The natural history of steroid-naïve eosinophilic esophagitis in adults treated with endoscopic dilation and proton pump inhibitor therapy over a mean duration of nearly 14 years

Seth Lipka, MD,[1] Jonathan Keshishian, MD,[2] H. Worth Boyce, MD,[3] David Estores, MD,[3] Joel E. Richter, MD, FACP, MACG[3]

Tampa, Florida, USA

Background: Despite the vast focus of research in eosinophilic esophagitis (EoE), the natural history of untreated EoE remains undefined. Current expert consensus panels are calling for natural history studies to define long-term risks, adverse events, and progression of the disease.

Objective: To address the natural course and long-term adverse events of EoE.

Design: Retrospective, single-center study.

Setting: Tertiary-care center. A cohort of patients from the year 1988 initially diagnosed as having congenital esophageal stenosis who were later reclassified as having EoE.

Patients: Ninety-five patients, with 13 meeting entrance criteria for idiopathic EoE with follow-up >5 years.

Interventions: Anti-acids and esophageal dilation.

Main Outcome Measurements: Clinical response, adverse events, long-term clinical outcomes, and progression of disease.

Results: Thirteen patients (mean age at diagnosis 30.3 years, 10 male) were evaluated over a 13.6-year mean follow-up (range 5-24 years). All patients experienced daily dysphagia, with 12 presenting with food impactions. Patients were treated with esophageal dilation (64% Maloney, 34% Savary, 2.5% through-the-scope balloon) and daily anti-acids. Patients were initially treated with an average of 3.2 dilations over the first year (range 1-6) to achieve a luminal size of 15.8 mm (range 14-18 mm). They were maintained successfully with dilations every 2 years, on average, based on symptoms. Two patients not adhering to recommended dilation schedules experienced repeat impactions. One adverse event from a mucosal tear required hospitalization (1 of 157, 0.6%). Seven of 13 had Barrett's esophagus, average length 2.4 cm (range 1-4 cm), 3 on initial EGD and 4 identified over a mean duration of 9.4 years. No patient developed dysplasia or malignancy.

Limitations: Retrospective, small sample.

Conclusion: The course of EoE over a 13.6-year mean duration, although persistent, appears benign and not associated with cancer risk. A program of regular esophageal dilations based on symptom recurrence appears to be a safe, long-term treatment. (Gastrointest Endosc 2014;80:592-8.)

(footnotes appear on last page of article)

Use your mobile device to scan this QR code and watch the author interview. Download a free QR code scanner by searching 'QR Scanner' in your mobile device's app store.

Since inception of the term *eosinophilic esophagitis* (EoE) into the medical literature in 1978, the disease has evolved from sporadic case reports to a significantly recognized cause of morbidity, with an estimated prevalence of 43 to 55 cases per 100,000 persons in the adult population.[1-3] EoE is defined as a chronic, immune and/or antigen-mediated disease characterized by symptoms related to esophageal dysfunction and histologically by

eosinophil-predominant inflammation.[4] The disease can present in any age group from newborn to the elderly[5]; however, it is found most often in young to middle aged white men.[6]

The histology and phenotype of the disease was first described by Attwood et al[7] in 1993 and later by Straumann et al[8] in 1994. According to the second EoE consensus statement, EoE is a clinicopathologic diagnosis defined as *symptoms related to esophageal dysfunction, ≥15 eosinophils per high-power field, eosinophilia that persists after a trial of proton-pump inhibitor (PPI) therapy, and exclusion of other secondary causes of esophageal eosinophila.*[4] In children, symptoms are typically vague in nature, usually presenting as abdominal pain, failure to thrive, heartburn, and vomiting.[9] In contrast, the predominant symptoms in adults consist of dysphagia, food impaction, and ongoing symptoms of GERD refractory to treatment.[10,11]

Despite the increased perception and vast focus of research on EoE, the course of disease over time left untreated or natural history remains a relative mystery. This deficiency in information prevents clinicians from comparing any true benefit of current therapeutic recommendations against the otherwise natural course of the untreated disease. Only one study in the adult literature describes the natural history of EoE, which was prospectively collected over a mean duration of 7.2 years.[12] Likewise, the natural history in pediatric EoE is limited, relying on retrospective data to characterize the disease course over time.[13-17] The majority of evidence supports a common pathogenesis for EoE in adults and children.[18] Although the natural history is currently limited, patients are generally warned that symptom recurrence and chronic need for long-term dietary or anti-inflammatory treatment are likely. Whether long-term sequelae from chronic esophageal inflammation and progression of disease exists remains to be demonstrated through natural history studies.[4,19]

We enjoyed the unique experience of following patients who had met the current criteria for EoE since 1988. Dr H. Worth Boyce at the University of South Florida initially identified patients with a primary complaint of dysphagia and endoscopic findings compatible with EoE, that is, strictures, multiple rings, and generalized esophageal narrowing. He called this disease "congenital esophageal stenosis" because of the similarity to a known pediatric disease, which was associated with trachealization of the proximal to mid-esophagus resulting from tracheobronchial tissue lingering in the esophagus from incomplete separation of the fetal trachea and esophagus.[20] Dr Boyce kept detailed records of patient demographics, symptoms, treatment, adverse events, and endoscopic features of this disease, including biopsy results, which on subsequent review were consistent with EoE.[21] These patients were not treated with steroids but were managed with anti-acid therapy and esophageal dilation because the histologic findings were interpreted at that time as chronic reflux disease, sometimes with excessive eosinophils. This cohort of patients offers the distinct opportunity to address the natural course and long-term adverse events of EoE when steroids are omitted.

Take-home Message

- The natural history of fibrostenotic eosinophilic esophagitis is a benign disease over a follow-up duration of up to 24 years.
- Biennial esophageal dilation and proton pump inhibitors give excellent long-term symptom relief with very low rates of adverse events.

METHODS

Sample population

Institutional review board approval was obtained from the University of South Florida and H. Lee Moffitt Cancer Center. Patients were selected from a database of patients diagnosed with congenital esophageal stenosis initiated in 1988 by Dr Boyce at the University of South Florida Joy McCann Culverhouse Center for Swallowing Disorders in Tampa, Florida. This is a predominantly white patient population found in an urban area of 2 million people located on the west coast of Florida. We reviewed the patient records of 95 patients from 1988 to 2013 diagnosed with congenital esophageal stenosis and/or EoE. Patient notes were assessed along with endoscopic reports. Biopsy reports from each endoscopic session interpreted as reflux esophagitis were sent for re-examination for diagnosis of EoE by a GI pathologist experienced with this disease. Over this period, most biopsy specimens were obtained from the distal esophagus, looking for Barrett's esophagus (BE) or progression to dysplasia, and selectively from ringed and/or stricture areas. Usually, 4-quadrant biopsy specimens were taken every 2 cm beginning just above the gastric folds and ending at the new Z line (range of 4-12 biopsies). Biopsies also were done on any focal mucosal abnormalities. Biopsies were not routinely done on the proximal and distal esophagus. Records of treatment and medications, including PPI/H2 receptor antagonist/steroid therapy and dilation, were collected for analysis. Results of patient dilations including esophageal lumen size, number of dilations, year of dilation, and adverse events were recorded for analysis.

Inclusion/exclusion criteria

Eligibility required chart documentation of dysphagia for solid foods with or without food impactions and endoscopic and/or histologic evidence of EoE. The general work-up for patients included ruling out other known causes of esophageal eosinophilia such as collagen vascular disease, autoimmune processes, or infections. Patients