosed as having GERD and EoE. Food allergy challenge and elimination diet resulted in a clinical improvement in 50% of patients with EoE (Table 2).

### Discussion

The prevalence of EoE was found to be 3.7% in this population of children with aerodigestive symptoms refractory to initial medical management. This represents only 14 cases of pediatric EoE identified over a 9-year period at a dedicated pediatric aerodigestive center. It is relatively more common in this population than in the general pediatric population, where prevalence has been described as low as 4.3 per 10,000 children. Saadah and colleagues observed that 0.85% of children with GI symptoms were diagnosed as having EoE in western Saudi Arabia. Pediatric prevalence was found to be 5.8% in children who presented with refractory GI symptoms in a US study, which is higher than the prevalence found in this study population of children with airway and GI symptoms. This underscores the rarity of the disease in children presenting with airway symptoms. Similar to others’ findings of a male predilection in this disease, of the 14 children in our EoE population, 11 (78.6%) were male.

Children who were ultimately diagnosed as having EoE in this study displayed airway symptoms in addition to the commonly described symptoms of choking, gagging, and food refusal on initial presentation, signaling a strong airway component to the aerodigestive symptomatology. The spectrum of presentation of EoE has been demonstrated to include airway symptoms, such as wheezing, asthma, rhinitis, sinusitis, and nasal congestion. Cooper and colleagues reported that 6.25% of children with croup and cough were found to have more than 15 eosinophils per high-power field in esophageal biopsy.

In our group of 14 children with EoE, there was 1 patient who demonstrated inflammatory subglottic stenosis, which highlights the variety of airway symptoms and findings within this disease. Hartnick et al first reported this significant laryngeal manifestation in a case of a child with recurrent airway symptoms and subglottic stenosis following surgical correction in the absence of treatment of EoE. In addition, Dauer and colleagues reported 1 case of subglottic stenosis in a child with EoE and no history of airway surgery.

Half of the patients with EoE who were treated medically according to our dietary algorithm showed improvement or resolution of their symptoms. This response rate may suggest that children with EoE and airway symptoms could have worse outcomes than their counterparts with purely GI symptoms; this is currently largely unknown. Literature describing long-term treatment outcomes in children is limited and focuses on children who present primarily with GI symptoms. In one such review by Liacouras and colleagues, 75 of 132 patients (56.8%) had improvement in symptoms with diet restrictions focused on allergy testing results and 160 of 167 patients (95.8%) had improvement with an elemental diet. Notably, this study eliminated noncompliant patients from its outcomes analysis, and it is known that this disease is chronic and symptoms typically recur without continued treatment. Presumably, our patients were continuing their treatment regimen as recommended; however, adherence was not evaluated in outcomes assessment. While this may represent a weakness in our study, it also gives a realistic evaluation of outcomes in a small group of children with EoE who present with airway symptoms in addition to GI symptoms.

There is evidence supported by validated questionnaires that EoE has a major impact on a child’s quality of life. In addition, it has been shown that patients with persistent eosinophilia of only 5 eosinophils per high-power field are symptomatic compared with controls. With this evidence, there is a push for outcome measures that include symptomatic improvement rather than histologic changes alone. One strength of this study is its focus on improvement or resolution of symptoms as measures of treatment outcome.

This study has established the prevalence of EoE in children with refractory aerodigestive symptoms. We describe a group of patients with frequent airway complaints in addition to the commonly recognized GI symptoms, with a range of airway manifestations that include subglottic stenosis. With airway symptoms within the scope of presentation, EoE will be an increasingly important diagnosis for pediatric otolaryngologists to consider. For future investigation, a detailed evaluation of treatment outcomes in this subgroup of children with EoE and airway complaints with a focus on improvement of outcomes is warranted.

### Table 2. Treatment Outcomes

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treated Medically Alone, No.</th>
<th>Children, No. (%)</th>
</tr>
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<tbody>
<tr>
<td>GERD alone</td>
<td>114</td>
<td>Improved 29 (25.4)</td>
</tr>
<tr>
<td>EoE alone</td>
<td>14</td>
<td>Improved 4 (28.6)</td>
</tr>
<tr>
<td>GERD + eosinophilic esophagitis</td>
<td>1</td>
<td>Improved 0</td>
</tr>
<tr>
<td>GERD + tracheomalacia</td>
<td>60</td>
<td>Improved 23 (38.3)</td>
</tr>
</tbody>
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Abbreviations: EoE, eosinophilic esophagitis; GERD, gastroesophageal reflux disease.
Analysis and interpretation of data: Hill, Ramakrishna, Sternberg, Ojha, Hartnick.
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Critical revision of the manuscript for important intellectual content: Hill, Fracchia, Sternberg, Ojha, Hartnick.
Statistical analysis: Hill, Ramakrishna, Sternberg, Ojha, Hartnick.
Administrative, technical, or material support: Infusino, Hartnick.
Study supervision: Fracchia, Hartnick.

Conflict of Interest Disclosures: None reported.

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REFERENCES