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EOSINOPHILIC ESOPHAGITIS

Recognizing the Clues

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If your patients complain that their throat makes a clunking sound, they have sticky saliva and a spicy throat, they ate a scratchy food, or their food gets stuck when they swallow; they may have a diagnosis of eosinophilic esophagitis (EoE). (Note: EoE, as opposed to *EE*, will be used here because of the confusion of *EE* with erosive esophagitis in the more traditional gastroenterology field). Children with EoE, especially young children, may note problems with eating and swallowing. (Haas & Maune, 2009; Jarocka-Cyrta, Wasilewska, & Kaczmarski, 2010; Mukkada et al., 2010; Pentiuk, Miller, & Kaul, 2007; Spergel et al., 2009). Most have grown well and appear normal, but on further questioning, many are found to have a variety of somewhat "unusual for age" complaints (see Table 1). For instance, on initial history, an adolescent boy may state that he has no problems in swallowing, but on further questioning, he is the last one to leave the table during meals, uses several glasses of water to wash his meals down after swallowing, or avoids certain textured foods like meats because they are difficult to swallow. Likewise, parents may note that toddlers may refuse to eat or spit food out after putting it in their mouth. These responses may be clues to esophageal inflammation that can be due to a variety of causes, but in many cases, it may be the result of EoE.

In this light, we present two case studies that reveal key historical features often encountered in children with EoE. These features represent early clues to the initial diagnosis that may prompt earlier evaluation with the

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TABLE 1. Symptoms Associated With Eosinophilic Esophagitis

List of symptoms
Abdominal pain
Chest pain (heartburn)
Coughing
Decreased appetite (forced to eat, but not hungry)
Dysphagia (food sticking—especially meat, bread, pasta, and pills; "toy car" in throat; "furball" in throat; sticky saliva; throat makes a clunking sound; food wads up; holds food in mouth for 15 minutes before swallowing; chews food finely; needs a lot of water to wash food down; and last one to leave the table)
Food impaction
Food refusal (spits out food; throws food away; self-limits food; fear of choking; and picky eater)
Choking/gagging
Nausea ("food smells make me sick")
Regurgitation
Sleeping difficulty
Throat pain (itchy, scratchy, spicy, and hot spit)
Vomiting
Weight loss, poor growth

institution of appropriate treatment. These scenarios are common presentations that both gastroenterology and allergy nurses may hear in the course of their usual busy days.

Case Reports

Case 1: Fear of Feeding

A 3-year-old African American boy presented at 13 months of age with complaints of vomiting, swallowing difficulties, and weight loss due to food refusal. Consistent with a history of gastroesophageal reflux disease (GERD), he would regurgitate after meals. In contrast to most children with GERD, he also appeared to have problems in swallowing foods, which eventually led to reduction in his oral intake. Pain did not appear to be the primary reason for his reduced intake. On further questioning, his parents noted that their child would self-limit the ingestion of solid foods, especially meats, and he eventually began to fall off his growth curve.

Treatment with a histamine-2 (H_2) receptor antagonist, metaclopromide, and a change in his formula to a protein hydrolysate were ineffective in improving his symptoms. Repeated attempts to advance the texture of his diet past stage 2 baby food without gagging were unsuccessful. In addition, he had a history of allergic diseases, including eczema, asthma, and food allergy to egg products. The child was referred to a pediatric gastroenterologist for evaluation.

An upper gastrointestinal series revealed normal anatomy, and the patient was started on lansoprazole 15 mg daily for possible GERD. Because symptoms persisted, an upper endoscopy revealed a grossly normal mucosa, but esophageal biopsies revealed 35 eosinophils per high-power field (HPF), with degranulating eosinophils noted in the distal esophagus and 15 eosinophils per HPF in the proximal esophagus. The gastric and duodenal mucosa was normal.

After discontinuing proton-pump inhibition for 5 days, a pH impedance-monitoring study was performed; the results of this test were normal. On the basis of this outcome, the child received a diagnosis of EoE, and treatment with fluticasone at a dose of 110 μg, one puff swallowed twice a day, was initiated. With the goal of identifying a therapeutic elimination diet, an allergist performed skin testing and allergen-specific IgE levels test (ImmunoCAPs, Portage, MI) to foods based on the child's diet. These tests identified sensitivity to milk, egg, soy, peanut, tree nuts, oat, wheat, peas, and sesame seed. As a result of this testing, consultation with a pediatric dietitian provided an age-appropriate elimination diet.

Because of persistent problems advancing textures, a feeding specialist was consulted. Three months after starting treatments, vomiting had decreased, the patient's swallowing had improved, and he began gaining weight. One year later, repeat analysis of the esophageal mucosa biopsies revealed significant improvement and his parents were pleased that he was growing, happier, social, and full of energy.

Discussion

Several features make this case study remarkable. First, limited literature and clinical experience suggest that EoE affects primarily Caucasian males, but the patient described here is of African American descent. More epidemiological studies will be required to determine the prevalence of EoE overall and its ethnic distribution specifically. Second, this patient had long-standing symptoms typically associated with GERD. GERD is more common than EoE, and thus, a therapeutic trial of antiacid treatment is reasonable as an initial step for the treatment of symptoms related to esophageal dysfunction. A pH/impedance study was performed to rule out GERD as an etiology for the esophagitis since the patient had not been on high-dose–proton-pump inhibition at the time of the

endoscopy. Finally, in this patient with EoE, the primary reasons for consultation were related to reduction in eating, which lead to failure to thrive. In this patient, the use of anti-inflammatory medications, diet restriction, nutritional rehabilitation, and feeding therapy led to a successful treatment of his disease.

Case 2: The Reluctant Carnivore

The second case study involves an 11-year-old boy with a history of GERD since infancy. The H_2 receptor antagonists had not been effective and were stopped 1 year before evaluation. Longstanding symptoms included abdominal pain, vomiting, dysphagia, and food sticking. While on a 3-week vacation, the patient experienced two episodes of food impaction of meat, both of which resolved spontaneously. Because of the fear of having another food impaction, the patient reduced his eating to the point that he lost 7 lb during the remainder of his trip. Further questions about his history uncovered a pattern of altered swallowing behaviors such as always having a glass of liquid with him during meals to wash food down and requiring long periods of time to chew his food.

Subsequent evaluation revealed a normal upper gastrointestinal series. An upper endoscopy showed white plaques coating the proximal and distal esophageal mucosa. Mucosal biopsies of the esophagus identified 40 eosinophils per HPF, with eosinophilic microabscesses in the distal esophagus and seven eosinophils per HPF in the proximal esophagus. After the upper endoscopy, fluticasone at a dose of 220 μg, two puffs swallowed twice a day, was started. The boy had seasonal allergic rhinoconjunctivitis, but referral to an allergist for evaluation and skin-prick testing to foods were unrevealing.

Six weeks after the onset of treatment, his appetite and symptoms had significantly improved, which helped to reduce his fear of future food impactions. Subsequent endoscopic analysis revealed normal-appearing mucosa, histopathology, and pH/impedance monitoring of the distal esophagus.

In contrast to the first patient, this older child demonstrates the acute impact of EoE. Although he had a history of unresolved and longstanding symptoms, the acute events of meat impactions led him to reduce his ingestion of foods that subsequently led to weight loss and eventual referral to a gastroenterologist. Subsequent analysis and his prompt response to topical corticosteroids led to a diagnosis of EoE, and the patient has since thrived. Recognition of this as a diagnostic possibility with its comorbid features is critical to nursing practice in allergy and gastroenterology.

Eosinophilic Esophagitis

EoE is a chronic inflammatory disease of the esophagus that is characterized by symptoms of vomiting, abdominal pain, dysphagia, and food impaction, which occur in the context of dense esophageal eosinophilia. (Furuta et al., 2007). Other causes of esophageal eosinophilia need to be ruled out; in EoE, the rest of the gastrointestinal tract mucosa is normal. EoE occurs with a prevalence of between 1 and 4 per 10,000 individuals, with men being most commonly affected. A family history of EoE or esophageal stricture is common, suggesting a genetic link.

Because of the common symptomatology, EoE is often confused with GERD. Symptoms of EoE include food refusal, feeding dysfunction, poor growth, chest pain, abdominal pain, nausea, and vomiting (see Table 1). Although not yet certain, some suggest that the variation in reporting occurs because of the inability of young children to relate exact symptoms or symptoms change over time due to progressive inflammation. In the former situation, children may not be able to adequately describe dysphagia and simply reduce their oral intake, as in our first case described previously, or complain of a sore throat. In the later situation, longstanding inflammation may lead to tissue remodeling and scarring, with resultant stricture formation.

Importantly, some children learn to accommodate to esophageal inflammation and thus develop coping behaviors that may not be reported on the initial history. Slow eating, being the last to leave the table after meals, washing food down with liquids, chewing foods excessively, inability of swallowing pills, avoiding highly textured foods such as meats, and limiting social engagements associated with eating are common occurrences but may not be spontaneously reported by children and teenagers due to embarrassment or because they have become commonplace parts of their lives (Haas & Maune, 2009; Heller, Freeman, & Furuta, 2009). Some of these symptoms were exemplified in the second case.

The diagnosis of EoE relies on the exclusion of other causes of esophageal eosinophilia. For instance, esophageal eosinophilia has been associated with a number of diseases, including, most commonly, GERD, but also, Crohn disease, collagen vascular disease, eosinophilic gastritis, parasitic infection, malignancy, and drug sensitivities (Fleischer & Atkins, 2009) (see Table 2).

A number of endoscopic findings characterize EoE. Although none of these are diagnostic, all represent evidence of acute inflammation or chronic remodeling of the esophagus (see Figure 1). Mucosal linear furrows,

TABLE 2. Diagnostic Criteria for Eosinophilic Esophagitis

Symptoms associated with esophageal dysfunction
Esophageal eosinophilia
Other causes of esophageal eosinophilia have been ruled out.

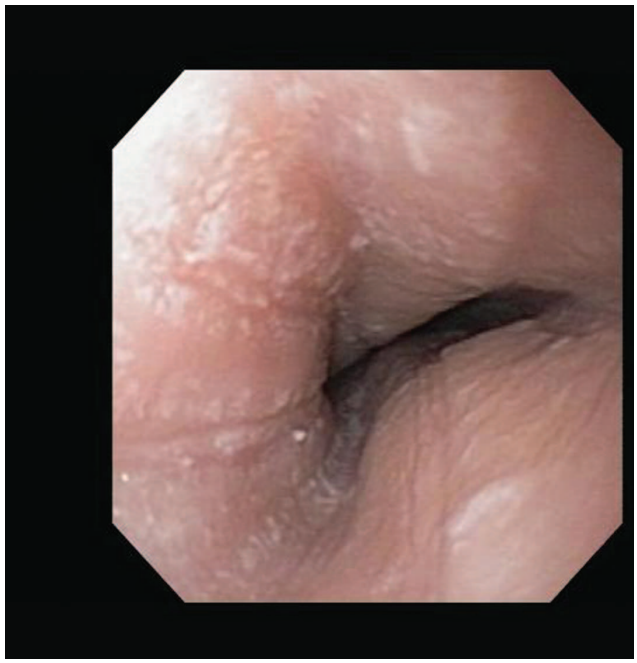

FIGURE 1. Endoscopic features of esophageal eosinophilia. Endoscopic appearance of acute inflammation in esophageal eosinophilia demonstrating lack of vascular pattern, white exudates, and linear furrows.

ridging, white exudates, and loss of vascular pattern are all indicative of the accumulation of inflammatory cells, such as eosinophils, in the esophageal mucosa (see Figure 1). Strictures, linear shearing, and long-segment narrowing are demonstrative of longstanding inflammation and complications of EoE.

Histologically, eosinophils increase in the squamous epithelia and may form microabscesses or line up along the luminal surface (Collins, 2008). Eosinophil degranulation, basal cell hyperplasia, rete peg elongation, and submucosal fibrosis are also associated features, but to date, no pathognomonic features have been identified (see Figure 2).

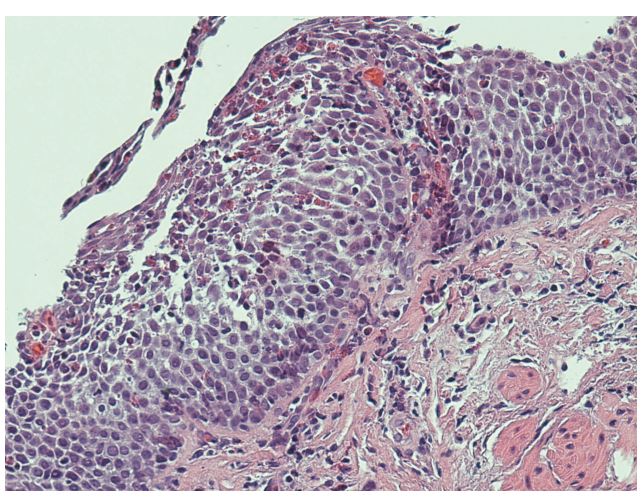

FIGURE 2. Histopathology associated with esophageal eosinophilia. Typical histological appearance of esophageal eosinophilia showing increased eosinophils, luminal layering rete peg elongation, and basal zone hyperplasia.

EoE is thought of as an allergic disease of the esophagus (Atkins & Furuta, 2010; Atkins, Kramer, Capocelli, Lovell, & Furuta, 2009; Brown-Whitehorn & Spergel, 2010; Spergel, 2007). In fact, a number of studies provide strong evidence for this link. Basic science studies have convincingly demonstrated that allergen challenge can lead to eosinophilic inflammation (Mishra, 2009; Rothenberg, 2009).

Clinical studies and experiences also support an allergic etiology. For instance, between 33% and 75% of patients with EoE have some form of allergic disease, including food allergies, asthma, eczema, allergic rhinitis, and environmental allergen sensitization. These findings have led to allergy evaluations that include skin-prick testing. ImmunoCAPs or specific IgE-serum–testing checks for the presence of IgE to specific foods in the bloodstream that indicates sensitization to specific foods, and in some circumstances, food allergy. *Food sensitization* is defined as the presence of food-specific IgE by skin testing or

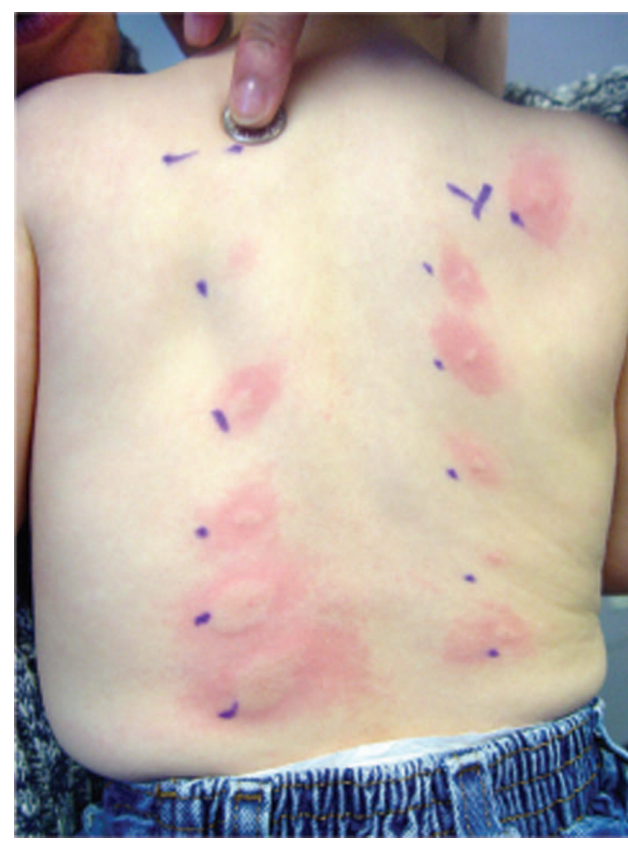

FIGURE 3. Skin-prick testing for food allergies. The procedure is performed on the child's back. Commercially available allergen extract drops are placed on the back and the skin is pricked with a device (much like a plastic tooth-pick) at a 45-degree angle with pressure to tent the skin. After 15 minutes, the test site is wiped to remove the extract and any swelling is measured. A *wheal* is defined as a palpable swelling at the site, whereas a flare represents erythema.

laboratory tests, whereas *food allergy* is defined as a reproducible physical response to a food that is immunologically mediated. These terms are not synonymous. Allergen skin-prick testing consists of applying commercially derived food protein extracts to the skin (see Figure 3).

These tests are selected on the basis of the child's diet. The utility of this type of testing has been demonstrated in a number of studies showing that exclusion of identified foods leads to successful treatment of the disease (Brown-Whitehorn & Spergel, 2010; Kagalwalla et al., 2006; Spergel, Andrews, Brown-Whitehorn, Beausoleil, & Liacouras, 2005).

A number of studies have documented complications of EoE that include food impaction and esophageal stricture formation (Dellon et al., 2010; Hurtado-Waasdorp, Furuta, & Kramer, 2011; Schoepfer et al., 2010; Straumann, 2008; Straumann et al., 2008). Between 25% and 55% of children and adults entering the emergency room with an esophageal food impaction receive a diagnosis of EoE. Barrett's esophagus and esophageal cancer have not been definitively linked with EoE (Francalanci et al., 2008; Mukkada, Atkins, & Furuta, 2008; Wolfsen, Hemminger, & Achem, 2007).

Treatment of EoE can often be confusing and represents an area of active clinical investigation (Rothenberg, 2009; Schroeder, Atkins, & Furuta, 2010). For instance, the definition of successful treatment is not yet certain and is defined by some as the resolution of symptoms alone, whereas others require both improvement symptoms and histological abnormalities. Despite these ongoing controversies, growth and development remain key in the successful treatment of children with EoE. Treatments include topical steroids and nutritional management. The use of swallowed topical steroids takes advantage of the off-label use of metered-dose inhalers and nebulized preparations formally used for asthma (see Table 3). Successful strategies must balance the risks and benefits of suggested therapies.

Consultation with a registered dietitian is critical when foods are eliminated to ensure provision of appropriate calories, protein, vitamins, and micronutrients (Santangelo & McCloud, 2009). As shown in the case studies, children with EoE may have feeding dysfunction, either as a result of the acute inflammation or as a result of coping with the inflammation (Haas & Maune, 2009). Regardless, the expertise of a feeding specialist is frequently helpful in overcoming this aspect of the disease. Finally, psychosocial consultation to help with coping with the disease or treatments are often very helpful (Klinnert, 2009).

TABLE 3. Topical Steroid Treatments for Eosinophilic Esophagitis[a]

Fluticasone (Flovent): 2 puffs twice a day
1–5 yr, 44 μg
11 yr, 110 μg
12 yr and older, 220 μg
Budesonide (Pulmicort): Respules mixed with Splenda twice a day
1–5 yr, 0.25 mg/2 ml
6–11 yr, 0.5 mg/2 ml
12 yr and older, 1 mg/2 ml

Note. Instruct patients that they should not rinse their mouth, eat, or drink for 30 minutes after topical steroid administration. For metered-dose inhaler, no spacer should be used, and patients should not inhale when the medication is sprayed into the mouth.
[a]Proposed doses based on clinical experiences and studies (Aceves, Bastian, Newbury, & Dohil, 2007; Arora, Perrault, & Smyrk, 2003; Dohil, Newbury, Fox, Bastian, & Aceves, 2010; Lucendo, De Rezende, Comas, Caballero, & Bellon, 2008; Schaefer et al., 2008; Straumann et al., 2010; and Teitelbaum et al., 2002).

Summary

Symptoms of EoE may present acutely, but frequently, they will not surface for a longer period of time. It is important for care team members to perform effective interviewing to further define the information that patients and families share. Careful listening skills can also uncover the necessary clues needed to recognize and confirm a diagnosis of EoE. ✪

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