Successful Food Elimination Therapy in Adult Eosinophilic Esophagitis

Not All Patients are the Same

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Abstract: Eosinophilic esophagitis (EoE) is a chronic, immune/antigen-mediated, esophageal disease characterized by esophageal dysfunction and eosinophilic inflammation, manifested mainly as dysphagia and frequent food impaction. EoE is recognized into the spectrum of food allergy, but food sensitization studies used not to be efficient to identify the triggering food, because of what patients are frequently treated with topic steroids or even endoscopic esophageal dilation. Herein, we describe 3 adult patients—all suffering from EoE, but with different sensitization patterns—who were treated successfully with elimination diets. Allergy tests indicated no food sensitization for patient 1, but challenge with milk and wheat were positive. Food IgE-mediated allergies were found in patients 2 and 3; inflammation was resolved with food elimination. Lack of food allergy sensitization does not exclude the possibility of food allergies as a cause of EoE; elimination diets must therefore be considered as an effective diagnostic and treatment tool.

Key Words: eosinophilic esophagitis, allergic esophagitis, challenge, food elimination, food allergy

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Eosinophilic esophagitis (EoE) is a chronic, immune/antigen-mediated, esophageal disease characterized by esophageal dysfunction and eosinophil inflammation.[1] The past few years have witnessed a progressive rise in diagnosed cases of EoE, making it the second cause of chronic esophageal disease behind gastroesophageal reflux.[2]

At the same time, research efforts aimed at providing efficient therapy for this chronic illness have also intensified. However, no treatment strategies have been commonly accepted to date, making adequate management of these patients somewhat controversial.[3] Nevertheless, 3 different therapeutic approaches have been used effectively in patients with EoE:

The first approach involves endoscopic dilation. Endoscopic or radiologic examinations are frequently able to identify alterations in the caliber of the esophagus, including a narrowing of the lumen.[4] From the earliest documented cases, mechanical dilation has been used as a treatment option for EoE, similar to the way it is used in other types of fibrous esophageal stenosis, such as peptic stenosis or after caustication. However, recent reports of cases of esophageal rupture and large tears and lacerations in these patients because of the extreme fragility of the organ as a result of eosinophilic inflammation[5] make this a less attractive option.

The classification of EoE as an immunoallergic disorder has led to a second approach, namely that of treating patients with drugs for bronchial asthma.[6] However, as no specifically approved drugs are currently available for EoE patients, these treatments must be used out label.

From the first studies carried out on children with EoE, allergies to certain dietary components have been shown to contribute significantly to its pathogenesis; indeed, it is well documented that both the symptoms and the histology levels improve after eliminating certain foods from the diet.[7] Initial studies based exclusively on elemental diets showed a huge efficacy in reverting EoE,[8] but this approach is not plausible in adults or chronic patients.

For this reason, a third treatment approach was developed that identified offending foodstuffs through allergic sensitization studies. Spergel et al[9] were the first to use skin prick tests (SPTs) and atopy patch tests (APTs) on pediatric patients with EoE to guide elimination diets, obtaining positive results in 77% of the cases. Unfortunately, these good results have not been reproduced by other research groups; moreover, there is no data from studies using the same strategy with adults.[1]

On account of this, dietary management of adult EoE remains controversial, although an approach algorithm has been published recently by our group[3] (Fig. 1). In this study, we describe 3 EoE adult patients who were treated successfully with the aid of dietary management.

CASE REPORTS

Patient 1

A 27-year-old woman exhibiting symptoms of dysphagia and pyrosis for 4 years and initially diagnosed with gastroesophageal reflux disease was irresponsive to antisecretory and prokinetic drugs. The endoscopic appearance was normal. Esophageal manometry and 24-hour pH-monitoring revealed no alterations, so the patient underwent a new endoscopic examination including biopsies, after which she was diagnosed with EoE. No additional allergy symptoms were presented. Allergy tests including SPTs and specific IgE (sIgE) were developed for inhalants and food, results of which are summarized in Table 1. APT developed with food including

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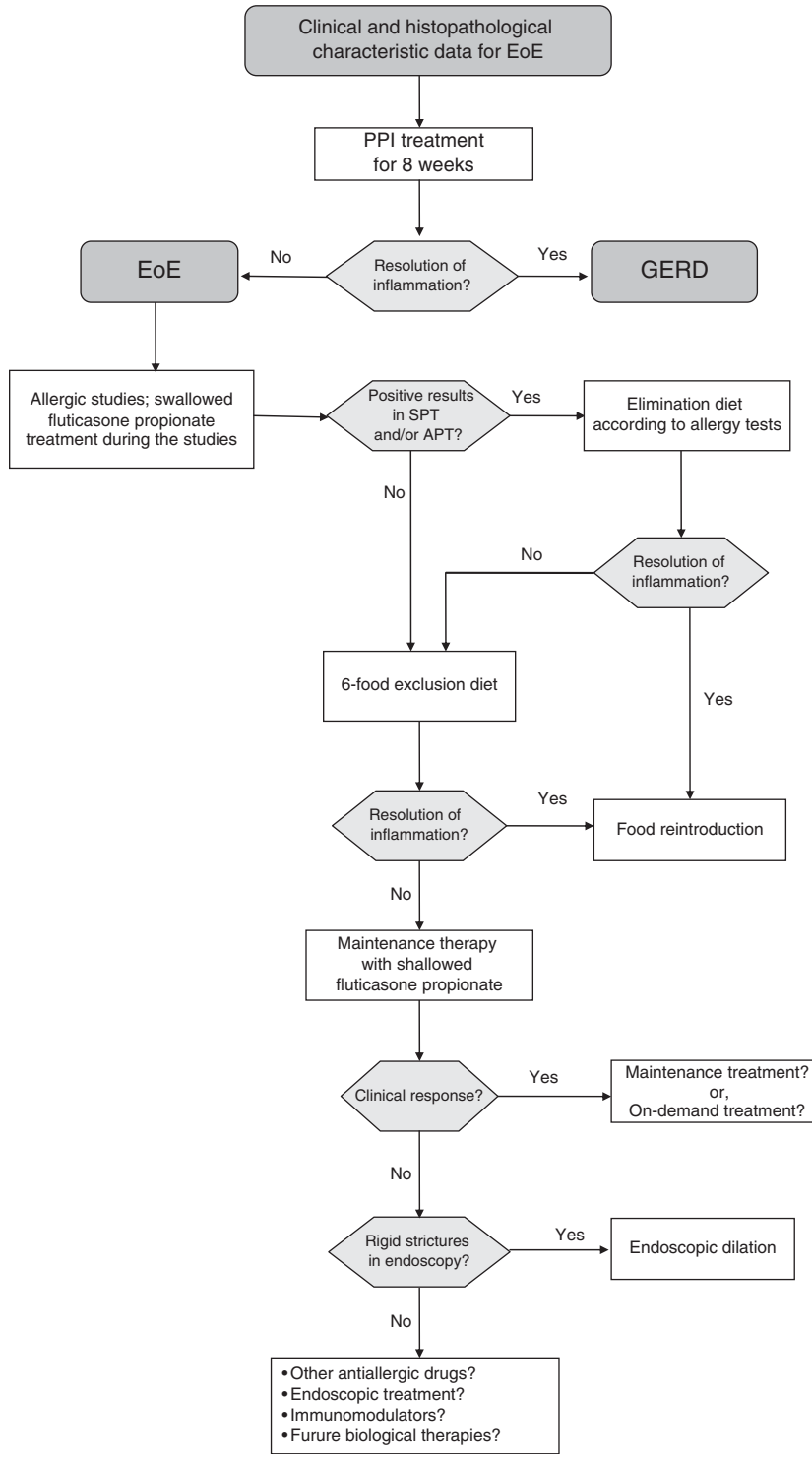

FIGURE 1. Proposal of sequential algorithm for treating eosinophilic esophagitis (EoE). APT indicates atopy patch test; GERD, gastroesophageal reflux disease; PPI, proton pump inhibitor; SPT, skin prick test.

milk, eggs, cereals, legumes, nuts, seafood, and meat also resulted negative. Despite these findings, a 6-food elimination diet was set up, avoiding cereals (wheat, rice, and corn), dairy products, eggs, legumes, nuts, and seafood, and given amino acid-based supplements. After 6 weeks, a new endoscopy with esophageal biopsies was performed, resulting normal with no eosinophilic mucosal inflammation. Food was then sequentially reintroduced with a new endoscopic examination with biopsies 6 weeks after challenge with each specific food. Eosinophilic inflammation and symptoms only reappeared after challenge with wheat and milk.

TABLE 1. Specific Immunoglobulin E to Aeroallergen and Food Results for Our 3 Patients

	Patient 1		Patient 2		Patient 3	
Allergen	**sIgE KU/L**	**SPT (mm)**	**sIgE KU/L**	**SPT (mm)**	**sIgE KU/L**	**SPT (mm)**
Cow's milk	< 0.35	0	2.84	11 × 8	< 0.35	0
Goat's milk	NA	0	0.65	6 × 4	< 0.35	0
Sheep's milk	NA	0	1.03	7 × 5	< 0.35	0
Casein	< 0.35	0	< 0.35	0	< 0.35	0
Egg white	< 0.35	0	< 0.35	0	< 0.35	0
Egg yolk	< 0.35	0	< 0.35	0	< 0.35	0
Codfish	< 0.35	0	< 0.35	0	< 0.35	0
Wheat	< 0.35	0	< 0.35	0	< 0.35	0
Peanuts	< 0.35	0	< 0.35	0	< 0.35	0
Soy	< 0.35	0	< 0.35	0	< 0.35	0
Lentils	< 0.35	0	< 0.35	7 × 6	< 0.35	0
Beans	NA	0	NA	0	0.72	7 × 6
Chickpeas	< 0.35	0	< 0.35	0	0.53	6 × 5
Rice	< 0.35	0	< 0.35	0	< 0.35	0
Anisakis	< 0.35	0	< 0.35	0	< 0.35	0
Veal	NA	0	0.81	8 × 5	NA	0
Pork	NA	0	3.52	12 × 7	NA	0
Lamb	NA	0	2.46	10 × 8	NA	0
Turkey	NA	—	< 0.35	0	NA	0
Dermatophagoides pteronyssinus	< 0.35	0	2.01	8 × 6	< 0.35	0
Olive	1.16	9 × 8	0.8	7 × 4	13.1	8 × 6
Phleum pretense	< 0.35	5 × 4	< 0.35	6 × 5	0.49	5 × 4
Dander (cat)	< 0.35	0	86.9	13 × 7	< 0.35	0
Epihelium (dog)	< 0.35	0	29.6	9 × 7	< 0.35	0

NA indicates not available; sIgE, specific IgE; SPT, skin prick test.

Patient 2

A 37-year-old man with seasonal rhinoconjunctivitis had suffered repeated food impaction after eating bread for 2 years, with no seasonal preference. He was diagnosed with EoE after endoscopy with esophageal biopsies. Allergy tests included SPT and sIgE for inhalants and food (results summarized in Table 1). The APT was negative for food (mentioned in patient 1). At this point, the patient was put on a diet according to the sIgE and SPT results observed, avoiding milk, lentils, and meat except for chicken and turkey. A new endoscopy was performed after 6 weeks, revealing resolution of eosinophilic inflammation. A sequential food reintroduction challenge was carried out accompanied by repeated endoscopies; esophageal eosinophilic inflammation and derived symptoms reappeared 6 weeks after reintroducing dairy products. Meats and lentils were completely tolerated.

Patient 3

A 37-year-old woman had presented pollen-induced rhinoconjunctivitis and chronic dysphagia and multiple episodes of solid food impaction for 6 years with no seasonal predominance. She was diagnosed with EoE 2 years ago, at which time oral treatment with swallowed fluticasone propionate was introduced (Flixonase 0.4 mg nasal drops, Glaxo-Smithkline, Durham, UK). This resulted in partial improvement of symptoms. Allergy tests were thus performed to guide elimination diet decisions (Table 1). APT performed with food (described above) resulted negative. According to the results, a diet avoiding legumes was subsequently recommended, and fluticasone was dropped out. Six weeks after starting the diet, no evidence of inflammation was observed in endoscopic or histopathologic examinations. Sequential challenge was thus begun by reintroducing beans, chickpeas, and lentils. Endoscopic and biopsy controls were repeated 6 weeks after every individual food was reintroduced. Eosinophilic infiltration and derived symptoms recurred after every reintroduction.

DISCUSSION

We have described 3 adults patients diagnosed with EoE from whom different diet therapies lead to the resolution of eosinophilic inflammation and other symptoms. Food allergy was determined to be the cause of the disease in all 3 patients. However, different sensitization patterns were observed for each patient; as described above, even though both patients 2 and 3 were able to manage the disease by following a diet avoiding those foods for which sIgE sensitization was demonstrated, patient 2 only developed symptoms after milk challenge despite the fact that he was also found to be sensitized to meat.

In contrast, no food sensitization was demonstrated in the allergy tests (sIgE and SPT) carried out on patient 1, who was sensitized only to grass and olive pollen. Despite this, a 6-food elimination diet successfully resolved his eosinophilic inflammation and other symptoms. The disease recurred only after the separate reintroduction of milk and wheat, pinpointing a food allergy as the cause of EoE in this patient.

Several interesting observations arise from this study:

EoE seems to be a heterogeneous disorder in which eosinophilic infiltration of the esophagus seems to be the common feature in patients who exhibit different food sensitization patterns. In fact, research has shown that patients suffering from EoE are also heterogeneous from a molecular point of view, as the esophageal biopsies of adult patients exhibit distinct profiles for cytokine gene expression.[10]

From recent research, we also know that IgE-mediated sensitizations seem to play an important role in the pathophysiology of EoE, as local IgE esophageal production has been observed in some EoE patients.[11] Nonetheless, these case studies show that the pathophysiology of EoE cannot be

explained by only attending to IgE-mediated sensitizations because on the one hand, not all IgE sensitizations detected with SPT or sIgE causes EoE; indeed, several of these sensitizations proved to be innocuous in our patients. In contrast, the absence of IgE-mediated food sensitization does not exclude the possibility of a food allergy as being the cause of EoE, as we have seen in the case of patient 1, in which a cell-mediated immunoallergic reaction might also be considered.

Further studies should evaluate the real relationship between EoE and food allergy, whether they are mediated by IgE or not. Nevertheless, sequential reintroduction of suspicious foods under monitoring with repeated endoscopic and histopathologic controls seems to be a very useful method in assessing the specific cause of EoE, which, in turn, allows doctors to establish a definitive and effective treatment for the disease.

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