

ORIGINAL ARTICLES—ALIMENTARY TRACT

A Shift in the Clinical Spectrum of Eosinophilic Gastroenteritis Toward the Mucosal Disease Type

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This article has an accompanying continuing medical education activity on page e88. Learning Objectives—At the end of this activity, the learner should be able to understand the clinical spectrum and clinical presentation of eosinophilic gastroenteritis and understand the imaging and pathological features of eosinophilic gastroenteritis.

See related articles, **Dohil R et al**, on page 418 in **Gastroenterology** and, **DuBay D et al**, on page xxii in this issue of **CGH**.

BACKGROUND & AIMS: Eosinophilic gastroenteritis (EG) is a rare disorder characterized by eosinophilic infiltration of the gastrointestinal (GI) tract. Despite the increasing prevalence of eosinophilic GI disorders, the epidemiology of EG has not been well studied. We evaluated the clinical spectrum of EG. **METHODS:** We reviewed data from patients diagnosed with EG, allergic gastroenteropathy, or eosinophilia and referred to gastroenterologists from 1987 to 2007 (n = 59; 52 with mucosal, 3 with muscularis, and 4 with subserosal disease). The study included subjects diagnosed with EG and those with a history that suggested EG, defined by GI symptoms; eosinophilic infiltration of the GI tract, eosinophilic ascites, or characteristic radiographic findings with eosinophilia; and no parasitic or extraintestinal disease. Findings were compared with those from patients with unexplained GI symptoms and peripheral eosinophilia (n = 11). **RESULTS:** Associations between clinical variables and EG subgroups did not differ between patients with EG and peripheral eosinophilia. Fifty percent of patients with EG who underwent food allergy testing had a positive test result; only 32% of those with EG who underwent radiographic imaging had positive test results. Patients with EG received steroid therapy; 75% with mucosal, 67% with muscle, and 100% with subserosal disease received prednisone. Eighty-eight percent of patients who received only steroids (mean follow-up period, 7 mo) and 94% of patients who received steroids in combination with another therapy (mean follow-up period, 4 mo) had improved or resolved disease. **CONCLUSIONS:** Unlike eosinophilic esophagitis, EG is rare. Results from this large study suggest that EG disease type has shifted toward that of the mucosal layer.

Keywords: Eosinophilia; Gastroenteritis; Allergic Gastroenteropathy; Clinical Trial.

Eosinophilic gastroenteritis (EG) is a heterogeneous and rare disorder characterized by eosinophilic infiltration of the gastrointestinal (GI) tract. Although originally described by Kaijser¹ in 1937, the etiopathogenesis for EG remains largely unknown, but eosinophilic inflammation from an allergic response is thought to have a central role, with a predominance of Th-2 proinflammatory cytokines and the chemokine eotaxin.² GI eosinophilic inflammation is associated with seasonal allergies, food allergies, asthma, eczema, and atopy.^{2–5} Klein et al⁶ further described that the depth of eosinophilic infiltration defines the likely clinical symptoms and presentation; a classification system based on maximal depth of tissue involvement (mucosal, muscle layer, or subserosal layer) was proposed. Talley et al⁷ evaluated clinical differences based on the Klein classification system in one of the largest series to date. Eosinophilic gastroenteritis has been found to have a myriad of clinical manifestations because symptoms appear dependent on both the site of the GI tract involved, as well as the depth of involvement of the gut wall.

The current generally accepted diagnostic criteria includes the presence of recurrent gastrointestinal symptoms, biopsies with histopathology showing predominant eosinophilic infiltration with sheets of eosinophils, and the absence of parasitic or extraintestinal diseases that may cause eosinophilia.^{7,8} Although peripheral eosinophilia commonly may be found, it generally is thought not to be required for diagnosis because it is not a universal finding.^{7,9,10} The epidemiology of EG is unclear and challenging to assess given the relative dearth of published data. It generally is reported that EG has been found to affect all age groups from infants to adults, usually presents in the third decade of life, and has been reported to have a slight male predominance.^{3,7,8}

Abbreviations used in this paper: EG, eosinophilic gastroenteritis; GI, gastrointestinal; HPF, high-power field; PEos, peripheral eosinophilia.

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Given that it is uncommon, there remains a significant lack of clinical data on EG. The available literature is largely limited to single case reports and small case series. This is in contrast to other eosinophilic gastrointestinal disorders such as eosinophilic esophagitis. Although first reported 3 decades ago, eosinophilic esophagitis has been well described in the literature and there is growing evidence that the prevalence and incidence of eosinophilic esophagitis have been increasing in recent decades.^{11,12} However, it is unknown whether there has been a similar parallel increase seen for eosinophilic gastroenteritis. Although a large pediatric series involving duodenal eosinophilia, dyspepsia, and treatment with montelukast recently was described, there remains a lack of investigation of EG in the adult population.¹³ In fact, the 40 subjects originally described by Talley et al⁷ remain one of the largest adult series in the literature. Given this, we sought to evaluate the clinical spectrum of EG in adult patients diagnosed at a major referral center over the past 2 decades.

Methods

Our previous experience with eosinophilic gastroenteritis from 1950 through 1986 was reported in 1990 and included 40 subjects.⁷ The present study was approved by the Mayo Foundation Institutional Review Board.

Patient Selection and Case Definitions

Charts from Mayo Clinic patients, from 1987 to 2007, with a diagnosis of eosinophilic gastroenteritis, allergic gastroenteropathy, or eosinophilia and referred to the GI clinic were reviewed. These medical records are readily available for review because the Mayo Clinic has maintained a common medical records system with its 2 affiliated hospitals (St. Marys and Rochester Methodist) for more than 100 years. All diagnoses and surgical procedures are recorded and indexed, including all diagnoses made from outpatients seen in the office or clinic consultations, emergency room visits, or nursing home care. Diagnoses also are recorded for hospital inpatients, at autopsy examination, or on death certificates. This system contains the medical histories of more than 4 million individuals, with only approximately 300 lost in the past 80 years.⁷

Review of appropriate medical records was used to identify and/or verify a clinical diagnosis of eosinophilic gastroenteritis, ensure eligibility based on exclusion criteria, and to abstract data points of interest. Subjects were excluded if they had a history or diagnosis of any of the following: eosinophilic esophagitis, Ménétrier's disease, inflammatory bowel disease (ulcerative colitis or Crohn's disease), celiac disease, connective tissue disease, vasculitides, amyloidosis, lymphoma, leukemia, malignancy, and hypereosinophilic syndrome. Source of referral for subjects (eg, self-referred vs outside physician referral) was not a factor for inclusion or exclusion. All subjects with a clinical diagnosis of eosinophilic gastroenteritis were included for analysis regardless of the number or duration of clinical visits surrounding the time of diagnosis at our center. For subjects with a history suggestive of eosinophilic gastroenteritis but with equivocal clinical diagnosis, accepted diagnostic criteria were used to identify subjects to be included in the study.⁷ Eosinophilic gastroenteritis was defined in these subjects by the following criteria: (1) presence of recurrent or chronic GI symptoms; (2) biopsies showing eosinophilic infiltration of one or

more areas of the GI tract, eosinophilic ascites, or characteristic radiographic findings with peripheral eosinophilia; and (3) no evidence of parasitic or extraintestinal disease; peripheral eosinophilia was not required as part of the diagnostic criteria. The same diagnostic criteria were used in a previous study.⁷

Patients with EG were divided into groups according to the Klein classification system: (1) mucosal disease, defined as infiltration of the mucosa by eosinophils and/or evidence of mucosal edema on barium studies, and without evidence of GI obstruction, eosinophilic ascites, or histologic evidence of infiltration beyond the mucosal layer; (2) disease of the muscle layer, defined as eosinophilic infiltration of the muscularis and/or documented complete or incomplete bowel obstruction, and without evidence of eosinophilic ascites; and (3) subserosal disease, defined by the presence of eosinophilic ascites with or without evidence of eosinophilic infiltration of the gut.⁶ Patients with histologic evidence of involvement of the mucosa and muscle layer were included in the latter group. Patients with evidence of mucosal disease and ascites were included in the subserosal group.

When available, histologic slides were reviewed by a single experienced expert gastrointestinal histopathologist (T.C.S.). All biopsy specimens were collected, processed, and reviewed at the Mayo Clinic Rochester. Biopsy specimens were fixed in formalin and embedded in paraffin, cut at 4 to 5 μ m, then stained with H&E. Histopathologic findings that were considered suggestive of eosinophilic gastroenteritis included dense and diffuse eosinophilic infiltration (often at >50 eosinophils per high-power field [HPF]), formation of sheets of eosinophils in the lamina propria, extension of eosinophilic infiltration into the submucosa, and lack of evidence of chronic changes or injury. Quantification of the degree of infiltration was performed on available slides.

A second group of subjects was identified who had gastrointestinal symptoms, unexplained peripheral eosinophilia, and no evidence of eosinophilic infiltration of the GI tract or parasitic infection. The exclusion criteria used earlier also were applied to this group. In addition, these subjects were required to have negative histologic findings. This group was identified as having unexplained peripheral eosinophilia (PEOs). The identification of this group was for comparison purposes with the EG group.

Statistical Analysis

Prespecified clinical features were evaluated and the association with EG subgroups (mucosa, muscularis, and subserosal), EG as a homogeneous group that included all subtypes, and the group with unexplained PEOs also was assessed. The association of group category with age at diagnosis, sex, presenting GI symptoms, years of symptoms, history of allergy, history of food allergy/intolerance, family history of allergy, body mass index, anemia at time of presentation, serum immunoglobulin E levels, absolute peripheral eosinophil count, and erythrocyte sedimentation rate was assessed using the Fisher exact test. A 2-tailed α level of .05 for each variable examined was used to assess statistical significance. Descriptive data were collected on demographic characteristics, endoscopic findings and sites of biopsies, and radiographic findings. Available histologic slides were reviewed by an expert histopathologist (T.C.S.) and results were compared based on the number of eosinophils per HPF.

Table 1. Sociodemographic Features Among Patients With EG and Unexplained PEos

	EG (n = 59)	Unexplained PEos (n = 11)
Mean age (SEM)	47 (2)	37 (4)
Sex, %		
Male	61	64
Female	39	36
Ethnicity (EG, n = 10 missing)		
White/Caucasian, %	98	100
Asian/Pacific Islander, %	2	0
Marital status, % (EG, n = 1 missing)		
Single	28	36
Married	66	55
Divorced	3	9
Widowed	3	0
Education level (EG, n = 6 missing)		
Less than high school	4	0
High school/some college	60	73
College/professional training	36	27
Employment status, % (EG, n = 3 missing; PEos, n = 1 missing)		
Employed	63	70
Unemployed	11	0
Retired	9	0
Student	9	20
Disability	3	0
Other	5	10
Alcohol use, % (EG, n = 2 missing)		
Never	40	45
Current user	49	45
Quit/use in past	11	10
Smoking, % (EG, n = 2 missing)		
Never	60	64
Current smoker	15	18
Quit/past smoker	25	18

SEM, standard error of the mean.

Results

A total of 59 patients with eosinophilic gastroenteritis were identified: 52 with disease of the mucosa, 3 with disease of the muscle layer, and 4 with subserosal involvement. Eleven patients were identified with unexplained peripheral eosinophilia and gastrointestinal symptoms. [Table 1](#) summarizes the sociodemographic findings for the EG and PEos groups. The mean age at presentation was 47 years for EG and 37 years for PEos patients. Among those with EG, 61% were male, 98% were Caucasian with 1 Asian/Pacific Islander subject, and 96% had at least completed high school (36% with college/professional training). No statistically significant association was detected between group membership and age, sex, ethnicity, marital status, education level, employment status, alcohol use, or smoking history.

The clinical findings are presented in [Table 2](#). No clinical variable was found to be associated significantly with subgroup membership. The body mass index for those with EG by subtype was 26 kg/m² with mucosal disease, 29 kg/m² for muscular disease, and 24 kg/m² for subserosal disease. For those with EG, most reported a personal history of allergy (63% mucosal disease, 67% muscle layer disease, and 50% serosal disease), but

only 27% reported a family history of allergy and this was limited to only those with mucosal involvement. Subjects with EG did not appear to have anemia at presentation or a profoundly increased erythrocyte sedimentation rate. Peripheral eosinophilia was seen commonly among all 3 EG groups with a median count between 0.9 and 3.3 kU/L. Serum immunoglobulin E levels appeared highest in the mucosal group of EG (622 U/L), but these levels were comparable with those found in the unexplained PEos group (690 U/L). Common presenting symptoms by EG subtype were mucosal disease with abdominal pain (63%) and diarrhea (52%); muscle layer disease with nausea/vomiting (100%), weight loss (67%), and diarrhea (67%); and serosal disease with ascites (100%), abdominal pain (67%), and diarrhea (67%). No unique presenting symptom was detected among any of the EG groups aside from ascites in serosal disease.

[Table 2](#) also summarizes the therapies used for each EG subtype as well as the PEos group. Possible therapies included steroids (eg, prednisone), dietary modification, antihistamine agents, mast cell inhibitors, leukotriene receptor antagonists, combined therapies, and therapy without steroids. Treatment for the EG group consisted largely of steroid therapy with 75% of mucosal layer, 67% of muscle layer, and 100% of subserosal disease patients receiving prednisone, and this was found to be associated significantly with group membership (eosinophilic gastroenteritis group vs the unexplained PEos group). Only 13% of the EG group (limited to the mucosal layer of disease group) received any type of therapy that did not include steroids. Combination therapy was common with 100% of the subserosal group receiving combination therapy that included steroids.

Of the patients with EG, 56 underwent endoscopic evaluation and all patients with PEos underwent endoscopic evaluation with either esophagogastroduodenoscopy or colonoscopy, or both procedures. All 3 EG patients who did not have an endoscopic evaluation underwent surgery; 2 for diagnostic purposes and 1 owing to gastric outlet obstruction. Of the patients who had some form of endoscopic evaluation, 58% of EG patients and 64% of PEos patients had positive endoscopic findings. Gastric erythema/gastritis (22%) and thickened gastric folds (10%) were the most common endoscopic findings for EG. The total number of unique biopsies obtained at each site of the GI tract also was recorded. The sum of these numbers will be larger than the total number of subjects because many had numerous biopsy specimens taken. When available, the histologic slides from subjects with EG were reviewed by an expert histopathologist (T.C.S.) and quantification of the number of eosinophils per HPF was recorded ([Figure 1](#)). The median eosinophil count per HPF for EG was 82 (interquartile range, 27–100). The overall range of eosinophils/HPF seen on biopsies from patients diagnosed with EG was from 4 to 300. [Table 3](#) summarizes for the EG group the number of biopsies based on site, number of patients with eosinophilic infiltration of 20 or more eosinophils/HPF per each biopsy site, and median eosinophil/HPF (interquartile range) seen on positive biopsies at each site. [Table 3](#) does not include any data for the PEos group because by definition this group was required to have negative histologic findings.

The sites as well as description of radiographic findings in the EG and unexplained PEos groups ([Figure 2](#)) were recorded. Radiographic techniques included computerized tomography, magnetic resonance imaging, ultrasound, computerized tomog-

Table 2. Clinical and Laboratory Features of EG by Disease Group and Unexplained PEos

Variables	Mucosal layer (n = 52)	Muscle layer (n = 3)	Serosa (n = 4)	All EG (n = 59)	GI symptoms and PEos (n = 11)
Age at diagnosis, y ^a	48 (2)	45 (14)	29 (8)	47 (2)	37 (4)
Years of symptoms, y ^a	3.4 (0.8)	2.8 (2.6)	7.0 (6.5)	3.6 (0.8)	4.6 (2.2)
History of allergy, %	63	67	50	63	73
Body mass index, kg/m ^{2a}	26 (0.8)	29 (3.4)	24 (2.9)	26 (0.8)	25 (1.7)
Family history of allergy, %	27	0	0	24	0
Food intolerance/allergy, %	19	33	0	19	18
Anemia at time of diagnosis, %	27	0	25	25	9
ESR ^{a,b}	15 (3)	4 (2)	21 (17)	15 (2.9)	7 (2)
Median blood eosinophil count, kU/L, (interquartile range) ^a	0.9 (0.3–1.9)	3.3 (0.4–3.8)	1.3 (0.9–2.0)	1.5 (0.3–2.1)	1.7 (0.7–2.3)
Serum IgE level, U/mL ^a	622 (278)	27	86 (49)	531 (234)	690 (301)
Presenting symptoms, %					
Abdominal pain	63	33	75	64	73
Nausea/vomiting	40	100	25	43	36
Bloating	8	33	0	9	27
Weight loss (≥5 lb)	19	67	25	22	9
Diarrhea	52	67	25	52	73
Constipation	8	0	0	7	0
Treatment, %					
Steroids (eg, prednisone) ^b	75	67	100	78 ^b	18
Dietary modification	23	33	50	27	36
Mast cell inhibitors	25	0	50	27	27
Antihistamines	35	33	50	38 ^b	0
Leukotriene receptor antagonists	4	0	0	4	9
More than one therapy	88	67	100	88 ^b	64
Treated without steroids (with one of the other noted therapies)	13	0	0	13 ^b	45

ESR, erythrocyte sedimentation rate; Ig, immunoglobulin.

^aMean (standard error of the mean).

^b*P* < .05 for total EG group versus unexplained PEos group.

raphy enterography, magnetic resonance enterography, upper GI series, and small-bowel follow-through. Only 32% of those with EG who had radiographic imaging had a positive finding. Most common sites were the stomach (10%) and small bowel (15%), with thickened walls commonly seen in the jejunum/ileum (17%) and stomach (8%). For the PEos group, 27% had a positive radiographic finding, with the most commonly involved sites being the duodenum (18%) and jejunum/ileum (27%), with thickened walls being the most common finding at 9% for both affected areas.

As shown in Table 4, the association of self-reported types of allergies with subgroup also was assessed for the EG and PEos groups; these included atopy, asthma, nasal polyps, hay fever,

drug allergy (self-reported drug allergy and recorded qualitatively as yes/no), eczema, food intolerance/allergy, and rhinitis. No significant association was found for any one particular type of allergy. Food allergy testing (either through radioallergosorbent or skin prick testing) was performed and reported on 22 subjects with EG and 2 with PEos. Types of foods tested by either method included dairy, meat, poultry, grains, seafood, vegetables, nuts, legumes, fruits, and spices. Only 50% of the EG subjects who underwent food allergy testing had a positive finding and the specific types of food allergies are reported in Table 5. No particular food group appeared to be over-represented.

A total of 30 subjects, 27 with mucosal disease and 3 with serosal disease, had follow-up evaluation after therapy available

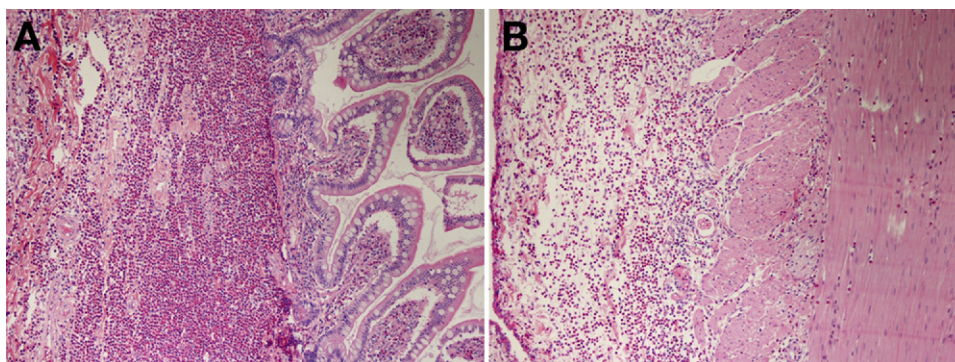


Figure 1. (A) Small-bowel biopsy from the jejunum that shows dense eosinophilic infiltration involving the submucosa as well as serosa. (B) Taken from the same jejunal biopsy as in panel A, this higher-magnification view of the subserosa shows the significant accumulation of eosinophils.

Table 3. Distribution of Biopsy Specimens and Degree of Eosinophilic Infiltration of Positive Biopsies From Patients Diagnosed With EG

	EG patients biopsied at each site, n	Patients with eosinophilic infiltration (>20 eosinophils/HPF), n	Median eosinophils/HPF for positive biopsies (interquartile range)
Site of biopsies, %			
Gastric antrum/body	39	21	83 (25–100)
Duodenum, proximal jejunum	26	11	69 (30–80)
Ileum	7	2	165 (30–300)
Colon	6	4	129 (65–192)
Rectum ^a	1	—	—
Gallbladder ^a	1	—	—
Appendix ^a	2	—	—
Other ^a	2	—	—

^aBiopsies unavailable for review.

for review. The mean length of follow-up evaluation for these 30 subjects was 6 months. Of these 30 subjects, most received therapy with steroids: 8 received steroid therapy alone, 16 received steroid therapy in combination with another therapy (eg, dietary modification, antihistamine agents, mast cell inhibitors, leukotriene receptor antagonists), and 2 received therapy other than steroids. Four subjects received no therapy. For the group that received only steroid therapy, which had a mean length of follow-up evaluation of 7 months, 88% had either improvement or resolution of symptoms. For the 16 subjects who received steroids in combination with another therapy, 94% had either improvement or resolution of symptoms, with a mean length of follow-up evaluation in this group of 4 months. The 2 subjects who received a therapy other than steroids had a mean length of follow-up evaluation of 2 months, and 1 had no improvement in symptoms and the other had resolution of symptoms. Interestingly, all of the 4 subjects who received no therapy had resolution of their symptoms, with a mean length of follow-up evaluation of 17 months.

Discussion

The present study reports our clinical experience with adult EG. A total of 59 patients with EG were seen in our center over the past 20 years and, when combined with our previous experience, a total of 99 patients with EG were seen over a 50-year period. The data suggest that unlike other eosinophilic GI disorders such as eosinophilic esophagitis, EG remains a rare

disorder with an average of only 2 to 3 cases diagnosed annually at a large tertiary referral center. This study evaluated numerous factors including sociodemographic characteristics, clinical features, endoscopic and radiographic findings, and types of self-reported allergies, as well as documented food allergies by specific type of food product. For applicable clinical features, a second group of patients with GI symptoms and unexplained PEos was compared against those with EG. No significant defining feature was found for EG as a whole and regardless of subtype, any of the particular EG types, or for the unexplained peripheral eosinophilia group.

Our findings that EG occurs largely in the third and fourth decades of life, has a male predominance, and occurs mostly in the Caucasian population is consistent with available literature.^{4,5,7,9} Most EG patients appear to have at least a high school degree or some college education and full employment. This finding may argue away from a relationship between EG and a primary allergic response because asthma and allergies are reported disproportionately in lower socioeconomic groups.^{14,15} However, our findings are similar to those reported for inflammatory bowel disease; ulcerative colitis and Crohn's disease appear to be more common in higher socioeconomic groups and those in white-collar occupations.^{16,17} Whether this may indicate a similar theorized etiopathogenesis, with absence of early antigen presentation in those from higher socioeconomic groups and subsequent lack of GI immunity for those with EG, is unclear.



Figure 2. Computerized tomography of the abdomen and pelvis of a patient diagnosed with EG with multiple computerized tomography findings. (A) Moderate ascites as noted (white arrows); (B) generalized mural thickening of the gastric antrum (white arrow); and (C) mild mural thickening and hyperemia of several loops of small bowel.

Table 4. Distribution of Types of Self-Reported Allergies Among EG and Unexplained PEos

	EG (n = 59)	Unexplained PEos (n = 11)
Type of allergy history, % (EG, n = 1 missing)		
Atopy	10	0
Asthma	24	9
Nasal polyps	5	0
Hay fever	7	0
Drug allergy	36	45
Eczema	2	0
Food intolerance/allergy	21	27
Rhinitis	21	9

Numerous clinical features were examined and compared between patients with unexplained GI symptoms and PEos, patients with EG regardless of subtype, and EG subjects segregated by degree of involvement per the Klein classification. No clinical feature was found to be associated significantly with any one group membership. However, notable is that increased PEos was found for all 3 groups of EG. This finding contradicts the historical perspective that PEos is not believed to be a prerequisite for diagnosis because it is not a universal finding.^{7,9,18,19} A possible explanation for this finding is that the majority of the patients reported a history of allergy; peripheral eosinophilia has been reported to occur more often in those with an allergic disorder such as atopy, asthma, or eczema.^{20,21} Another consideration is that secondary to increased clinical awareness of EG, patients who presented with PEos and GI symptoms were more likely to undergo diagnostic evaluation that was focused on confirming or excluding a diagnosis of EG. Although clinical experience would support the view that peripheral eosinophilia is not a universal finding and not required for diagnosis, our findings may reinforce that clinical vigilance and suspicion for EG should be high in the context of GI symptoms, PEos, and a history of allergy. Other laboratory parameters including anemia at time of diagnosis, increased erythrocyte sedimentation rate, and serum immunoglobulin E levels did not appear to be helpful diagnostic tests for EG, and this is consistent with past experience.⁷

A history of allergy appeared common for all groups of EG; specifically drug allergy, asthma, and food intolerance/allergy were the most common types of allergies. Twenty-two subjects with EG underwent food allergy testing. Although a variety of types of food allergies were identified, it is notable that 50% of all tested subjects had negative food allergy testing. Our findings, in conjunction with the low sensitivity and high rates of false-positive results of commonly available allergy tests, may argue for great caution when contemplating the use of these tests for suspected EG patients.⁸

Body mass index also was evaluated and most groups were largely overweight but without overt obesity. Increasing weight may be relevant in the pathogenesis of EG given that obesity has been reported to be associated with allergic diseases such as asthma and atopy.^{22,23} One proposed explanation for this association is that obesity results in decreased immunologic tolerance and a shift of the immune system toward a Th-2 cytokine profile, which increases the risk for allergy and other immune-mediated diseases.²³ Th-2 cytokines (interleukin-3, interleu-

kin-5, and interleukin-13) are especially relevant for EG in that they are thought to play a critical role in the pathogenesis.⁸ Finally, gastrointestinal symptoms including abdominal pain, nausea, vomiting, and diarrhea were common but not unique to any one particular group.

Endoscopic features were examined and the predominance of proximal findings likely is secondary to the use of upper endoscopy as part of the diagnostic evaluation. Furthermore, the use of upper endoscopy in clinical practice has been increasing over this same time period.^{12,24} This is reflected by the common identification of gastric erythema/gastritis, as well as the stomach and duodenum/proximal jejunum being the most common sites of biopsy, consistent with previous investigation.⁷ Radiographic features also were reported and the findings appear to often involve the stomach or small bowel, with a thickened gut wall being the common abnormality. Finally, available histologic slides were reviewed and the intensity of eosinophilic infiltration was quantified. Interestingly, we found a significant level of eosinophilia seen on reviewed biopsies that were positive with a median of 82 eosinophils (interquartile range, 27–100). This finding is much greater than the minimum level of 20 eosinophils per HPF commonly used as part of the diagnostic criteria.

Finally, the distribution of types of EG in our study is notably different from our previous experience. In 1990, Talley et al⁷ reported on a group of 40 subjects with EG that comprised 23 mucosal, 12 muscle layer, and 5 subserosal disease patients. Although our findings continue to show a predominance of mucosal disease, there appeared to be a greater shift toward mucosal disease and away from disease of the muscularis, with our finding of 52 mucosal, 3 muscle layer, and 4 subserosal disease. The change may reflect diagnostic bias with the greater use of upper endoscopy in the evaluation of GI symptoms since that original report in 1990,^{12,24} but another consideration would be the hypothesis that the pathogenesis of EG involves an inward-out pathway; EG initially may involve the mucosa and that progression of the disease involves greater depth of invasion of the gut wall. This hypothesis in conjunction with greater use of diagnostic upper endoscopy could explain the shift in types of EG observed secondary to diagnosis at an earlier stage. This is supported by our findings that the fraction of those with serosal involvement also appeared to decrease during this same time period; we presume the serosal

Table 5. Types of Food Allergies Found in EG

	EG (n = 22)
Type of food allergy, % ^a	
Dairy	23
Meat	23
Poultry	18
Grains	32
Seafood	23
Vegetables	36
Nuts	27
Legumes	23
Fruits	27
Spices	9
None	50

^aDiagnosed by either radioallergosorbent immunoglobulin E test or skin prick test.

group represents those with advanced disease and we now see less of this with more aggressive and earlier investigation.

Finally, this study describes response to therapy in 30 subjects. Steroid therapy, either as monotherapy or in combination with another therapy, remains the cornerstone of treatment for EG, and most patients appeared to have a significant clinical response within a relatively short period of time after therapy. Although 88% responded to steroid therapy alone, combination therapy with steroids appeared to be superior to monotherapy with 94% having either clinical improvement or resolution of symptoms at follow-up evaluation.

In conclusion, this study reports a large and comprehensively described clinical experience with adult EG. We reviewed 59 patients with EG disease and 11 patients with GI symptoms and unexplained PEos. Our data suggest that EG remains a rare disorder and does not appear to be increasingly diagnosed despite increasing prevalence and incidence of other eosinophilic GI disorders. PEos was seen in the majority of our cases and extent of involvement appears to have shifted toward that of the mucosal layer. It often presents with nonspecific GI symptoms, occurs largely in the third and fourth decades of life, has a male predominance, occurs mostly in the Caucasian population, and most patients have a higher level of education. Steroid therapy appears to be a highly effective treatment with a clinical response seen in just months, and the response may be even greater when used in combination with another therapy. Although a history of allergy is common, food allergy testing did not appear to have a useful role as part of the evaluation for EG. Finally, our findings suggest that clinical vigilance is warranted especially when evaluating a patient presenting with even mild PEos and GI symptoms.

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Conflicts of interest

The authors disclose no conflicts.