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Endoscopic assessment of eosinophilic esophagitis

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ABSTRACT

Eosinophilic esophagitis (EoE) is a clinicopathologic, inflammatory disease of the esophagus with increasing prevalence. In adults, the condition presents with dysphagia and may result in food impaction. There are a number of endoscopic findings in patients with EoE that include esophageal rings, linear furrowing, white plaques, strictures, and edema. Although individually each of these features may be seen in other esophageal diseases; when combined they have a high specificity for the pathologic finding of esophageal eosinophilia. Prospective studies have identified the presence of endoscopically identified, esophageal signs in most children and adults with EoE. In this article, we highlight a number of recent studies, including the development of an endoscopic classification and grading system to describe the esophageal manifestations of EoE. We also discuss the results of randomized controlled trials with end points assessing endoscopic findings before and after diet therapy and corticosteroids. Fibrostenotic sequelae are common in patients with EoE, and a technique to measure esophageal distensibility, which has been shown to be a predictor of risk of future food impactions and need for esophageal dilation, is discussed. Endoscopic features of EoE play an important role in our current understanding of the complications of EoE and are an important component of the assessment of disease severity and treatment response.

1. Introduction

Eosinophilic esophagitis (EoE) is a clinicopathologic inflammatory disease of the esophagus that has been increasing in prevalence [1]. This condition frequently leads to symptoms of dysphagia [2] and an increased risk of esophageal food impaction [3–6]. Biopsies taken of the esophagus at the time of endoscopy demonstrate eosinophilic inflammation of the squamous epithelium and tissue injury including subepithelial fibrosis and basal cell hyperplasia. Biopsies taken of the proximal and distal esophagus demonstrating 15 or more eosinophils per high-powered field characterize the pathologic aspects of EoE [7]. EoE prevalence is dependent on the population assessed. In the general population, the prevalence of EoE is 4-10 cases per 10,000, while among patients undergoing upper endoscopy for evaluation of dysphagia, the prevalence of EoE is 10%-15% [8,9].

There are several endoscopic findings that may be identified in patients with EoE although none are pathognomonic. These include longitudinal furrows, white exudates (plaques), rings (trachealization), strictures, edema (mucosal pallor or decreased vascularity), and a narrow-caliber esophageal lumen [7,10,11]. Patients have been described to have fragility of the esophageal mucosa ("crepe-paper esophagus"), which may lead to esophageal lacerations because of the passage of the endoscope [7,12]. Tracking of blood after esophageal biopsies can aid in improving visualization of furrowing of the esophagus in patients with EoE. Recently, increased resistance when extracting the forceps during esophageal tissue acquisition, a "tug sign," has been described as an additional feature [13]. A small minority of patients with EoE may exhibit subtle or absent visible endoscopic findings of the disease, making it important that all patients suspected of harboring the disease undergo esophageal biopsies.

In recent years, endoscopically determined mucosal healing has become an important therapeutic goal in Crohn's disease and is increasingly used as a predictor of clinical remission [14]. Mucosal healing in Crohn's disease is assessed as a goal beyond symptom control and as a primary end point in clinical trials. Although EoE is a distinct disease, the diseases share similarities as both are chronic immune disorders that result in clinically relevant fibrostenotic complications. Endoscopic features of both disorders are important considerations in the assessment of disease severity and treatment response.

2. What is the evidence?

A number of studies over the past decade have reported data regarding endoscopic findings in this disease. A recent meta-analysis systematically evaluated the prevalence and diagnostic utility of endoscopic features of EoE [10]. A total of 80 original articles and 20 abstracts incorporating 4678 patients with EoE

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were included with an overall pooled prevalence of 44% for esophageal rings, 21% for strictures, 9% for narrow-caliber esophagus, 48% for linear furrows, 27% for white plaques, and 41% for pallor or decreased vasculature. When limited to prospective studies, the authors noted that 7% patients with of EoE exhibited an unremarkable appearance of the esophagus at the time of endoscopy. Among the prospective studies, the prevalence of esophageal rings was 59%, strictures 17%, narrow-caliber esophagus 11%, linear furrows 61%, white plaques or exudates 44%, pallor or decreased vasculature 57%, and erosive esophagitis 15%. The diagnostic sensitivity for each of the endoscopic features was less than 50% but overall sensitivity was 87% if allowing for any single feature to be indicative of disease. The inclusion of patients who may have had concomitant gastroesophageal reflux disease (GERD) or proton pump inhibitor–responsive esophageal eosinophilia was a limitation to the findings of this study.

As highlighted by this meta-analysis, substantial heterogeneity exists in the currently used descriptions of the esophageal features of EoE. This observation reflects the lack of standardized definitions of the features as well as inconsistent reporting of each feature by different endoscopists and medical centers. The use of variable terminology such as "trachealization," "corrugation," "ringed esophagus," and "felinization" can create confusion. Several features, such as mild strictures or mucosal pallor, are often overlooked or inconsistently reported, especially in retrospective series. The lack of endoscopic or radiologic criteria for a narrow-caliber esophagus is problematic. Prospective studies offer greater appreciation for the diagnostic yield of endoscopy in EoE than retrospective studies. In recent prospective studies, the diagnostic sensitivities for endoscopically identified esophageal features exceeded 93%. The substantial increment in detection of the endoscopic signs in prospective compared with retrospective studies emphasizes the importance of careful and systematic inspection and nomenclature to optimize diagnostic capabilities of endoscopy.

Endoscopic findings in patients with EoE have been shown to vary by age. Younger patients are more likely to have findings of white plaques and a normal-appearing esophagus whereas adult patients are more likely to have strictures, narrow-caliber esophagus, rings, and crepe-paper mucosa [15–17]. Fibrostenotic features including strictures and severe rings are commonly identified in adults with active EoE but only among a minority of pediatric patients with EoE. The entity of pediatric EoE is more commonly characterized by an inflammatory phenotype including severe mucosal exudates. The presence of linear furrows and edema has been shown to be similar between age groups. These observations indicate a key distinction in the prevalence of fibrostenotic consequences of esophageal eosinophilia in different age groups. Furthermore, the endoscopic findings correlate with typical clinical presentations that are characterized by GERD-like symptoms in children and dysphagia in adults [16].

3. Diseases that mimic the endoscopic features of EoE

Diseases of the esophagus other than EoE may exhibit similar endoscopic findings. Esophageal rings may be found in patients with lichen planus, congenital esophageal stenosis, or graft vs host disease, although the appearance is not identical. A narrow-caliber esophagus may be seen in patients with a history of caustic ingestion, radiation treatment, long segment Barrett esophagus, or prolonged insertion of a nasogastric tube. Esophageal exudates can also be seen in the setting of GERD or in the setting of food residue in the esophagus, esophageal candidiasis, or after application of a topical anesthetic agent before endoscopy. Endoscopic findings must be interpreted in the context of a patient's histologic findings and clinical history so as to properly diagnose EoE.

4. Endoscopic REFerence Scoring system: A novel classification and grading system

A novel classification and grading system designed to assess endoscopic findings in EoE has recently been proposed and validated. The acronym for the Endoscopic REFerence Scoring system (EREFS) designates 5 major features of EoE (edema, rings, exudates, furrows, and stricture) [11]. This metric was created to standardize endoscopic assessment among endoscopists, but it also incorporated grading of major esophageal findings (Table). The validation process included the determination of interobserver agreement amongst private practice and academic, pediatric, and adult gastroenterologists with varying experience with EoE. Good interobserver agreement was

Table
Modified classification and grading system for the endoscopic assessment of the esophageal features of eosinophilic esophagitis [11].

Major features	
Fixed rings (also referred to as concentric rings, corrugated esophagus, corrugated rings, ringed esophagus, or trachealization)	• Grade 0: none • Grade 1: mild (subtle circumferential ridges) • Grade 2: moderate (distinct rings that do not impair passage of a standard adult diagnostic endoscope) • Grade 3: severe (distinct rings that do not permit passage of a standard adult diagnostic endoscope)
Exudates (also referred to as white spots or plaques)	• Grade 0: none • Grade 1: mild (lesions involving $<10\%$ of the esophageal surface area) • Grade 2: severe (lesions involving $>10\%$ of the esophageal surface area)
Furrows (also referred to as vertical line or, longitudinal furrows)	• Grade 0: absent • Grade 1: present
Edema (also referred to as decreased vascular markings or mucosal pallor)	• Grade 0: absent (distinct vascularity present) • Grade 1: loss of clarity or absence of vascular markings
Stricture	• Grade 0: absent • Grade 1: present (specify estimated luminal diameter)
Minor features	
Crepe-paper esophagus (mucosal fragility or laceration upon passage of diagnostic endoscope but not after esophageal dilation)	• Grade 0: absent • Grade 1: present