How I Approach the Management of Eosinophilic Esophagitis in Adults

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Eosinophilic esophagitis (EoE) is diagnosed in patients presenting with esophageal symptoms and histologic evidence of eosinophil-predominant inflammation without identifiable secondary causes of esophageal eosinophilia. Consequences of EoE in adults include a negative impact on quality of life, particularly centering on eating behaviors, and food impaction that may necessitate ER visits and pose an, albeit uncommon, risk of esophageal perforation (1,2). In this section, I have summarized advice regarding the management of EoE that is derived both from my experience as well as from an evolving evidence base.

ENDOSCOPIC FEATURES: SEEING IS BELIEVING

Studies have demonstrated that endoscopic severity is a major determinant of physician assessment of overall disease severity of EoE in adults (3). For clinical practice, I believe that the use of standardized nomenclature to characterize and grade the endoscopic features can facilitate communication between gastroenterologists (4). A validated endoscopic scoring tool is currently available in Provation as a pull down menu. "Seeing is believing" and improvement in endoscopic appearance can support decisions regarding the effectiveness of treatment (Figure 1). This may be pertinent in individual cases where the histologic response is indeterminate (e.g., a reduction from 100 to 15 eos/hpf) but endoscopic mucosal healing is evident (i.e., disappearance of previously identified exudates, furrows, and edema). If a previous endoscopy showed marked, diffuse inflammatory features, perhaps endoscopic mucosal healing is more relevant than a single microscopic high-power field demonstrating a focus of inflammation? On another practical level, endoscopy provides a means of detecting remodeling consequences in the form of strictures that are not assessed by means of standard histology and that inform decisions regarding esophageal dilation.

PPI: MORE THAN JUST ACID SUPPRESSION?

One of the more controversial subjects in EoE is the rationale and necessity for a proton pump inhibitor (PPI) therapeutic trial in patients with dysphagia and esophageal eosinophilia indicative of a diagnosis of EoE. Prospective studies have demonstrated that 25–50% of such patients will show histologic response to a PPI trial. More recent data have demonstrated that such patients are symptomatically, endoscopically, histologically, and genetically indistinguishable from "guideline-defined EoE" patients (i.e., those with persistent eosinophilia on PPI) (5). These observations have called into question the utility of the PPI trial to "rule out GERD." Given this ambiguity, I discuss with my patients the concept of reversal of a reflux-induced epithelial barrier defect that may prevent immune activation by swallowed antigen.

I generally perform a baseline endoscopy in patients I suspect of having EoE prior to PPI initiation. If patients with eosinophilia on this index upper endoscopy (EGD) show evidence of erosive esophagitis or demonstrate a significant reduction, but not normalization, of eosinophilia on follow-up EGD on PPI, I will continue the PPI and add medical or diet therapy. While performing the baseline EGD after treating with PPI may be more efficient and cost effective, the PPI will mask underlying coexistent reflux esophagitis and the magnitude of a partial histologic response. In patients who fail to demonstrate convincing symptom and histologic improvement, I stop the PPI and switch to steroids or diet. I continue PPI therapy in patients who demonstrate symptom and histologic response to PPI. For patients who achieved this response on high-dose PPI, I will typically perform a follow-up examination in the following year on a lower PPI dose realizing that a small proportion of patients may relapse.

DIET THERAPY: THE FIRST COURSE AND NOT JUST FOR LEFTOVERS

Currently, there are no trials that directly compare the efficacy of topical steroids with an elimination diet for EoE. Nevertheless, both forms of therapy have a high degree of effectiveness. When offered both options, many of my patients voice a strong preference for one form of therapy over the other. Steroids offer an easy and rapidly effective response, but patients may have concerns with the long-term reliance on medications and uncertain.

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HOW I APPROACH IT

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I routinely discuss known adverse effects of Candidiasis and logical delivery method compared with the aerosolized modality. Packets within the diskus can be swallowed and provide a more logical delivery system but are also cumbersome to prepare when the released mist. Liquid formulations of budesonide are a more used in clinical practice, patients report challenges in swallowing the released mist. Liquid formulations of budesonide are a more logical delivery system but are also cumbersome to prepare when mixed with sucralose or honey to increase viscosity. On the basis of an idea shared with me by Dr Alex Straumann, I have switched the released mist. Liquid formulations of budesonide are a more logical delivery system but are also cumbersome to prepare when mixed with sucralose or honey to increase viscosity. On the basis of an idea shared with me by Dr Alex Straumann, I have switched

from the inhaler to the diskus formulation of fluticasone. Individual doses of powdered fluticasone contained within foil-lined packets within the diskus can be swallowed and provide a more logical delivery method compared with the aerosolized modality. I routinely discuss known adverse effects of Candidiasis and potential, but unlikely, risks of adrenal insufficiency and reduced bone density. Until long-term safety data is available, I do annual testing with serum cortisol and plasma adrenocorticotropic hormone (ACTH) for my patients on long-term steroids.

STERIOD FORMULATION. PUFF BUT DON’T INHALE

Topical steroid formulations that are currently used are neither designed for esophageal delivery nor Food and Drug Administration approved for EoE. While the fluticasone inhaler is commonly used in clinical practice, patients report challenges in swallowing the released mist. Liquid formulations of budesonide are a more logical delivery system but are also cumbersome to prepare when mixed with sucralose or honey to increase viscosity. On the basis of an idea shared with me by Dr Alex Straumann, I have switched from the inhaler to the diskus formulation of fluticasone. Individual doses of powdered fluticasone contained within foil-lined packets within the diskus can be swallowed and provide a more logical delivery method compared with the aerosolized modality. I routinely discuss known adverse effects of Candidiasis and potential, but unlikely, risks of adrenal insufficiency and reduced bone density. Until long-term safety data is available, I do annual testing with serum cortisol and plasma adrenocorticotropic hormone (ACTH) for my patients on long-term steroids.

SETTIN PATIENT EXPECTATIONS: TREAT TO TARGET

Symptoms of dysphagia or food impaction are the impetus for my patients to seek medical attention and integral to the diagnosis of EoE. However, symptoms are unreliable as a sole determinant of disease activity. Dissociation between the presence and magnitude of esophageal eosinophilia and symptom severity exists as exemplified by the observation that dysphagia may resolve after esophageal dilation without reduction in eosinophilia (6). Moreover, symptoms may improve as the result of careful mastication, avoidance of hard texture foods, and prolonged meal times that may mask the presence of high-grade esophageal stenosis. Taking a page from the inflammatory bowel disease literature, my goals of therapy in EoE are to “treat to target.” (i) elimination of esophageal eosinophilia (<5–15 eos/hpf), (ii) resolution of dysphagia in the absence of avoidance of hard-to-chew foods, and (iii) maintenance of an esophageal diameter of 16 mm or greater (6).

DILATION: SHORT-TERM PAIN FOR LONG-TERM GAIN

Although steroids and diet are highly effective at reducing esophageal eosinophilic inflammation, they provide less consistent benefits in terms of reversal of existing esophageal strictures. Reversal of remodeling may be more effective in children or with long-term administration. For my adult patients with strictures, I view esophageal dilation as a highly effective, immediate, and safe means of alleviating dysphagia that can provide long-term relief of dysphagia with or without concomitant use of medical or diet therapy.

“Guess-stimation” of stricture diameter prior to dilation is challenging and may improve in the future with use of the functional luminal imaging probe. I fully concur with the dictum of “start low and go slow” advocated in Dr Joel Richter’s recent editorial in this journal earlier this year. I have a general preference for use of bougie dilation on the basis of the longer and multiple strictures in EoE, as well as ability to feel stricture resistance as a means of assessing stricture diameter. Balloon dilation is effective for short strictures and allows for immediate visualization of treatment effect. I routinely inspect the esophageal mucosal after 1–2 mm dilation increments or after encountering resistance to bougie passage. I will typically terminate a dilation session once an adequate degree of mucosal disruption has been achieved, regardless of the number of millimeters to which the esophagus has been enlarged (deviating from the “rule of threes”) (Figure 2). On the basis of published data and our own institutional experience, I do not view dilation as having a significantly higher perforation risk than for benign strictures of other causes (6). Nevertheless, I caution my patients about the almost universal, "short-term pain" after dilation owing to the greater length of mucosal lacerations.

MAINTENANCE. CAN A PUFF A DAY KEEP THE DILATOR AWAY?

Studies have shown that both eosinophilic inflammation and symptoms recur within weeks to months after cessation of either diet or steroid therapy in EoE. In addition, retrospective studies point to progression of strictures in association with duration of untreated disease and that more frequent use of topical steroids is associated with a lower risk of food impaction. Such
observations provide the rationale for use of maintenance therapy. In my practice, I taper steroid dosing to the lowest dose needed to maintain histologic healing. I readily acknowledge that it is not clear that every patient benefits from long-term medication use. Thus, when counseling patients, I assess their individual disease severity and course to tailor decisions for as needed (PRN) or low-dose maintenance therapy. Until more data are available, clinical monitoring for progression without chronic therapy may be appropriate for selected patients with mild disease severity without evidence of progression.

The optimal management of EoE continues to evolve. The satisfaction of diagnosing EoE extends beyond simply giving a name to describe a patient’s condition and extends to the ability to provide highly effective medical, dietary, and endoscopic interventions that alleviate troublesome symptoms and should prevent disease progression. For the gastroenterologist, this will hopefully translate to fewer “wake up” calls at 2 in the morning for yet another food impaction!

CONFLICT OF INTEREST
Guarantor of the article: Ikuo Hirano, MD.
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REFERENCES
1. What percentage of patients with esophageal eosinophilia will have a histologic response to PPI therapy?
   a. 5-10%
   b. 75-85%
   c. 22-50%
   d. 15-20%

2. Regarding dilation for EoE
   a. perforation is more common than dilation for other etiologies
   b. pain after dilation is more common than after dilation for other etiologies
   c. goal is to reach 16mm in the first or second endoscopy
   d. Bougie dilation may be more efficient than balloons for multiple or long strictures

True or False

3. Patients who prefer to go on an elimination diet must be prepared to undergo an additional 5-6 endoscopies

4. A patient who becomes totally asymptomatic on therapy for EoE does not need a repeat endoscopy to assess for response

5. Fluticasone diskus formulation provides a powder that can be swallowed and is easier than using the inhalers

6. If long or deep “lacerations” are noted on the esophageal mucosa after dilation, the patient should have a gastrografin swallow prior to discharge from the endoscopy unit.

7. The severity of endoscopic findings on initial EGD will determine which patients are likely to respond to PPI alone

8. Patients who fail to improve after PPI therapy, steroids or diet therapy should be added to the PPIs.

9. After 6-12 weeks of steroid therapy, most patients who achieved a complete response can successfully discontinue therapy