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## CLINICAL VIGNETTE

# Eosinophilic Esophagitis: An Increasingly Common Cause of Upper GI Disease

By Brian S. Morris, MD

### **Case Report**

The patient is an 8-year old female with a lifelong history of GERD who is seen by her pediatrician because of complaints of dyspepsia, weight loss, and early satiety. Her recent symptoms began approximately six months ago and had become progressively worse over the last few weeks.

Her past medical history is remarkable for a lifelong history of GERD, which was previously treated with a proton pump inhibitor. Her upper GI symptoms began shortly after birth and included projectile vomiting, indigestion, and difficulty sleeping. As a newborn, she was treated with ranitidine and was eventually switched to a proton pump inhibitor when the H-2 blocker became ineffective. She is currently on no medications. She is allergic to penicillin and bactrim. Her social history is unremarkable. Her family history is remarkable for asthma, atopic dermatitis, autoimmune thyroid disease, and food allergies.

Vital signs include blood pressure of 105/60 mm hg., pulse of 70 beats/minute, temperature of 36.6 C, Her physical examination is unremarkable.

Laboratory evaluation revealed an eosinophilia with an absolute eosinophil count of 1100/uL (0-700). The remainder of the CBC was unremarkable as were basic chemistries. Total IgE was 568 IU/mL (8-150). Thyroid function was within the normal range. Because of the progressive nature of the symptoms, an EGD was performed.

### **General Discussion**

Eosinophilic esophagitis (EE) is an allergic, inflammatory condition of the esophagus where the walls of the esophagus become infiltrated with eosinophils<sup>1</sup>. Many names have been used to describe this condition including eosinophilic esophagitis (EE or EoE), primary eosinophilic esophagitis (PEE), allergic eosinophilic esophagitis (AEE), and idiopathic eosinophilic esophagitis<sup>2</sup>. EoE is a *clinicopathologic*

disorder characterized by an eosinophilic infiltration of the walls of the esophagus in association with upper GI symptoms that tend not to respond well to treatment to proton pump inhibitors. Patients typically complain of heartburn, chest pain, food intolerances, dysphasia, reduced appetite, and odynophagia. Most cases of EoE are allergic in nature with food allergies being the most common precipitant<sup>3</sup>. Wheat, eggs, dairy, soy, nuts, and fish appear to be the most common food-based precipitants of EoE<sup>4</sup>. EoE is commonly associated with atopic dermatitis, asthma, chronic urticaria, allergic rhinitis, and peripheral eosinophilia<sup>5</sup>.

### **Epidemiology**

EoE has been reported in patients around the world (including North America, Europe, Asia, Australia, and South America) but has, thus far, not been reported in Africa. Studies have suggested a geographical variation in incidence with this condition being more common in the northeast of the United States and less common in the west<sup>6</sup>. EoE was first reported in the late 1960's and was initially confused with GERD as their pathological specimens can look very similar.<sup>7</sup> Over the past 25 years, the incidence of of EoA has been increasing and, in some states, is now more common than inflammatory bowel disease<sup>7,8</sup>. Among children and adults, EoE is more common in males than females<sup>8</sup>. Genetics do play a role in EoE and appear to be carried at least in part on chromosome 5q22<sup>9</sup>.

### **Diagnosis and Pathogenesis**

The diagnosis of eosinophilic esophagitis should be based upon symptoms, endoscopic appearance, and findings on histological evaluation. In patients suspected of having eosinophilic esophagitis, the first diagnostic test is usually an EGD with biopsies. Many gastroenterologists prefer the EGD to be performed following 1-2 months of treatment with a proton pump inhibitor to eliminate any superimposed GERD<sup>10</sup>. Patients need to have at least 15 eosinophils per high

power field in at least one esophageal biopsy specimen<sup>11</sup>. Five or six biopsies are often required to ensure a proper histological diagnosis. Other histological findings can include eosinophilic microabscesses, extracellular eosinophil granules, subepithelial and lamina propria fibrosis and inflammation, basal cell hyperplasia, and mast cells<sup>12</sup>. Although laboratory and other radiologic tests can support the diagnosis, such tests cannot alone make the diagnosis. A positive biopsy (usually taken from the proximal and distal esophagus) also requires the appropriate clinical setting to make a definitive diagnosis of eosinophilic esophagitis. Allergy testing has been used historically to help guide dietary recommendations, but such testing has many pitfalls and food elimination diets have become first-line therapy in many centers<sup>4</sup>.

The pathogenesis of EoE involves both environmental and genetic factors and involves T-cell immunity as well as interleukins (such as IL-5, IL-13, and IL15)<sup>13</sup>. Fibroblast growth factor-9 appears to play roles in the recruitment and/or function of the inflammatory process in EoE<sup>14</sup>. Common findings on EGD include stacked circular rings (“feline” esophagus), white plaques, linear furrowing, strictures, and small caliber esophagus<sup>15</sup>.

### ***Clinical Features and Outcomes***

In adults, common clinical presentations include dysphagia, chest pain, GERD-like symptoms, abdominal pain, and food impaction<sup>7</sup>. In children, clinical presentations vary and can sometimes be very subtle and unremarkable<sup>16</sup>. The most common symptoms in the pediatric population include nausea, GERD-type symptoms, generalized feeding dysfunction, dysphagia, and abdominal pain<sup>11</sup>. The generalized feeding dysfunction usually includes various eating strategies such as only eating liquid/soft foods or avoiding certain types of quantities of foods<sup>17</sup>. Children are more likely than adults to have a normal appearing esophagus on EGD although most of these patients have abnormal histology on biopsy<sup>16</sup>.

### ***Treatment***

Treatment of EoE includes dietary treatments, pharmacologic therapies, and procedures. The mainstay of dietary treatment is an elimination diet or elemental diet<sup>18</sup>. Elimination diets are based on the idea that avoiding foods known to trigger EoE (either specific to each patient or foods that generally affect many patients) is an effective strategy<sup>19</sup>. Thus, patients are sometimes referred to an allergist for allergy testing

to try to identify which foods may be triggering the EoE. Such testing can be performed with skin prick testing, serum RAST IgE levels, and/or patch testing although the sensitivity and specificity of such results aren't always reliable<sup>20</sup>. This targeted strategy though allows for a more focused approach to dietary avoidance and may also assess for when airborne allergens may be playing a role in the EoE.

The second type of elimination diet involves avoiding the most common food allergens that trigger EoE<sup>21</sup>. These include peanuts, eggs, soy, cow's milk, wheat, and tree nuts with wheat, milk, soy, and eggs being the most common<sup>4</sup>. Patients on any elimination diet may need to be followed by a nutritionist to prevent dietary deficiencies. Because of these factors, elimination diets require the patient to be motivated and have a strong understanding of nutrition and food choices to ensure proper compliance. In addition, such patients also often require repeated endoscopies to document the status of the disease. The other type of dietary program to limit exposure to potential food allergens is the elemental diet where the patient's diet is comprised of amino acids rather than the proteins that are more likely to serve as allergens. Unfortunately, many of these elemental programs are expensive and unpalatable making this a challenging diet to follow. However, elemental diets can be effective in certain circumstances<sup>22</sup>.

Pharmacologic therapies include proton pump inhibitors and various formulations of corticosteroids. Proton pump inhibitors are used prior to EGD to ensure that the patient truly has EoE rather than GERD. PPI's can also help patients with EoE by reducing acid-related symptoms that these patients may also have<sup>23</sup>.

Topical steroids are also used for these patients. Fluticasone (MDI without a spacer) is swallowed and can be quite effective and well-tolerated<sup>24</sup>. Long term safety studies (especially in children) have not been performed in EoE patients and possible safety concerns include growth delay, cataracts, and osteoporosis. Viscous budesonide is also used in certain patients. Although topical steroids have a high efficacy rate, there is also a high rate of relapse upon discontinuation of the treatment. Thus, a combination of dietary modification and pharmacological therapy is sometimes the most effective therapy. Systemic steroids are occasionally used for severe cases<sup>25</sup>.

Another type of therapy is dilation with EGD. This type of therapy is reserved for those with high-grade strictures or those who have failed medical/dietary management<sup>26</sup>. These patients have a relatively high risk of esophageal perforation on EGD, so dilation should be reserved for select patients<sup>27</sup>.

## Prognosis

The prognosis for patients with EoE is variable. Some patients respond quite well to dietary modification and/or medications while others suffer a complicated, rocky course with strictures and nutritional deficiencies<sup>28</sup>. There does not appear to be an increase risk of malignancy<sup>29</sup>.

## Clinical Course and Follow-Up

The patient's EGD revealed patches of linear exudates, friability, edema, and white plaques as well as a generalized pallor to the superficial tissues. A focal area of narrowing was noted distally in the esophagus. Multiple esophageal biopsies were taken which showed eosinophils (25 per high powered field), microabscesses, lengthening of the lamina propria papillae, and basal-cell hyperplasia. The patient was referred to an allergist and testing revealed several potential food allergies. After eliminating these foods from her diet, the patient noted a nearly complete resolution of her symptoms.

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