Food Allergy and Eosinophilic Esophagitis: What Do We Do?

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Eosinophilic esophagitis (EoE) is an inflammatory disease of the esophagus triggered by foods and possibly environmental allergens. Common conditions that mimic EoE include gastroesophageal reflux disease and proton pump inhibitor-responsive esophageal eosinophilia. These need to be excluded before confirming the diagnosis of EoE. Identification of food triggers for EoE using standard allergy tests remains challenging. Dietary therapy for EoE so far consists of test-directed elimination of foods, empiric elimination of common food allergens, or exclusive feeding of amino acid-based formulas, with variable success. No FDA-approved medications yet exist for EoE. Topical corticosteroids to the esophagus are being used. EoE is a chronic disease; therefore, long-term therapy seems to be necessary to avoid potential long-term complications such as esophageal remodeling and strictures. Optimal long-term therapies and follow-ups are still not established; therefore, discussion with patients and families regarding the choice of therapy is important to ensure the best possible outcomes from a medical and social standpoint. In this article, we discuss all the above issues in detail by using a hypothetical case; highlighting in a stepwise manner what is known with respect to diagnosis, work-up, and management of EoE; and discussing gaps in knowledge that need to be addressed in the future. © 2015 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2015;3:25-32)

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AC is a 15-year-old female with a 3-year history of intermittent epigastric abdominal pain and solid-food dysphagia that occurs daily, especially with bread and meat. Her past medical history is notable for IgE-mediated cow's milk (CM) and egg allergies, which she outgrew after she passed oral food challenges (OFCs) to CM and egg at the age of 4 and 6 years, respectively. She also experiences mild persistent asthma controlled on 2 puffs once daily of fluticasone 110 mcg with a spacer, and seasonal allergic rhinitis controlled on 10 mg once daily of cetirizine and 2 sprays once daily of fluticasone.

As an infant and toddler, she had gastroesophageal reflux disease (GERD), and was treated with a proton pump inhibitor (PPI) from the age of 2 to 15 months. Several weeks before coming to your office (allergist's office), she had an esophageal food impaction that consisted of steak that required flexible endoscopic removal performed by a pediatric surgeon. Biopsies obtained during the procedure revealed 35 eosinophils/high-powered field (hpf) in the proximal esophagus and 65 eosinophils/hpf in the distal esophagus. She was not taking PPI medication at the time of the endoscopy. The surgeon referred AC to a gastroenterologist for further evaluation of esophageal eosinophilia.

Confirmation of diagnosis:

1. *AC was told that the biopsies were consistent with eosinophilic esophagitis (EoE). Does esophageal eosinophilia alone confirm a diagnosis of EoE?*

It is important to differentiate EoE from esophageal eosinophilia as a descriptive finding, as the latter is not pathognomonic for EoE. Based on the most recent consensus guidelines, EoE is defined as "a chronic, immune/antigen-mediated esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation."[1] Inflammation occurs only in the esophagus, and other etiologies for these features must be ruled out before assigning this diagnosis. Table I summarizes a list of diseases where esophageal eosinophilia can be seen.

Two common clinical conditions presenting with esophageal eosinophilia deserve particular attention: GERD and the newly

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Abbreviations used
CM- Cow's milk
EoE- Eosinophilic esophagitis
GERD- Gastroesophageal reflux disease
hpf- High-powered field
OFC- Oral food challenge
PPI- Proton pump inhibitor
PPI-REE- PPI-responsive esophageal eosinophilia
SFED- Six-food elimination diet (SFED)
TCS- Topical corticosteroids

described entity proton pump inhibitor-responsive esophageal eosinophilia (PPI-REE). Patients with GERD present with similar symptoms to EoE, such as heartburn and retrosternal chest pain. Patients with GERD typically have symptom relief when taking antacids and may have esophageal erosions or ulcers on gross endoscopic examination. Esophageal reflux can be assessed by pH probe monitoring.

A growing body of literature and clinical experiences identified PPI-REE as a clinicopathological entity described by symptoms, and endoscopic and histological findings consistent with EoE, which resolved with the use of PPIs.[2-4] The etiology of PPI-REE is still unknown. It is not yet determined as to whether patients with PPI-REE have severe GERD that mimics EoE (though pH probe results are normal in a subset of patients with PPI-REE); GERD that triggers EoE, hence the response to PPI therapy; or EoE that is responsive to PPI therapy by some anti-inflammatory mechanism. Thus, histology alone does not confirm the diagnosis of EoE.

2. What is the best method to confirm an EoE diagnosis?

To date, the best method to confirm a diagnosis of EoE, ie, ruling out GERD and PPI-REE, is empiric therapy with high-dose PPI followed by repeat endoscopy with biopsies, documenting persistent esophageal eosinophilia. pH probe monitoring, although positive in the majority of patients with acid-induced GERD, is not always positive in those with PPI-REE. In fact, it was shown to be poorly predictive of response in those with PPI-REE, both in children and in adults.[2,4,5]

Therefore, when symptoms of esophageal dysfunction and esophageal eosinophilia (≥15 eosinophils/hpf) are found, the following are recommended to confirm EoE: (1) a thorough history to rule out other potential causes of esophageal eosinophilia, (2) biopsies that demonstrate the absence of pathology in the remainder of the gastrointestinal tract, and (3) a diagnostic trial of high-dose PPI followed by clinical and histological reevaluation.[1]

AC underwent a pH probe that showed no evidence of acid-induced GERD. Gastric and duodenal biopsies were normal, and she ingested wheat regularly, ruling out celiac disease. There were no clinical indicators of inflammatory bowel disease or cancer. The gastroenterologist started AC on lansoprazole 30 mg twice daily for 6 weeks. She underwent a repeat upper endoscopy that showed significant esophageal eosinophilia (32-68 eosinophils/hpf), which confirmed the diagnosis of EoE. AC's gastroenterologist refers her to you for further EoE management (see Figure 1 for management considerations). AC's family has done some research on the Internet regarding treatment of EoE with diet and/or medication, and they come to you with a list of questions.

Allergy testing and treatment:

1. My gastroenterologist gave me a choice of eliminating more foods from my diet or starting swallowed topical corticosteroids (TCS). How do we choose which treatment is best?

You explain to AC that there is evidence for successful treatment using dietary elimination, with varying success rates depending on the exact diet used (Figure 2). Dietary elimination can take the form of a targeted approach, in which the results of skin prick and patch testing are used; an empiric approach, in which the most common food allergens, consisting of CM, wheat, egg, soy, nuts (peanut/tree nuts), and seafood (fish/shellfish), therapy referred to as the six-food elimination diet (SFED), are eliminated; or an exclusive elemental formula. In children, skin prick combined with patch test-targeted elimination diets have success rates of 53-65%.[6,7] Empiric elimination diets have success rates of 70-74% in adults and children.[8,9] The elemental formula has success rates of >90% in almost all studies.[7,10] Centers that utilize skin prick testing often will start by obtaining a food consumption history and test those foods commonly consumed by the patient along with the common foods that cause EoE. Skin patch tests are usually performed using single-item baby foods or dry powders to an empiric panel. Then, the combinations of positive tests on prick and patch testing are utilized to build an elimination diet.[6] Because of the poor predictive value of patch testing to milk, some centers often eliminate milk empirically in addition to those foods to which the patient tests positive.[6] Reports on use of targeted elimination diets have shown that CM and wheat are the most common EoE triggers in both pediatric and adult populations in the United Sates and Europe.[7,11-14] Spergel et al identified the most common food combinations used in elimination diets to control EoE (Table II).[6] The definition of the SFED varies between treating physicians; for example, in Spanish studies all legumes are avoided, whereas in U.S. studies soy is the only legume avoided. The SFED has been utilized in both children and adults with success.[8,11-13] Because aeroallergens can also cause esophageal eosinophilia, it may be helpful to avoid these triggers.[15-18] Based on the observations of seasonal EoE, animal models that demonstrate mold and dust mite-induced EoE,[17,18] and new reports that specific immunotherapy for aeroallergens can help in EoE management,[19] skin prick testing for aeroallergens can be justified in EoE.

TCS are also successful therapy for children and adults with EoE, with success rates in symptom reduction and histological remission ranging from 50% to >80%.[20-25] Because no FDA-approved EoE therapies exist, TCS, including fluticasone and ciclesonide, have been reported to be administered with metered dose inhalers, in which the steroid is swallowed to coat the esophageal mucosa. Administration of TCS for EoE does not use a spacer, and thus thorough instructions are critical for success. Oral viscous budesonide has been developed as an alternative delivery method, in which a viscous suspension is made with sucralose and maltodextrin. Long-term side effects of esophageal TCS have not been determined to date, but esophageal deposition will allow for first-pass metabolism to occur, and hence minimal systemic absorption of corticosteroids.

You explain to AC that EoE is a chronic disease, cessation of therapy results in disease recurrence,[26-28] and chronic untreated inflammation likely leads to esophageal stricture formation.[29,30]