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An Atypical Case of Eosinophilic Gastroenteritis Presenting as Hypovolemic Shock

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Key Words

Eosinophilic gastroenteritis · Hypovolemic shock · Diarrhea · Acute renal failure

Abstract

Eosinophilic gastroenteritis is an uncommon condition characterized by focal or diffuse infiltration of eosinophils in the gastrointestinal tract in the absence of secondary causes. The pathogenesis of this condition is not well understood and its clinical presentation depends on the segment and layer of the gastrointestinal tract affected. The definition of eosinophilic gastroenteritis may be difficult, as the normal ranges of eosinophil numbers in normal and abnormal gastric and intestinal mucosa are not standardized. We present the case of a 59-year-old male who came to the hospital with hypovolemic shock and lethargy secondary to severe diarrhea. Laboratory analysis was significant for peripheral eosinophilia, and pathology from both the duodenum and colon showed marked eosinophilic infiltration.

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Introduction

Eosinophilic gastroenteritis (EG) is a rare disease characterized by focal or diffuse eosinophilic infiltration of the gastrointestinal tract, in the absence of secondary causes like adrenal insufficiency, medication hypersensitivity reactions, collagen vascular disease, malignancy, hypereosinophilic syndrome or parasitic infection. In 2011, the prevalence of EG in

the United States was estimated to be 22–28 per 100,000 persons [1]. EG can affect patients of any age, but it is diagnosed most frequently in the third through fifth decade of life [2–4] and is reported to be more common in men [3]. This condition has been associated with a personal or family history of allergic disorders, such as asthma, hay fever or eczema, which are present in 60–70% of patients diagnosed with EG [5].

Evidence supports the concept that EG develops as a result of the interplay of genetic and environmental factors. Approximately 10% of patients who are diagnosed with EG have an immediate family member with this condition [6]. The pathogenesis of this disease has yet not be fully explained, however it is hypothesized to be a polygenic allergic disorder between immunoglobulin E (IgE) and delayed Th2 response, but not fitting completely into either category [7]. A variety of clinical and experimental models support the critical role for allergens, eosinophils, Th2-type cytokines and eotaxin-1 in mediating eosinophilic inflammation [7]. It is suggested that food allergens activate and drive the differentiation of IL-5+ Th2 cells, leading to gut eosinophilia [8, 9]. Furthermore, the presence of eotaxin enhances the recruitment of eosinophils into the gastrointestinal tract [9]. Once eosinophils are present in the gut, they are able to persist through the release of eosinophil-active cytokines, such as IL-3, IL-5 and granulocyte-macrophage colony-stimulating factor [10]. In addition to this, eosinophils cause local inflammation by releasing major basic proteins and cytotoxic cationic protein [5].

Patients with EG have a variety of problems, including nausea, vomiting, abdominal pain, diarrhea, weight loss and malabsorption [11–13]. These clinical manifestations may vary by the involved organ and by the layer of tissue targeted by the infiltrative process [2, 14]. The diagnosis is established by demonstrating eosinophilic infiltration on biopsies obtained on endoscopy, laparoscopy or laparotomy. Multiple biopsies may be required because of the patchy nature of the disease [15]. We present the case of a male patient with EG who presented with severe diarrhea, acute renal failure and hypovolemic shock.

Case Report

A 59-year-old male with a past medical history significant for obesity status post gastric bypass surgery, hypertension and hyperlipidemia was admitted to the hospital with multiple episodes of diarrhea for the last 6 days which had started in Australia prior to his arrival to New York City for his vacation. He described the diarrhea as large-volume and watery with more than 15 episodes per day, with no similar episodes in the past. There was no complaint of abdominal pain, fevers and chills and no evidence of mucus or blood in the stool. He denied any prior recent trip when he was in Australia. In addition to denying a personal or family history of colon or small bowel malignancy, he also denied consuming alcohol, smoking and illicit drug use. He had no known allergies and his home medications included only olmesartan and simvastatin. Before presenting to the hospital, he had been prescribed erythromycin for his diarrhea which he took for 2 days, and subsequently it had been switched to ciprofloxacin for 1 day without any relief.

On admission he was in hypovolemic shock, with hypotension and lethargy. His physical examination was notable for dry mucous membranes, whereas his cardiovascular, respiratory and gastrointestinal examination was unremarkable. He was found to have severe dehydration, electrolyte abnormalities and acute kidney insufficiency. His initial laboratory results were remarkable for a BUN of 56 mg/dl and a creatinine level of 7.30 mg/dl. His complete blood count was notable for white blood cells of 29,600/ μ l and hemoglobin of 17.8 gm/dl, platelets of 322,000/ μ l and eosinophilia of 14% (absolute eosinophil count 4.0).

His liver function panel showed mild hypoalbuminemia of 3.5 gm/dl (table 1, table 2). Additionally, the patient had negative white blood cells in his stools, four negative stool studies for ova and parasites and negative stool cultures. More specifically, *Vibrio cholerae* test and *Clostridium difficile* toxin were negative. His HIV test was nonreactive and thyroid-stimulating hormone, gastrin, somatostatin and vasoactive intestinal peptide levels were within normal limit.

During the hospital course his daily laboratory tests were remarkable for constant leukocytosis with eosinophil predominance (ranging between 14 and 31%). His IgE serum level was 1,534. He had an abdominal computed tomography scan that showed mild dilation and thickening of the proximal jejunum with incidental transient intussusceptions reflecting altered motility (fig. 1).

The patient received aggressive intravenous hydration with electrolyte repletion. His lethargy resolved and blood pressure improved. His kidney function significantly improved over the hospital course; however, he continued to have several episodes of watery diarrhea every day. On the third day of hospitalization he had a colonoscopy which showed a semi-sessile 15-mm polyp localized in the descending colon which was removed with a hot snare; the rest of the colon mucosa appeared to be normal, with no evidence of erythema or ulceration, and random biopsies were obtained. The patient also underwent esophagogastroduodenoscopy, which revealed a normal esophagus with vertically banded gastropasty, nodular gastroesophageal junction and erythematous mucosa in the pylorus (fig. 2, fig. 3).

The pathology report (fig. 4) demonstrated markedly increased eosinophils in the lamina propria (>40/high-power field [HPF]) of the duodenum, stomach and colon. The duodenal aspirate was negative for parasites. Subsequently, the diagnosis of EG was made. The diarrhea started to improve and resolved by day 10 of hospitalization; his kidney function returned back to normal. The treatment was mainly supportive care, consisting of intravenous fluids and electrolytes repletion. He was discharged on day 10 to resume the rest of his vacation.

Discussion

EG is a rare inflammatory condition which may affect the entire gastrointestinal tract from the esophagus to the colon and where eosinophils are present in excess of 20/HPF in either the mucosal, muscular or subserosal layers [2, 16]. The clinical manifestations depend on the affected region of the gastrointestinal tract [14]. For example, with gastric and colonic mucosal disease, the most common symptoms are abdominal pain, nausea, vomiting, early satiety and diarrhea [2]. In contrast, dominant duodenal disease may present with malabsorption, protein-losing enteropathy and failure to thrive. Additionally, the extent of invasion of the eosinophils into the various layers can affect presentation. For instance, eosinophilic invasion of the muscular layer causes muscular wall thickening and impaired motility causing intestinal obstruction, leading to nausea, vomiting and abdominal pain and, in severe cases, perforation or obstruction of the gastric outlet, small bowel or colon [2]. Patients with subserosal EG can suffer from isolated ascites, causing abdominal distention and discomfort. In our case, eosinophils were more predominant in the mucosa of the stomach, duodenum and colon, which usually manifests with diarrhea. In the abdominal computed tomography we visualized mild thickening and dilation of the jejunal folds; since jejunal and ileal biopsies are not routinely obtained on endoscopy, we do not know how much these gut segments contributed to the patient's presentation.

Severe diarrhea and gastrointestinal enteropathy have recently been recognized as an adverse effect of the angiotensin II receptor antagonist olmesartan [17, 18]. The first case series to describe an association included 22 patients with enteropathy refractory to standard therapy interventions but who responded to discontinuation of olmesartan. Similar to our case, those patients presented with severe diarrhea leading to hospitalization and hemodynamic deterioration. However, in those patients the pathology material revealed increased intraepithelial lymphocytes, villous atrophy and subepithelial collagen deposition most consistent with a sprue-like condition [17–20].

The pathogenesis of EG is not well understood. In general, patients with EG have elevated serum IgE and an allergy component has often been suggested as a possible etiology [21]. Several studies have shown an improvement in disease with changes in the patient's diet [22–25]. The hypothesis is that exposure of patients to foods they are allergic to can cause activation of interleukins that express allergen-specific T helper cells in EG, leading to intestinal eosinophilia [8].

Patient with EG may have various significant laboratory findings. Serum eosinophil counts are usually elevated, but can be normal in approximately 20% of patients, and counts are usually higher in patients with mucosal and subserosal EG [26]. D-Xylose test can be abnormal in mucosal EG because of carbohydrate malabsorption [14]. Additionally, patients with mucosal disease may present with hypoalbuminemia secondary to protein-losing enteropathy, associated with increased mucosal permeability [27]. Eosinophilic EG can also cause anemia due to impaired iron absorption when the duodenal mucosal layer is involved [27].

The diagnosis of EG is based on the presence of eosinophils in a gastrointestinal tract biopsy or ascitic fluid. Before suspecting a diagnosis of EG, other etiologies of eosinophilia need to be excluded, such as parasites (*Ancylostoma*, *Anisakis*, *Strongyloides*, *Toxocara*, *Trichiura* and *Trichinella*), medications (antimalarials, penicillins, cephalosporins, sulfonamides, tetracyclines, nitrofurantoin, angiotensin-converting enzyme inhibitors, antituberculosis therapies, anticonvulsants, nonsteroidal anti-inflammatory drugs, proton pump inhibitors, H₂ receptor antagonists and chlorpropamide) [28], dietary and herbal supplements, ingestions of raw or undercooked meat and a history of residing in or traveling to parasite-endemic areas. Stool and serologic studies should be collected and should include microscopy for ova and parasites and serologies for *Strongyloides* and *Toxocara* species, to exclude parasitic infections as a secondary cause of eosinophilic EG [2].

Endoscopically, mucosal disease can appear relatively nonspecific with nodularity, polypoid gastric mucosa, erythema or erosions, therefore the diagnosis is made histologically. Because of the nonspecific nature of mucosal disease, biopsies should be taken from both normal- and abnormal-appearing mucosa, as normal-appearing mucosa can also have eosinophilic infiltration [29]. The diagnosis of EG is made by the presence of more than the number of expected eosinophils seen on a random gastrointestinal tract biopsy [30]. While there is not a designated cutoff number of eosinophils to make a diagnosis, most reports have defined EG when there are >20 eosinophils/HPF [2, 31, 32]. However, an experienced gastrointestinal pathologist should always analyze the specimens to assess whether the number of eosinophils is greater than expected in the tissue biopsy [30]. Our patient had >40 eosinophils/HPF visualized in the lamina propria from the stomach, duodenum and colonic mucosa. Patients with mucosal biopsies who have excluded mucosal disease but still present with gastrointestinal symptoms may need to undergo laparoscopic full-thickness biopsy as mucosal biopsy alone cannot rule out muscular or subserosal EG [2, 14].

Initial treatment begins with diet modification in an attempt to eliminate potential food allergens [24]. If dietary changes do not improve symptoms or patients experience recurrent

symptoms or flares, a short to long course of prednisone should be initiated, depending on the severity of the patient's symptoms [33].

Author Contributions

M. Martillo and M. Herman wrote the manuscript; J. Abed and P.K. Mankal reviewed and edited the manuscript; K. Munot provided the esophagogastroduodenoscopy/colonoscopy images; E. Abed edited the images and contributed to the manuscript; W. Shi provided the pathology images; R. Gurunathan, G. Ionescu and D.P. Kotler reviewed the manuscript.

Statement of Ethics

The patient gave his verbal consent for publication of this case report. It is documented in his electronic medical record.

Disclosure Statement

The authors have no conflicts of interest or financial disclosures to report.

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Table 1. Laboratory results: chemistry and hematology

	Reference range	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
<i>Chemistry</i>								
Sodium	136–146 mmol/l	138	143	144	139	142	142	136
Potassium	3.5–5.1 mmol/l	3.4	3.5	3.7	3.0	4.0	3.6	3.7
Chloride	98–107 mmol/l	111	112	113	113	114	114	108
CO ₂	22–30 mmol/l	14	21	19	20	21	20	21
BUN	8–24 mg/dl	50	46	31	17	10	7	7
Creatinine	0.66–1.25 mg/dl	5.7	4.20	2.10	1.30	1.10	1.00	1.00
Glucose	74–106 mg/dl	95	94	84	79	74	73	69
Est. GFR		10	15	32	57	69	76	76
Anion gap	7–16 mmol/l	13	10	12	6	7	8	7
Magnesium	1.6–2.3 mg/dl	2.0	1.9	1.9	–	1.7	1.6	1.6
Calcium	8.4–10.3 mg/dl	7.4	8.0	8.2	7.9	8.5	8.3	8.4
Phosphorus	2.5–4.5 mg/dl	10.2	4.6	–	–	–	2.9	–
<i>Endocrinology</i>								
TSH	0.55–4.78 mIU/ml							1
Gastrin	≤100 pg/ml							74
VIP	20–42 pg/ml							36
<i>Hematology</i>								
WBC	3.9–9.8 K/μl	26.9	19.7	22.5	20.1	19.4	19.3	16.1
Hemoglobin	13.0–17.0 g/dl	14.9	13.9	14.1	12.7	12.8	12.2	12.9
Hematocrit	38.0–51.0%	43.9	41.4	41.1	38.5	38.5	36.2	38.7
Platelet count	150–450 K/μl	264	246	233	212	225	196	174
RBC	4.20–5.60	4.86	4.53	4.49	4.22	4.15	3.94	4.10
Basophils automated	0.1–1.4%	0.4	0.5	0.6	0.3	0.4	0.7	0.9
Eosinophils automated	0.7–8.0%	14.9	20.1	19.5	25.7	26.4	31.2	21.1
Lymphocytes automated	18.0–44.0%	16.4	20.1	22.9	22.6	22.0	21.5	20.8
Monocytes automated	4.0–9.0%	3.8	3.8	5.5	4.2	4.2	4.0	4.3
Neutrophils automated	40.0–74.0%	64.5	55.5	51.5	47.2	47.2	42.6	52.9
Sedimentation rate	0–13 mm/h			7				

Bold values indicate markedly elevated eosinophils seen in eosinophilic gastroenteritis.

Table 2. Laboratory results: immunology

Immunology	Reference range	Serum values
IgA, serum	70–400 mg/dl	271
IgM, serum	40–230 mg/dl	54
Gliadin Ab IgG	<20 U	2
Gliadin Ab IgA	<20 U	4
IgE, serum	≤114,000 U/l	1,534
IgG subclass 4	4.0–86.0 mg/dl	80.9
IgG subclass 3	22–178 mg/dl	15
IgG subclass 2	241–700 mg/dl	366
IgG subclass 1	382–929 mg/dl	519
TTG Ab IgA	<4 U/ml	1

Bold values indicate elevated IgE seen in eosinophilic gastroenteritis.

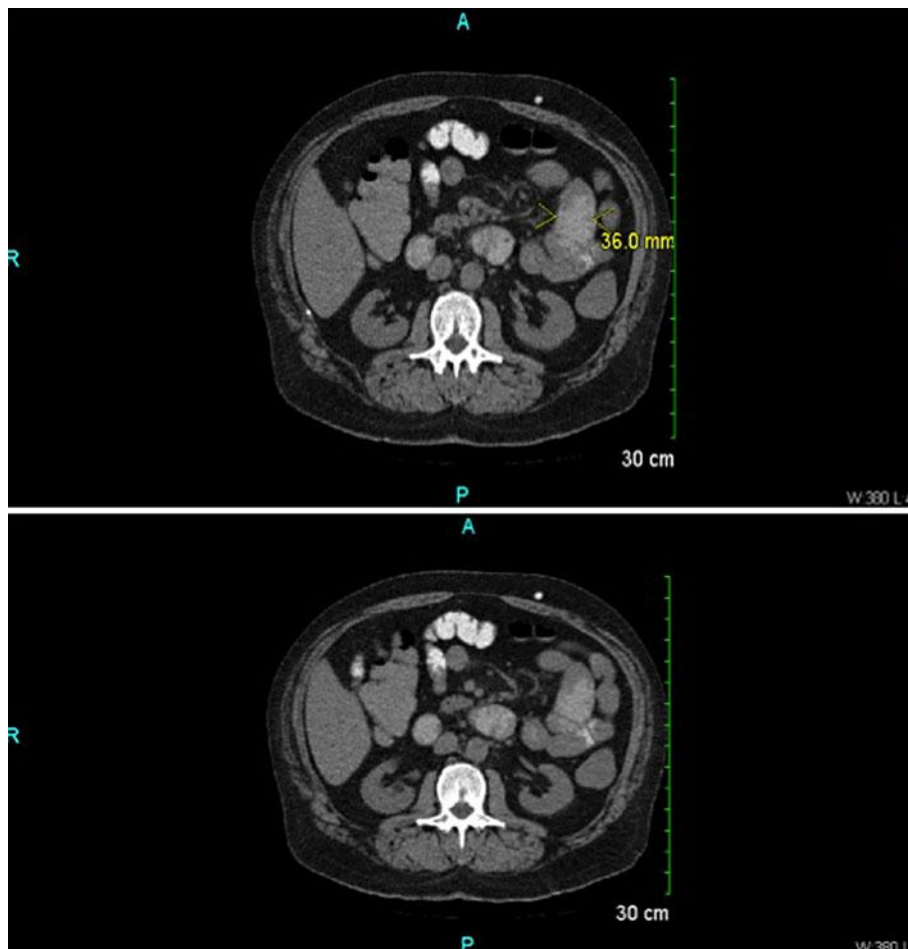


Fig. 1. Proximal jejunal dilation (up to 36 mm in diameter) and mucosal thickening and possibly transient intussusception in the proximal jejunum (nonobstructing).

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Fig. 2. Normal colon mucosa with no evidence of erythema or ulceration.



Fig. 3. Erythematous mucosa in the pylorus of the stomach.

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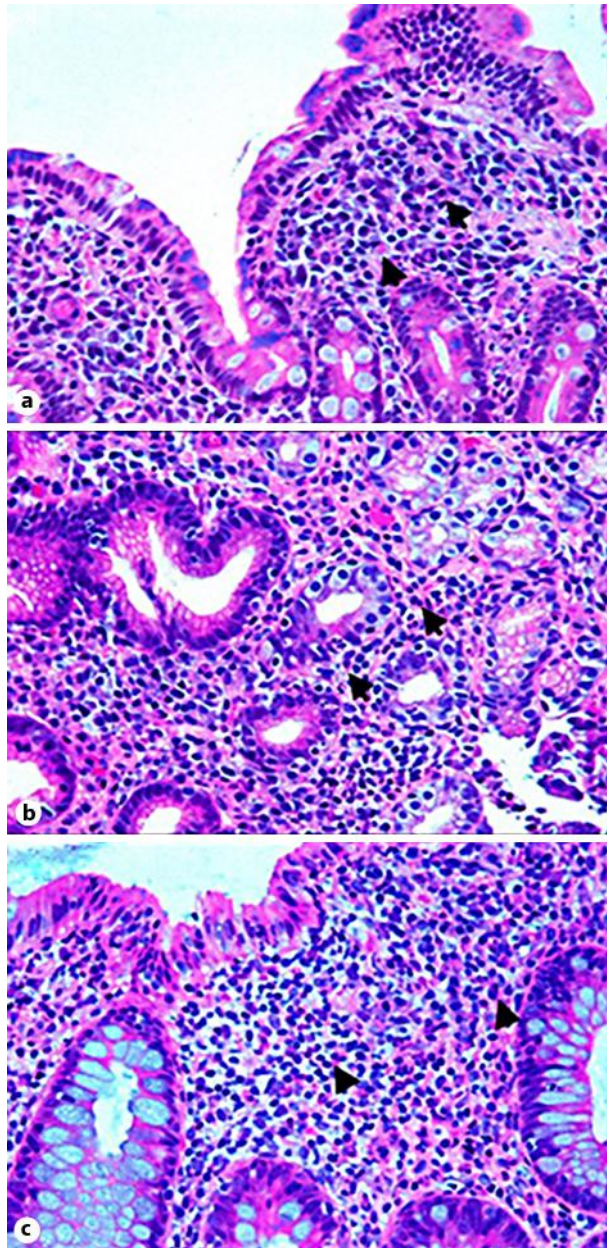


Fig. 4. Markedly increased eosinophils (arrows) in the lamina propria of the duodenum (a), stomach (b) and colon (c) (hematoxylin and eosin; magnification $\times 400$).