The Clinical Characteristics and Treatment Outcomes of Concomitant Eosinophilic Esophagitis and Inflammatory Bowel Disease

Siri A. Urquhart, MD,[*] *Kevin P. Quinn, MD,*[†] *Karthik Ravi, MD,*[†] *and Edward V. Loftus, Jr, MD*[†]

Background: The clinical characteristics and treatment outcomes in patients with eosinophilic esophagitis (EoE) and inflammatory bowel disease (IBD) have not been extensively investigated.

Methods: We determined treatment outcomes and frequencies of disease-related complications in patients with EoE and IBD.

Results: Among 69 patients who met inclusion criteria, 39 (56.5%) had a diagnosis of Crohn disease. Clinical and histologic response rates to proton pump inhibitors and topical steroids were 25.9% and 24.4%, respectively.

Conclusions: Lower than expected clinical and histologic response rates for EoE suggest the combination of EoE and IBD is a medically refractory phenotype with more difficult to treat EoE.

Lay Summary

The clinical and microscopic tissue response rates of eosinophilic esophagitis (EoE) in this group appeared lower than what we would anticipate, perhaps suggesting EoE is more difficult to treat when patients have both EoE and inflammatory bowel disease combined.

Key Words: eosinophilic esophagitis, Crohn disease, ulcerative colitis, indeterminate colitis

INTRODUCTION

The gastrointestinal (GI) mucosa comprises the largest host–environment interface of the body, using both innate and adaptive immune mechanisms to provide protective responses.[1] Eosinophilic esophagitis (EoE) and inflammatory bowel disease (IBD) are distinct chronic inflammatory conditions involving the GI system.[2] While eosinophil-predominant inflammation involving the esophagus is the hallmark of EoE, the presence of eosinophilic infiltration in GI mucosa has been observed as a histopathological feature of IBD, being described in both Crohn disease (CD) and ulcerative colitis (UC). An association between EoE and CD has been previously described in the literature, giving rise to speculation about a shared idiopathic dysregulated mucosal immune response that results in chronic inflammation.[3,4] The number of intestinal mast cells and eosinophils is altered in patients with IBD as compared to controls, suggesting both cell types are involved in the pathogenesis of chronic intestinal inflammation. Prior studies have demonstrated focal eosinophilic mucosal infiltration in CD is more common than epithelioid cell granulomas, and is an important parameter in the histologic differential diagnosis between colonic CD and UC.[5,6]

IBD and EoE are highly prevalent disorders in the Westernized world with recent estimates indicating IBD now affects 71.3–734 patients per 100,000 persons in Western Europe and 236.1–604.8 per 100,000 in North America.[7] The

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*Division of Internal Medicine, Mayo Clinic, Rochester, Minnesota, USA; †Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, Minnesota, USA

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Address correspondence to: Siri A. Urquhart, MD, Mayo Clinic, 200 1st Street SW, Rochester, MN 55905, USA (urquhart.siri@mayo.edu).

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prevalence of EoE has been estimated to be between 45 and 56 per 100,000.[8] However, some studies have suggested an increased risk of EoE among patients with IBD.[2,4] Limited data have also suggested a more severe disease phenotype in this subset of patients with both EoE and IBD.[4] However, the clinical characteristics and treatment outcomes in patients with concomitant EoE and IBD have not been extensively studied. Thus, we sought to determine the clinical characteristics and outcomes of disease-specific therapy in patients with an established diagnosis of both EoE and IBD, and to assess the relationship between phenotypic features and outcomes.

MATERIALS AND METHODS

Patient Population

This retrospective study was approved by our center's Institutional Review Board. Using a search of the electronic medical record, we identified all patients ≥18 years old who were evaluated at our institution with diagnoses of EoE and IBD between 2000 and 2019 using ICD-9 and ICD-10 diagnostic codes. The medical records of only patients who did not withdraw research authorization were included. This was followed by manual review of individual patient charts to confirm each diagnosis. In patients meeting inclusion criteria with confirmed EoE and IBD diagnoses, clinical data were then abstracted for various demographic, clinical, endoscopic, and histopathological outcomes. The date of first visit recorded for either diagnosis was recorded as the index date. Patients were excluded for the following reasons: <18 years old at time of last follow-up; no upper endoscopy with esophageal biopsies performed at our institution; and no follow-up at our institution following index visit.

Eosinophilic Esophagitis

The diagnosis of EoE was confirmed by the presence of esophageal dysfunction as described in the electronic medical record and histologically at our institution with ≥15 eosinophils per high power field as per the 2013 American College of Gastroenterology (ACG) guidelines.[9] Clinical response was defined as complete resolution of clinical symptoms including, but not limited to, dysphagia, food impaction, chest pain unresponsive to antacids, gastroesophageal reflux-like symptoms, or upper abdominal pain as documented in the electronic medical record. Histologic response was defined as a decrease to <15 eosinophils per high power field on subsequent esophageal biopsies following initiation of a specific therapy. Food impaction was defined as food sticking for greater than 5 minutes as documented at any point in the electronic medical record. Patient medical records were also reviewed to identify patients who required emergent endoscopic disimpaction. The need for esophageal dilation was determined based on review of available endoscopy reports and/or clinical history reporting esophageal dilation at any point in the electronic medical record. The date of EoE diagnosis was defined as when a diagnosis was first described in the patient's medical record and supported by clinicopathologic data as above. Patients with a clinical diagnosis of eosinophilic gastroenteritis were excluded.

Inflammatory Bowel Disease

IBD was diagnosed based on clinical diagnostic criteria as per the treating gastroenterologist and review of the medical record. Diagnosis was supported by characteristic endoscopic, radiographic, and/or histologic findings. Patients with an IBD diagnosis were then subcategorized as having CD, UC, or indeterminate colitis (IC) based on review of the medical record. Clinical response was defined as improvement in clinical symptoms, including abdominal pain, urgency, tenesmus, diarrhea, or hematochezia. Endoscopic response was defined as improvement or resolution of ulcerations, erythema, erosions, pseudopolyps, friability, or edema as documented on review of available endoscopy reports. The date of IBD diagnosis was defined as when a diagnosis was first described in the patient's medical record and confirmed histologically at our institution.

Data Collection and Analysis

Patient charts were manually reviewed for pertinent demographic and clinical data including dates of diagnosis of EoE and IBD, dates of initiation of typical treatments for either condition, clinical and/or histologic response, and dates of response. Patient charts were manually reviewed to determine need for surgical intervention and number of hospitalizations from the time of IBD diagnosis to last follow-up. Available esophagram data were also manually extracted to determine minimum and maximum esophageal diameter. Endoscopic reports were also reviewed for endoscopic features associated with EoE. Descriptive statistics included means, medians, and ranges. Continuous variables were reported as a median with range. Categorical variables were reported as a unique count and percentage of the sample.

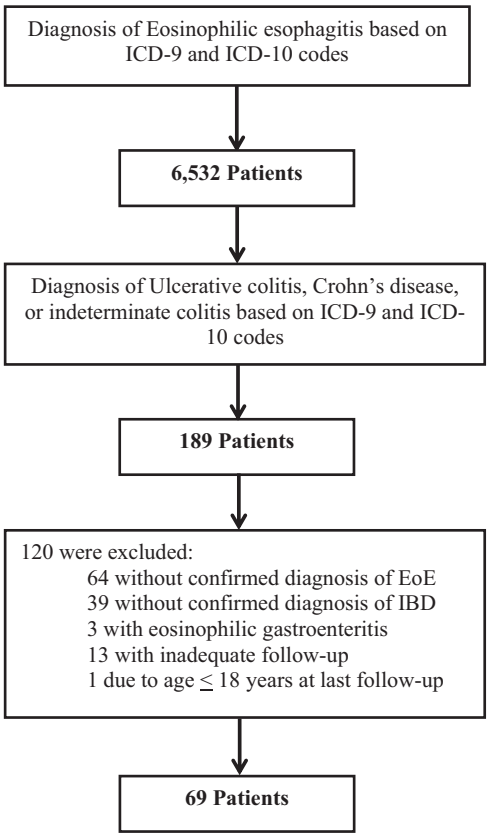
RESULTS

The initial data search identified 189 patients with suspected diagnoses of both EoE and IBD. After manual review, 69 patients were included in the final analysis, and 120 were excluded due to absence of confirmed diagnosis of EoE and/or IBD, presence of eosinophilic gastroenteritis, lack of sufficient follow-up, or pediatric age at last follow-up (see Fig. 1, which demonstrates the screening process of patients).

Demographics

Baseline characteristics including demographic data and median follow-up time are summarized in Table 1. The majority of patients were male with a median age in the mid-to-upper 30s. Median duration of follow-up from index visit was

approximately 5–6 years. Forty-eight patients were diagnosed with IBD prior to EoE diagnosis (69.6%) with a median time between diagnoses varying from 7.5 months to 9 years (Table 2). Twenty-seven patients (39.1%) were initially diagnosed with CD, 20 (29.0%) with UC, and 1 (1.4%) with IC prior to EoE.



Key: EoE, eosinophilic esophagitis; IBD, inflammatory bowel disease.

FIGURE 1. Screening of patients for study inclusion. Utilizing ICD-9 and ICD-10 diagnostic codes for EoE, a master computer system at our institution was used to search for patients with the diagnosis of EoE who had research authorization. ICD-9 and ICD-10 diagnostic codes for IBD were then utilized to identify EoE patients with IBD. A total of 120 patients were excluded.

Eosinophilic Esophagitis

The diagnosis of EoE was confirmed histologically in all 69 patients. At the time of EoE diagnosis on esophageal biopsy, the median eosinophil count per high power field was 27.5 for CD patients, 40 for UC, and 45 for IC. The median peripheral eosinophil count at time of EoE diagnosis was 0.21 × 10(9)/L for CD and 0.45 × 10(9)/L for UC. The median peripheral eosinophil count at time of IBD diagnosis was 0.22 × 10(9)/L for CD and 0.40 × 10(9)/L for UC. At EoE diagnosis, 35 patients had the presence of rings and/or strictures (48.7% with CD) while 34 had edema, furrows, and/or exudates (38.5% with CD) (Table 3).

The most common treatments for EoE were proton pump inhibitors (PPIs) (78.3%) and topical steroids (59.4%), which included fluticasone and budesonide (Table 4). Overall, 51.9% of patients treated with PPI and 63.4% with topical steroids had complete resolution of clinical symptoms alone compared to combined clinical and histologic response (25.9% and 24.4%, respectively). Of the 31 patients with CD treated with PPI therapy for EoE, 13 (41.9%) demonstrated complete resolution of clinical symptoms alone while 12 (38.7%) demonstrated both a clinical and histologic response. Of the 23 UC patients treated with PPI therapy for EoE, 15 (65.2%) demonstrated complete resolution of clinical symptoms alone while 2 (8.7%) demonstrated both a clinical and histologic response.

Twenty-two patients with CD, 18 patients with UC, and 1 patient with IC were treated with topical steroids. Twelve patients with CD (54.5%) had complete resolution of clinical symptoms alone while 7 (31.8%) had both a clinical and histologic response. Thirteen patients with UC (72.2%) had complete resolution of clinical symptoms alone while 3 (16.7%) had both a clinical and histologic response. Only 1 patient with IC demonstrated complete resolution of clinical symptoms alone.

Of the 20 patients who had an esophagram performed, the median minimum esophageal diameter was 13 and 16 mm for CD and UC, respectively. The median maximum esophageal diameter was 22 and 21 mm for CD and UC, respectively. Two patients with CD and 1 patient with UC had a minimum esophageal diameter ≤15 mm. Two patients with CD and 2 patients

TABLE 1. Baseline Characteristics of Patients With EoE and IBD

	EoE + CD (N = 39)	EoE + UC (N = 28)	EoE + IC (N = 2)
Median age, years (range)	39 (18–82)	39.5 (22–78)	35 (20–50)
Male gender, n (%)	21 (53.8)	24 (85.7)	2 (100.0)
Median follow-up, years (range)	5 (0–18)	6 (0–23)	6 (6)
Disease extent of IBD, n (%)	Colonic 6 (15.4) Ileocolonic 18 (46.2) Ileal 12 (30.8) No luminal involvement 3 (7.7) Proximal GI involvement 5 (12.8) Perianal involvement 5 (12.8)	Proctitis 4 (14.3) Left-sided disease 9 (32.1) Extensive 15 (53.6)	

TABLE 2. Subsequent Development of EoE in IBD and Subsequent Development of IBD in EoE, Stratified by Gender

Initial Diagnosis	Subsequent Diagnosis	Overall, n (%)	Male Gender, n (%)	Female Gender, n (%)	Median Time Between Diagnoses (in Years)
CD	EoE	27 (39.1)	14 (29.8)	13 (59.1)	9
UC	EoE	20 (29.0)	17 (36.2)	3 (13.6)	7.5
IC	EoE	1 (1.4)	1 (2.1)	0 (0)	3
EoE	CD	8 (11.6)	5 (10.6)	3 (13.6)	1.5
EoE	UC	4 (5.8)	3 (6.4)	1 (4.5)	4
EoE	IC	1 (1.4)	1 (2.1)	0 (0)	0.58
CD + EoE*	—	4 (5.8)	2 (4.3)	2 (9.1)	—
UC + EoE*	—	4 (5.8)	4 (8.5)	0 (0)	—

*Four patients with CD and 4 patients with UC had the same date of diagnosis for both diseases due to documentation of dates in the electronic medical record.

TABLE 3. Eosinophil Burden and Endoscopic Features at Time of EoE and IBD Diagnoses

	EoE + CD, N = 39	EoE + UC, N = 28	EoE + IC, N = 2
Median no. eosinophils on esophageal biopsy at time of EoE diagnosis, eos/HPF (range)	27.5 (15–100)	40 (15–200)	45 (20–70)
Median peripheral eosinophil count at time of IBD diagnosis [×10(9)/L] (range)*	0.22 (0.09–0.41)	0.40 (0.17–0.47)	—
Median peripheral eosinophil count at time of EoE diagnosis [×10(9)/L]*	0.21 (0.01–1.00)	0.45 (0.15–0.66)	—
Presence of strictures/rings on upper endoscopy at EoE diagnosis, n (%)	19 (48.7)	16 (57.1)	0 (0)
Presence of edema/furrows/exudates on upper endoscopy at EoE diagnosis	15 (38.5)	18 (64.3)	1 (50.0)

*Both patients with IC did not have peripheral eosinophil counts at time of IBD or EoE diagnosis.
eos, eosinophils; HPF, high power field.

with UC had a maximum esophageal diameter ≤20 mm. Eight patients with CD (20.5%), 12 with UC (42.9%), and 1 with IC (50%) had at least 1 episode of food impaction (Table 5) with 9 patients in total (4 with CD and 5 with UC) requiring emergent endoscopic disimpaction.

Inflammatory Bowel Disease

Thirty-nine patients had a diagnosis of CD (56.5%), 28 UC (40.6%), and 2 IC (2.9%). A majority of patients with CD had ileocolonic involvement (46.2%) with 5 patients having proximal GI involvement and 5 patients with perianal involvement. A majority of patients with UC had extensive (proximal to splenic flexure) involvement (53.6) of disease. The most common treatments for IBD were oral 5-aminosalicyclic acid (69.6%) compounds, oral corticosteroids (66.7%), azathioprine (44.9%), and adalimumab (43.5%), with 35.4%, 47.8%, 32.3%, and 53.3% of patients demonstrating clinical improvement, respectively (Table 6). Fourteen patients with CD (35.9%), 8 with UC (28.6%), and 1 with IC (50%) required surgical intervention for IBD. Eighteen patients with CD (46.2%), 8 with UC (28.6%), and 1 with IC (50%) required hospitalization for IBD (Table 7).

DISCUSSION

While both EoE and IBD are distinct chronic inflammatory conditions, they share similar potential mechanisms for pathogenesis including genetic–environmental interactions, epidemiologic trends, diagnostic considerations, and general therapeutic principles.[2] However, the clinical characteristics and treatment outcomes in patients with whom these diseases coexist are not well described in the current literature.

Several of our study findings were notable. The majority of study patients were male with a median age range in the mid-to-upper 30s, which is consistent with the fact that EoE is more common in young male patients.[10] We found that IBD was most often diagnosed prior to EoE. A majority of patients with either CD or UC had ileocolonic (46.2%) or extensive involvement (53.6%), respectively. Only 5 patients with CD had confirmed proximal GI involvement (12.8%) in this cohort. Several associations between IBD and EoE have already been described. Studies have shown a relationship between EoE and immune-mediated diseases.[2] Additionally, prior studies have shown an increase in the number of serum and mucosal eosinophils in IBD. This perhaps leads to worsened clinical outcomes

TABLE 4. Response to Typical Treatments for EoE in Patients With Both IBD and EoE

	IBD Subtype			Median Time From Initiation to Reassessment (in Months)	Response of EoE to Treatment				
	CD, N = 39	UC, N = 28	IC, N = 2		No Response	Clinical Only	Clinical and Histologic	Not Assessed*	Discontinued Due to Side Effects
PPI, n (%)	31 (79.5)	23 (82.1)	0 (0)	3	4 (7.4)	28 (51.9) CD 13 (41.9) UC 15 (65.2) IC 0 (0)	14 (25.9) CD 12 (38.7) UC 2 (8.7) IC 0 (0)	7 (13.0)	1 (1.9) due to palpitations
Topical steroid, n (%)	22 (56.4)	18 (64.3)	1 (50.0)	5	2 (4.9)	26 (63.4) CD 12 (54.5) UC 13 (72.2) IC 1 (100.0)	10 (24.4) CD 7 (31.8) UC 3 (16.7) IC 0 (0)	4 (9.8)	0 (0)
Oral corticosteroid, n (%)	2 (5.1)	2 (7.1)	0 (0)	1	1 (25.0)	2 (50.0)	1 (25.0)	0 (0)	0 (0)
Elimination diet, n (%)	3 (7.7)	1 (3.6)	0 (0)	3	1 (25.0)	3 (75.0)	0 (0)	0 (0)	0 (0)
Esophageal dilation, n (%)	7 (17.9)	8 (28.6)	0 (0)	2	1 (6.7)	14 (93.3)	0 (0)	0 (0)	0 (0)

*Patients did not have a documented initiation or reassessment date and therefore were not included in the median time from initiation to reassessment.

TABLE 5. EoE-Related Complications in Patients With Both IBD and EoE

	EoE + CD, N = 39	EoE + UC, N = 28	EoE + IC, N = 2
Esophagram			
Esophagram performed, n (%)*	12 (30.8)	8 (28.6)	0 (0)
Median minimum diameter (in mm)†	13	16	0
Median maximum diameter (in mm)‡	22	21	0
No. patients with abnormal minimum esophageal diameter, n (%)	2 (5.1)	3 (10.7)	0 (0)
No. patients with abnormal maximum esophageal diameter, n (%)	6 (15.4)	0 (0)	0 (0)
Food impaction, n (%)	8 (20.5)	12 (42.9)	1 (50.0)
Required emergent endoscopic disimpaction, n (%)	4 (10.3)	5 (17.9)	0 (0)
Need for esophageal dilation, n (%)	8 (20.5)	8 (28.6)	0 (0)

*A total of 20 patients had esophagrams performed.
†A total of 8 patients had minimum esophageal diameter reported.
‡A total of 9 patients had maximum esophageal diameter reported.

including increased healthcare utilization, and use of more aggressive medical treatment with corticosteroids and biologic agents. Presence of peripheral blood eosinophilia has been associated with elevated C-reactive protein levels, and may suggest a higher level of resultant inflammation in IBD patients with peripheral eosinophilia.[11] However, peripheral eosinophil counts that were measured at the time of EoE and IBD diagnoses in this group were not significantly elevated.

The most commonly utilized pharmacotherapies for EoE in our study cohort included PPIs and topical glucocorticoids, with clinical response rates of 51.9% and 63.4%, respectively. This appears consistent with clinical response rates reported in other studies. However, it is known that clinical response or remission does not always correlate with histologic response.[12] This appears true in our study which demonstrated lower than expected histologic response to conventional therapy with PPIs and topical steroids (Table 2). A systematic review and meta-analysis of 33 studies (including 11 prospective studies) with 619 patients demonstrated a pooled clinical response rate of 60.8% and histologic remission rate of 50.5% to PPI therapy.[13] Other studies in the literature have reported histologic response rates ranging from 25% to 57%.[14,15] Additionally, it is important to note that the current guidelines for diagnosis of EoE do not require exclusion of gastroesophageal reflux disease as a diagnosis or a trial of PPI therapy.[16]

TABLE 6. Response to Typical Treatments for IBD in Patients With Both EoE and IBD

	IBD Subtype			Median Time From Initiation to Reassessment (in Months)	Response of IBD to Treatment					
	CD, N = 39	UC, N = 28	IC, N = 2		No Response	Clinical	Endoscopic	Clinical and Endoscopic	Not Assessed*	Discontinued Due to Side Effects
5-ASA										
PO, n (%)	23 (59.0)	23 (82.1)	2 (100.0)	5	11 (22.9)	17 (35.4)	3 (6.3)	2 (4.2)	14 (29.2)	1 (2.1) due to palpitations
Topical, n (%)	1 (2.6)	11 (39.3)	1 (50.0)	7	3 (23.1)	6 (46.2)	2 (15.4)	0 (0)	2 (15.4)	0 (0)
Budesonide										
PO, n (%)	15 (38.5)	8 (28.6)	1 (50.0)	4	5 (20.8)	11 (45.8)	1 (4.2)	2 (8.3)	4 (16.7)	1 (4.2) due to dizziness/syncope
Topical, n (%)	2 (5.1)	1 (3.6)	0 (0)	36	1 (33.3)	0 (0)	0 (0)	0 (0)	2 (66.7)	0 (0)
Corticosteroid										
PO, n (%)	22 (56.4)	23 (82.1)	1 (50.0)	1	6 (13.0)	22 (47.8)	0 (0)	2 (4.3)	16 (34.8)	0 (0)
Topical, n (%)	1 (2.6)	7 (25.0)	0 (0)	3.5	3 (37.5)	4 (50.0)	0 (0)	0 (0)	1 (12.5)	0 (0)
Immunomodulator										
AZA, n (%)	11 (28.2)	20 (71.4)	0 (0)	3	3 (9.7)	10 (32.3)	1 (3.2)	5 (16.1)	7 (22.6)	5 (16.1) due to nausea/vomiting (2), abdominal pain, and rash (1), headache and weakness (1), and skin cancer (1)
6-MP, n (%)	12 (30.8)	5 (17.9)	1 (50.0)	5	7 (38.9)	7 (38.9)	0 (0)	0 (0)	3 (16.7)	1 (5.6) due to nausea
Anti-TNF agents										
Infliximab, n (%)	18 (46.2)	8 (28.6)	1 (50.0)	6	4 (14.8)	12 (44.4)	1 (3.7)	7 (25.9)	2 (7.4)	1 (3.7) due to myalgias
Adalimumab, n (%)	21 (53.8)	8 (28.6)	1 (50.0)	6	5 (16.7)	16 (53.3)	0 (0)	8 (26.7)	1 (3.3)	0 (0)
Certolizumab, n (%)	5 (12.8)	0 (0)	0 (0)	2	1 (20.0)	4 (80.0)	0 (0)	0 (0)	0 (0)	0 (0)
Other biologics										
Vedolizumab, n (%)	5 (12.8)	4 (14.3)	0 (0)	6	3 (33.3)	3 (33.3)	0 (0)	3 (33.3)	0 (0)	0 (0)
Ustekinumab, n (%)	3 (7.7)	1 (3.6)	0 (0)	5	1 (25.0)	1 (25.0)	0 (0)	2 (50.0)	0 (0)	0 (0)

*Patients did not have a documented initiation or reassessment date and therefore were not included in the average.
5-ASA, 5-aminosalicyclic acid; 6-MP, 6-mercaptopurine; AZA, azathioprine; PO, per os or "oral".

The expected histologic response rate to topical steroids for EoE varies in the literature with small case series and retrospective studies reporting response rates ranging from 50% to 95%.[17–21] In a systematic review and meta-analysis consisting of 5 studies with a total of 174 EoE patients treated with topical fluticasone and budesonide, the pooled complete and partial histologic remission rates were 57.8% and 82%, respectively.[22] Prior data have also suggested the dose and mode of delivery of topical steroids may play a role in EoE treatment response, with high-dose viscous topical steroid preparations demonstrating a more modest effect compared to low-dose topical steroids or capsules.[23] In our study, histologic response (decrease in eosinophils to <15 per high power field) was seen in only 25.9% and 24.4% of those treated with PPI therapy and topical steroids, respectively. This may suggest that EoE in the presence of IBD is less responsive to conventional therapy with PPIs or topical steroids. In comparison of histologic response between IBD subtypes, patients with CD seemed to have a greater response to PPIs and topical steroids than patients with UC, despite similar median number of eosinophils per high power field on esophageal biopsy at EoE diagnosis. This may suggest CD and EoE share similar biologic targets, but lack a final common inflammatory pathway which inhibits complete response.[3]

Endoscopic findings of EoE are highly suggestive but not diagnostic of the disease. In fact, the incidence of endoscopically normal EoE is approximately 10%. Rings and strictures are typically associated with fibrostenotic disease, while exudates, edema, and furrows are more commonly associated with inflammatory disease phenotypes.[24] In this study population,

TABLE 7. IBD-Related Complications in Patients With Both EoE and IBD

	EoE + CD, N = 39	EoE + UC, N = 28	EoE + IC, N = 2
Surgical intervention			
Required surgical intervention for IBD, n (%)	14 (35.9)	8 (28.6)	1 (50.0)
Median time from IBD diagnosis to first surgical intervention (in years)	4*	5	8
Hospitalization			
Required hospitalization for IBD, n (%)	18 (46.2)	8 (28.6)	1 (50.0)
Median total no. hospitalizations	1	1.5	7
Median time from IBD diagnosis to first hospitalization (in years)	5†	4.5	2

*One patient with CD underwent surgical intervention 8 years prior to diagnosis of CD and thus was not included in median.
†One patient with CD had an unknown date of first hospitalization and thus was not included in median.

approximately half of CD patients had the presence of rings and strictures, or edema, exudates, and furrows which suggest either phenotype may be associated with IBD activity. Only 5 patients with CD had confirmed proximal GI involvement (12.8%) of disease in this cohort. De Felice et al described the endoscopic appearance of CD of the esophagus in 24 patients. In these cases, patients had superficial ulcerations, erythema and/or erosions, deep ulcerations, pseudopolyps, as well as fistulizing disease on endoscopy.[25]

A small subset of patients underwent esophagrams to assess esophageal diameter and presence of fibrostenotic disease. Esophagrams are not universally utilized in the diagnosis, surveillance, and management of EoE, at least based on the most recent ACG guidelines. Nonetheless, esophagrams are useful to characterize anatomic changes within the esophagus, particularly in patients with EoE.[9] Two patients with CD and 1 patient with UC had a minimum esophageal diameter ≤15 mm. Two patients with CD and 2 patients with UC had a maximum esophageal diameter ≤20 mm. In a study by Lee et al, approximately 50% of EoE patients had normal esophageal diameter; however, use of topical steroids resulted in an increase in maximum and minimum esophageal diameters when abnormal at baseline by means of increasing esophageal expansion and improving compliance.[26] Few patients in our study demonstrated abnormal minimum and/or maximum esophageal diameter, which seems to align with that encountered in the EoE population.

This study illustrated that about one-third of patients required surgical intervention and/or hospitalization for IBD-related complications. However, about one-third experienced food impaction and/or required esophageal dilation at least once based on review of the electronic medical record. Approximately 13% required emergent endoscopic disimpaction. Both IBD and EoE have been reported to begin with an inflammatory phenotype, with some developing fibrotic complications over time in the absence of appropriate therapy.[2] Given the more common initial diagnosis was IBD in this group of patients, typical treatment modalities for IBD may in fact reduce the risk of fibrostenotic complications associated with EoE including narrow-caliber esophagus and esophageal stricture. Furthermore, this cohort of patients displayed a similar risk of IBD-related complications that we would expect at a tertiary care center. This suggests eosinophils in this context may have some role in perpetuating ongoing tissue damage rather than serving an innate protective role by preventing inflammation.[2,3,10]

As expected in a tertiary IBD population, pharmacotherapy for our IBD cohort frequently included use of oral corticosteroids, antitumor necrosis factor (anti-TNF) agents, and other biologics such as ustekinumab and vedolizumab. The rates of hospitalization and surgical intervention for patients with IBD, particularly CD, have been reported to be 50%.[27] Need for surgical intervention ranged from 28.6% to 50% and hospitalizations related to IBD ranged from 28.6% to 50%. EoE appears to be less responsive in this subset of patients, but IBD-related treatment outcomes seem to be consistent with that experienced in a tertiary care institution.

Biologic therapies such as anti-TNF agents are commonly used for treatment of IBD. However, they have not been shown to be effective in treatment of EoE. Novel monoclonal antibodies have recently been developed and utilized in phase 2 trials, demonstrating promise in EoE patients with more refractory disease.[28] There have also been reports in the literature regarding the use of vedolizumab, an anti-α4β7 integrin agent which inhibits leukocyte trafficking,[29] for intractable EoE. Vedolizumab mediates T-helper 2 cell (Th2) cytokine effects by binding with high affinity to eosinophils and CD4 T cells.[30] Infliximab has also been used for treatment of adult EoE in prospective T1 translational studies for patients with steroid-dependent EoE with mixed results.[31]

Typically, EoE has been described as being associated with a Th2 inflammatory response[32] while IBD, and particularly CD, is mediated by a Th1/Th17 response with interleukin (IL) 10 involvement.[3] However, both disease conditions share common cytokine and T-helper cell-mediated mechanisms. In the current literature, CD can manifest increased mucosal

expression of IL-5 while increased expression of eotaxin (chemoattractant for eosinophils) can be seen in UC.[4] IL-5 has been associated with eosinophilic activation in tissues, and may participate in early mucosal damage in CD.[32] There is also increased expression of proinflammatory cytokines, including IL-5 and TNF-α, in the esophageal epithelium in patients with IBD.[1,33] This may suggest EoE and IBD share similar biologic targets, but lack a final common inflammatory pathway which inhibits complete response.[3]

The limitations of this study include it being performed at a tertiary referral center which may result in bias, limiting the study's generalizability. This study also had limited follow-up (median 6 years), which may not capture the full spectrum of EoE- or IBD-related complications in this group. This was also a retrospective study, and as a result, there was significant reliance on documentation within the electronic medical record. Retrospective studies come with their own limitations, including missing and incomplete data. For example, not all patients were reevaluated for treatment response based upon documentation within the electronic medical record which may have impacted our results. Some patients within this cohort were unable to be included in statistical analysis due to lack of date of diagnosis, time of initiation of treatment, reassessment to treatment response, unknown dates of hospitalizations and/or surgical procedures, and/or incomplete esophagram data. Perhaps significant fibrostenotic disease is more prevalent in patients with both EoE and IBD than what we have shown based on limited available esophagram data. Diagnosis and reassessment dates had to be inferred based on description within the individual electronic medical record. This study also lacked a control group (EoE without IBD and/or IBD without EoE). However, we utilized a large patient database and identified all possible patients with EoE and IBD at our institution. Rigorous data extraction protocols and strict criteria were utilized to categorize patients and confirm case status.

CONCLUSIONS

In conclusion, we demonstrated that IBD is the more frequent initial diagnosis in patients with concomitant EoE and IBD. Recent literature has shown an association between IBD and EoE, and as such, it is important to be vigilant for signs and symptoms suggestive of EoE in patients with IBD and evaluate accordingly. The IBD-related medications utilized, hospitalization, and surgical intervention rates are quite similar to that which we see at a tertiary care center. However, the clinical and histologic response rates of EoE in this cohort appear lower than what we would anticipate, perhaps suggesting the combination of EoE and IBD is a medically refractory phenotype with more difficult to treat EoE.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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