

Eosinophilic Gastroenteritis

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Eosinophilic gastroenteritis (EG) is commonly regarded as a synonym for eosinophilic gastrointestinal disorders (EGID), referring to a broad spectrum of clinical presentations produced by prominent eosinophilic infiltration through a variable depth of one or more gastrointestinal sites, and thus including eosinophilic esophagitis, gastritis, enteritis, and proctocolitis. Alternatively, the term has been used to refer to eosinophilic inflammation limited exclusively to the stomach and small intestine. To avoid redundancy in this issue of *Gastroenterology Clinics of North America*, this article is restricted to a focused and updated review of eosinophilic gastroenteritis as limited to the latter definition.

EPIDEMIOLOGY

Because of a notable scarcity of published data on the epidemiology, it is difficult to determine the true burden of EG. An English language literature review does not reveal a well-analyzed published case series describing primary EG in the last 3 years, suggesting that it is an uncommon and perhaps difficult-to-diagnose disorder. Nevertheless, several case reports of EG have emerged recently in different parts of the world [1–5]. The diagnosis affects most ethnicities, and all ages of both genders [6–10]. It is diagnosed most frequently in the third decade of life [6,7,10,11]. A personal or family history of allergic disorders, such as asthma, hay fever, or eczema, is present in 60% to 70% of patients [12].

A report from India on EG documented only 7 young adults during a 10-year period [10], and a hospital in China identified 15 patients who had EG, including 2 children, during 18 years [6]. Talley and colleagues [7] reported one of the largest case series of EG by characterizing 40 patients diagnosed during a 30-year period.

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PATHOGENESIS

EG may be primary, also known as allergic, or secondary to one of many conditions that provoke eosinophilic inflammation (see later section on differential diagnosis), with parasitic infections being the leading cause. The cause cannot be precisely determined in a small but important minority of patients, who are regarded as having idiopathic EG.

Eosinophils and Key Mediators

EG, like other allergic diseases, is characterized predominantly by a Th-2 type of inflammatory response. This response, in concert with eosinophils and their granular proteins and eotaxin-1, a selective chemoattractant, are all critical to the pathogenesis of EG.

Eosinophils, the hallmark of the pathology of EG, normally reside in the gastrointestinal tract lining beyond the esophagus, and are believed to have a role in host defense (eg, against parasitic infections). Reported normal densities of eosinophils vary throughout the length and depth of the gastrointestinal tract (see later discussion of diagnostic evaluation).

Eosinophils function as antigen-presenting cells and mediate inflammatory effects by releasing preformed granular proteins, such as eosinophil cationic protein (ECP), eosinophil derived neurotoxin (EDN), eosinophil peroxidase, and major basic protein (MBP) [12,13]. Extracellular deposits of ECP and MBP have been demonstrated in the small intestine of patients who have EG; electron microscopy has provided further evidence for eosinophil degranulation in duodenal mucosal samples from patients who have EG [14,15]. Eosinophils also secrete Th-2-type proinflammatory cytokines, such as interleukin (IL)-3, IL-4, IL-5, IL-18, and transforming growth factor, and lipid mediators that are cytotoxic to human intestinal epithelium [12,16,17].

Further new and exciting insights into the mechanism of intestinal mucosal eosinophilia have been made possible through the study of the BioBreeding (BB) lymphopenic (lyp) rat model [18]. The lyp gene encodes a molecule known as GTPase of the immunity-associated protein, which may protect lymphocytes against apoptosis. Homozygosity of the lyp gene mutation in this murine model is associated with intense eosinophilia of the small and large intestinal mucosa, an overall Th-2 phenotype expressed by cell cultures derived from lymph nodes and spleen, with increased levels of IL-4, IL-5, and IL-13 RNA, and increased serum levels of IgE. Furthermore, the rats develop clinical features of wasting, bloating, intestinal distention, splenomegaly, and mesenteric adenopathy. An interesting feature observed even before the histopathology findings was the presence of an autoantibody, BB rat serum IgG, bound to intestinal cells that resembled fibroblasts. This finding has led to the speculation that a novel autoantigen in the subepithelial layer may provoke mucosal eosinophilic invasion.

Allergy

Excess circulating eosinophils are considered a hallmark of atopy, and hence it is no surprise that the frequency of allergies in patients who have EG is 25% to

75%. Peripheral eosinophilia is present in 50% of those who have both EG and atopic diseases, such as asthma, eczema, and hay fever [19–21]. EG-associated allergies are reported variably as mediated by either IgE or non-IgE mechanisms. Mice challenged by oral antigens produce correlates of human EG disease: antigen-specific serum antibodies, prominent eosinophilic intestinal infiltrates, and clinical manifestations, including diarrhea, gastromegaly, dysmotility, and cachexia [22].

Genetics/Familial

Genetic susceptibility is also now being implicated in the pathogenesis, as evidenced by the presence of a family history of an EGID in 10% of patients [19].

CLINICAL PRESENTATIONS

Patients who have EG have heterogeneous clinical presentations, some of which overlap with more familiar diagnoses, such as functional GI disorders and inflammatory bowel disease. Presenting symptoms may be vague and non-specific (eg, recurrent abdominal pain [23]) or dramatic (eg, gastric ulcer perforation [24]). Symptom onset may be at any age, but most patients are diagnosed as young adults, between the third and fifth decades of life. Often patients experience symptoms for many months and undergo an elaborate evaluation before the diagnosis of EG is correctly established. The natural history of EG is not well studied, although the course is usually characterized by waxing and waning symptoms.

Patients who have EG have selective involvement of the stomach (26%–81%) and small intestine (28%–100%) [7,11,25]. As alluded to earlier, however, EG is popularly used to refer to those cases of prominent gastric or small intestinal eosinophilia that may have concurrent, although less prominent, eosinophilia of the esophagus, large intestine, or rectum. It is debated, for example, whether the occasional patient presenting with apparent eosinophilic esophagitis (EE) and marked eosinophilic inflammation extending to other segments of the gastrointestinal tract represents primary EE or EE as part of EGID.

The most common presenting complaint is abdominal pain, reported by two thirds of patients in most case series, followed by the symptoms of nausea, vomiting, and diarrhea [7,20,26].

Classification

The Klein classification describes EG clinical presentations in terms of the variable depth of eosinophilic infiltration: mucosal, submucosal, and serosal subtypes [27].

Mucosal

The mucosal subtype is the most common one (25%–100%), perhaps because of the accessibility to diagnosis by routine endoscopy and biopsies. Patients who have mucosal EG present with common, albeit nonspecific, complaints of abdominal pain, nausea, vomiting, diarrhea, occult gastrointestinal bleeding,

anemia, weight loss, or protein-losing enteropathy [1,8,21]. Because of their nonspecific nature, these clinical presentations may be confused with irritable bowel syndrome, dyspepsia, pancreatitis, acute appendicitis, or inflammatory bowel disease. Intestinal loss of blood and protein is a unique presentation in children who have allergic EG, and is suspected to be attributable to increased intestinal permeability induced by eosinophilic inflammation. Frequent coexisting findings in patients who have mucosal EG are atopy and high serum IgE levels.

Muscular

This subtype of EG is diagnosed in 13% to 70% of all EG cases, and is best known to present with a clinical picture of gastric outlet or intestinal obstruction [2,4,28]. Abdominal pain is usually characterized as colicky. EG presenting as gastric outlet obstruction can mimic hypertrophic pyloric stenosis, and has been successfully managed with a hypoallergenic formula rather than surgery [9]. Intestinal obstruction attributable to enteric strictures, although rare, occurs most frequently at the level of the jejunum, and has been described in children and adults [2,4,29,30].

Serosal

The serosal layer is involved in 12% to 40% of cases of EG. Most commonly affected are adults who present classically with ascites. Other notable findings in these patients are significant bloating, a higher level of peripheral eosinophilia, and a better response to steroids [7,31–34].

DIFFERENTIAL DIAGNOSIS

A broad range of conditions are associated with gastrointestinal mucosal eosinophilia and the following is a brief review of some of the important differential diagnoses.

Infections

Parasitic infestations

Among parasites, helminths are most characteristically associated with peripheral eosinophilia, probably as a reflection of an immunologic response to their tissue migration. Tissue eosinophilia also may be found with several other parasites, including hookworms (*Ancylostoma caninum*), pinworms (*Enterobius vermicularis*), *Eustoma rotundatum*, *Giardia lamblia*, *Anisakis*, *Trichinella spiralis*, *Ascaris*, *Trichuris*, *Schistosomiasis*, *Toxocara canis*, and *Strongyloides stercoralis*. Diagnosis should be pursued in the appropriate clinical situation using studies such as stool for ova and parasites, stool giardia antigen, serology, paracentesis (in the case of ascites), duodenal aspirate, and endoscopy with biopsies [35–40].

Helicobacter pylori

H pylori gastritis has been observed in patients who have diffuse intestinal eosinophilia in the absence of food allergies. The significance of these coexisting findings, beyond coincidence, is not clear [41].

Cytomegalovirus

Cytomegalovirus (CMV) gastroenteritis evident by serology and pathology, the latter also consistent with EG, has been reported in an immunocompetent child presenting with protein-losing enteropathy [42]. Whether the allergic mucosa predisposed to reactivation of latent CMV or CMV triggered prominent intestinal eosinophilia could not be elucidated from this report. Interestingly, this patient had complete resolution of clinicopathologic features without specific antiviral or antiallergy therapy within 4 weeks.

Medications

Several medications have been implicated in producing gastrointestinal eosinophilia as an allergic response. Examples include interferon [43], gemfibrozil [44], enalapril [45], carbamazepine [46,47], clobazamine [48] and co-trimoxazole [49]. Tissue eosinophilia is usually reversible with cessation of the medication.

Connective Tissue Disease and Vasculitis

Various connective tissue disorders (eg, scleroderma, dermatomyositis, lupus) and vasculitis (eg, Churg-Strauss syndrome, polyarteritis nodosa) are associated with fluctuating peripheral and gastrointestinal eosinophilia [50–53]. The presence of specific clinicopathologic and autoimmune markers is helpful in their differentiation from primary EG.

Inflammatory Fibroid Polyps

Rarely diagnosed, these benign localized polyps, also known as fibroma, inflammatory pseudotumor, submucosal granuloma, or localized EG, originate in the submucosa and are accompanied by a variable eosinophilic infiltrate. These lesions are most commonly located in the stomach (~35% of cases) and the small bowel (~50%), and come to attention because of obstructive presentations. Surgical excision is a cure for symptomatic patients [54,55].

Hypereosinophilia Syndrome

Hypereosinophilia syndrome is a rare heterogeneous disorder with features of unexplained marked peripheral hypereosinophilia (>1500 cells/ μL for more than 6 consecutive months) despite an extensive evaluation, and presence of organ damage or dysfunction related to hypereosinophilia [56–58]. The heart, skin, and central nervous system are the major targets, whereas occasional intestinal involvement is reported. Recently, hypereosinophilia syndrome has been classified as either myeloproliferative or lymphocytic indicating an underlying hematologic basis for these variants.

Inflammatory Bowel Disease

Peripheral and intestinal eosinophilia is often noted in patients who have irritable bowel disease, in the context of classic clinicopathologic features that allow differentiation from primary EG and other conditions.

Transplantation

Recipients of solid organ transplantation may develop intestinal eosinophilia as a consequence of immunosuppression, an imbalance of Th-1/Th-2 lymphocytes,

and de novo food allergies. A substantial number of patients are on immunosuppressive regimens composed of tacrolimus, a calcineurin inhibitor that is strongly implicated in inducing intestinal eosinophilia. A high total IgE and food allergen-specific IgE levels are observed in this subgroup of patients and dietary therapy has proved to be satisfactory [59–61].

DIAGNOSTIC EVALUATION

Diagnosis of EG requires suspecting the disease, excluding other disorders in the differential diagnoses, confirming the definitive diagnosis, and assessing for potential complications. Currently accepted diagnostic criteria are the presence of gastrointestinal symptoms, an intense eosinophilic infiltrate on histopathologic examination, and exclusion of other causes of intestinal eosinophilia. Tests considered useful in the evaluation of EG and its differentials are presented in Table 1 [62].

A single diagnostic algorithm may not be universally applicable, because, for example, the screening evaluation may follow the demonstration of tissue eosinophilia. The following aspects of evaluation usually complement each other.

History and Physical Examination

The history and physical examination should be aimed at eliciting information pertaining to food-related adverse effects, stigmata of atopic diseases (wheezing, eczema, rhinitis), and evidence of malnutrition (edema, anemia, failure to thrive).

Laboratory

In the context of gastrointestinal symptoms, peripheral eosinophilia, present in 50% to 100% of those who have EG, is indeed a useful clue to EG, but is not definitive. Peripheral eosinophil concentrations fluctuate and may reflect the effects of circadian rhythms. Tests on stool and duodenal aspirates for parasites (particularly helminths) are strongly recommended to exclude secondary causes of EG, particularly in high-risk geographic areas. Other potentially useful laboratory investigations are directed toward evaluation for anemia (complete blood count), hypoalbuminemia (serum albumin), enteric protein losses (stool α -1 antitrypsin), autoimmune associations (autoantibodies), the eosinophilic intestinal inflammatory process (eosinophils and their remnants—ie, Charcot-Leyden crystals in stools), and eosinophilic ascites (paracentesis). In the near future, serum, stool, and urine assays of active eosinophil inflammation (eg, ECP, EDN) may be used for follow-up and response to therapy.

Allergy Evaluation

Commonly available tests for allergy include skin prick tests (SPT) and in vitro quantitative CAP-fluorescent enzyme immunoassay (CAP-FEIA), formerly known as radioallergosorbent test (RAST), which detects allergen-specific IgE antibody. The results of both should be interpreted with caution because of low sensitivity and a high rate of false-positive results [63,64]. It has also

Table 1
Diagnostic evaluation of eosinophilic gastroenteritis

Evaluation	Significance
Complete blood count with differential	Anemia, absolute eosinophilia
Total protein and albumin	Hypoalbuminemia, edema, protein-losing enteropathy, ascites, malnutrition
Quantitative immunoglobulins	Protein-losing enteropathy
Stool α -1 antitrypsin	Protein-losing enteropathy
Stool eosinophils	EG diagnosis and follow-up
Stool for eosinophil-derived granular proteins (eg, ECP)	EG diagnosis and follow-up
Stool giardia antigen, ova and parasite	Exclusion of parasite-induced EG
Radiology	
Barium contrast studies	Thickening of folds, stenoses/strictures, inflammation, lymphadenopathy;
Computerized tomography	exclusion of differentials (eg, appendicitis)
Ultrasound	Ascites
Food Allergy	
Serum CAP-FEIA	IgE-mediated allergies
Skin prick tests	IgE-mediated allergies
Skin patch tests	Non-IgE-mediated allergies
Endoscopy	
Gross	Erythema, erosions, ulcers, polyps, nodules
Microscopy	Dense eosinophilic infiltrates, epithelial and glandular invasion, abscesses; exclusion of differentials
Surgery and pathology	Establishing diagnosis, relief of obstruction
Paracentesis	Eosinophilia in serosal EG
Miscellaneous	
Liver enzymes	Evaluation of differentials and multi-organ involvement
Pancreatic enzymes	
Erythrocyte sedimentation rate	
C-reactive protein	
Tissue transglutaminase antibody	
Autoimmune antibodies	
Stool calprotectin, lactoferrin	

Abbreviation: CAP-FEIA, CAP-fluorescent enzyme immunoassay.

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been shown that the probability of a true positive food challenge, and hence the positive predictive value, is high if allergen-specific IgE to a few select foods (milk, soy, egg, wheat, peanut, and fish) exceeds certain values [65]. The high negative predictive value of SPT is useful in confirming the absence of IgE-mediated reactions, if good quality food extracts are used.

In the evaluation of non-IgE-mediated food allergies, patch testing is now available in Europe and North America, but has not been studied specifically in EG, and remains of limited usefulness because of lack of standardized

criteria [66]. Double-blind placebo-controlled food challenges are not practical in the clinical setting, and may also have limited usefulness in EG, because delayed hypersensitivity reactions may not be apparent for a few days. In children strongly suspected to have allergic EG, therefore, the clinician is often faced with the challenge of balancing the benefits of eliminating offending foods against the risks of unnecessarily restricted diets caused by the institution of time-limited dietary trials.

Radiographic Evaluation

Barium contrast studies in patients who have EG may reveal irregular gastric or small intestinal folds, a string sign in gastric outlet obstruction, or strictures [9,43]. Ultrasound of the abdomen is useful in detecting serosal EG and ascites [67]. Deep layer infiltration and intestinal wall thickening may also be appreciated on computerized tomography [68]. White blood cell Tc-99m scintigraphy may demonstrate inflammation in EG, but without differentiating EG from other inflammatory causes [69].

Endoscopy and Pathology

The macroscopic features of EG are few, but include erythema, whitish specks, focal erosions, ulcerations, thickening of folds, polyps, nodules (Fig. 1), and friability [5,42]. A fair number of cases are not associated with any visible mucosal abnormalities (Fig. 2A).

Histopathology is the gold standard for diagnosis (Figs. 3 and 2B), but the precise criteria differentiating normal from pathologic states remain a matter of debate. The factors currently taken into consideration for differentiating



Fig. 1. The endoscopic appearance of the gastric mucosa in a patient who had eosinophilic gastroenteritis. The diffuse mucosal nodularity, as shown here, mimics *H pylori* nodular gastritis.

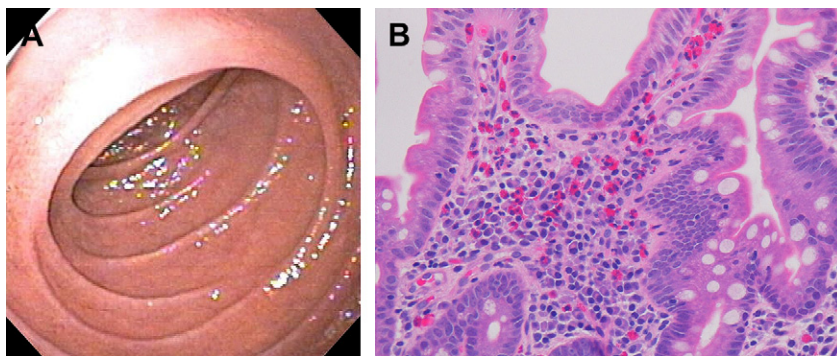


Fig. 2. Eosinophilic duodenitis in a patient who had grossly normal duodenum (A) depicts histologic features of normal villous surface, hypercellular lamina propria, predominant eosinophilic inflammation, and eosinophilic microabscesses (B).

normal gastrointestinal tissue from any type of EGID are: eosinophil density, location along the gastrointestinal tract (ie, within the normal digestive tract, the highest number of eosinophils—up to 68 per high power field—are found in the appendix and cecum, and the lowest—none—in the esophagus), eosinophil distribution through the wall depth (eg, it is unusual to find eosinophils infiltrating the normal epithelium and crypts, or forming superficial aggregates or abscesses), eosinophil degranulation, and the absence of features pathognomonic for other diseases (eg, granulomata in Crohn disease) [70,71]. Normal eosinophil levels were determined retrospectively in 28 children who did not have apparent pathology, most of whom underwent an endoscopy for abdominal pain [71]. The mean (maximum) number of eosinophils per high power

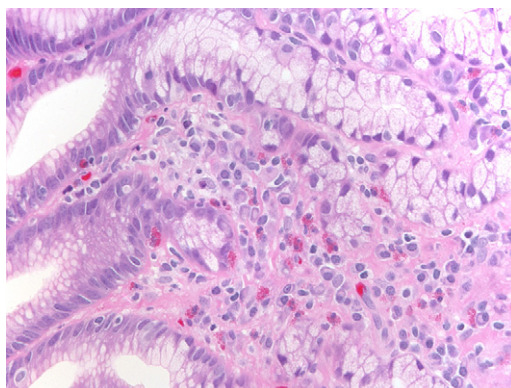


Fig. 3. A photomicrograph of a gastric mucosal biopsy from the same patient shows hypercellularity of the lamina propria, up to 20 eosinophils per high power field with focal epithelial involvement, and subepithelial collagen. A Diff-Quick stain for *H pylori* was negative.

field in the lamina propria of the gastric antrum and duodenum were 1.9 ± 1.3 (8) and 9.6 ± 5.3 (26), respectively. The diagnosis may be missed despite endoscopy and biopsies because of patchy disease distribution, and also because of sparing of the mucosa in some forms of muscular and serosal EG.

The diagnosis of muscular or serosal EG is particularly challenging and requires diligence. The diagnosis of these subtypes can be confirmed on pathology specimens obtained at laparoscopy or laparotomy [4,72]. Capsule endoscopy and balloon enteroscopy may prove useful in patients who have EG, but the inability to procure biopsies is likely to limit the value of these techniques in the diagnosis of EG [73–75].

MANAGEMENT

Various treatments may be beneficial in EG [76]. Our current knowledge of the treatment of EG is derived virtually exclusively from small studies and anecdotal experience. Evidence for the true efficacy of any therapy suffers from the lack of well-designed and controlled studies. Nevertheless, corticosteroids and dietary therapy are two treatment interventions for which the data are convincingly favorable. Emerging treatments in development are biologics and selective anti-eosinophil agents.

Diet

The particular EG presentation, the patient's age, and the expected compliance may be the most important determinants of the type of dietary therapy. Dietary therapy assumes the form of either an elimination diet or an elemental diet; both benefit from guidance by allergy evaluation. To ensure success with dietary therapy, it is important to support the patients and parents with relevant educational sources and dietary consultation.

Elemental diets are indicated in those who have multiple food allergies, and produce improvement of symptoms and histology in 4 to 9 weeks [5,8]. The efficacy and safety of long-term dietary therapy has not been studied in EG. Moreover, these diets are aversive because of their poor palatability and impractical because of the high cost and extreme restriction.

Directing food elimination by way of routinely available allergy testing (CAP-RAST and SPT) may be effective but does not always produce a favorable response in EG, probably because the immunologic reactions to foods in EG are mediated by non-IgE as well as IgE mechanisms. A food diary monitoring routine food consumption and its relation to adverse reactions may be used to decide the extent of food elimination. The empiric removal of the six major food allergens (milk, soy, wheat, egg, nuts, peanut, seafood), termed “the six food elimination diet,” has been shown to be effective and safe in EE [77]. It is a practical empiric approach in all patients who have primary EG who do not have obvious food allergies on allergy testing.

Caution should be used in the implementation of an extremely restricted or elemental diet for longer than 6 to 8 weeks. In those assessed clinically as responders, a new food may be introduced every 5 to 7 days with continued

vigilant follow-up. Repeat endoscopic evaluation is not routinely indicated, but may be advantageous in selected cases to guide complex treatment decisions.

Steroids

Systemic steroids produce symptomatic and histologic improvement in EG, regardless of type, within a few days to weeks of initiation [21,31,76]. Steroids are indicated in those patients who have EG who have failed to respond to, or declined, dietary therapy, and in those who have severe clinical presentations. The usual dosage, taper, and duration of therapy are equivalent to the treatment in inflammatory bowel disease. The use of 1 to 2 mg/kg/d for at least a month induces remission, and is then tapered over 2 to 3 months. The tapering and discontinuation may result in disease relapse, necessitating repeated use of steroids. Patients who have a disease course marked by chronic symptoms and relapses are candidates for steroid-sparing options to minimize the multitude of steroid-related serious side effects. These side effects include fluid and electrolyte imbalance, hyperglycemia, cushingoid state, growth suppression, bone demineralization, pituitary and adrenocortical hyporesponsiveness, and posterior subcapsular cataracts. Non-enteric-coated budesonide, with its extensive first pass metabolism and relatively favorable side effect profile, is a potentially safe option in those who have EG affecting the ileocecum and right colon [2,78].

Fluticasone may be used as a topical alternative to systemic steroids in treating EE [79,80] presenting concurrently with EG.

Mast Cell Inhibitors

A limited number of case reports favor the use of oral disodium cromoglycate and ketotifen as treatment options in EG [81,82].

Antihistamines

Current evidence does not support the use of antihistamines (H-1 receptor antagonists) in EG, except in the patient who has concurrent environmental allergies.

Leukotriene Receptor Antagonists

Montelukast is a selective and competitive antagonist of leukotriene Cys-LT₁ receptors expressed on bronchial smooth muscle cells and eosinophils. It is therefore an attractive steroid-sparing option in EG, acting by blocking the inflammatory effects of eosinophils. Studies report mixed results in induction of clinical and histologic remission, however [33,83].

Biologic Therapies

Anti-interleukin-5 (mepolizumab)

Early experience with humanized monoclonal antibody against IL-5 are limited to a small number of patients who had hypereosinophilia syndrome and EE, but may be seen as encouraging for future application in EG [84,85].

Anti-IgE therapy (omalizumab)

Omalizumab is a humanized anti-IgE monoclonal Ab that has been shown to be effective in allergic asthma and allergic rhinitis. There is new evidence to support its use in EG. It was administered as a subcutaneous infusion every 2 weeks for eight doses in nine patients (12–76 years) who had EG. Omalizumab use was associated with decreased absolute eosinophil counts, a nonsignificant reduction in tissue eosinophilia, lowered IgE levels, and improved symptom scores [86].

Novel and Emerging Treatment Agents

Several new therapeutic options are under investigation. These anti-eosinophil agents include eosinophil selective adhesion molecules, a monoclonal eotaxin antibody (CAT-213), and agents to enhance eosinophil apoptosis [87–89].

Surgery

Surgery is sometimes necessary to relieve, and occasionally cure, symptoms in patients who have obstructive EG presentations [4,90]. Close postoperative follow-up and consideration of adjuvant medical or dietary therapy are important because of the potential for disease recurrence.

NATURAL HISTORY

There is a dearth of information about the long-term course of patients who have treated or untreated EG. Most experts regard primary EG as a chronic disorder characterized by relapses and remissions, and hence the recommendations for close follow-up and perhaps repeated endoscopic surveillance in selected cases. The natural history of EG has not been well described, but clinical studies point to a chronic relapsing course for patients who have this diagnosis. The long-term follow-up (2.5 to 5.5 years) of six children who had EG and protein-losing enteropathy initially treated successfully with an elemental diet has been described recently: despite some liberalization of the diet, clinical remission could be maintained only by continued dietary restrictions [8]. This study emphasizes the chronic nature of EG and the importance of long-term follow-up. Larger, prospective, multicenter studies are needed to investigate further the pathogenesis, safe and effective management options, natural history, and long-term outcome of patients who have EG.

SUMMARY

EG is an uncommon, yet important, entity in the spectrum of primary EGIDs, selectively affecting the stomach and small intestine with an eosinophilic inflammatory process. Multiple clinical presentations are recognized because of the variability in the location and depth of eosinophilic infiltration. History of atopy and allergies is present in 25% to 75% of cases. Recent investigations providing an insight into the pathogenesis of EG support a critical role for allergens, eosinophils, Th-2-type cytokines, and eotaxin-1 in mediating eosinophilic inflammation. The diagnosis is confirmed by demonstrating prominent tissue eosinophilia on histopathology. Treatment strategies include the use of

restricted diets, corticosteroids, leukotriene receptor antagonists, mast cell stabilizers, and antibodies against IL5 and IgE. Many unanswered questions remain with regard to the natural history, optimal duration of therapy, safer steroid-sparing long-term treatment agents, and the means of reliable and non-invasive follow-up.

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