

Simultaneous Mucosal and Subserosal Eosinophilic Gastroenteritis: A Rare and Severe Presentation

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Eosinophilic gastroenteritis (EG) is a rare condition of undetermined cause that is characterized by peripheral eosinophilia, infiltration of the gastrointestinal tract by eosinophils, and gastrointestinal symptomatology.^{1,2} In EG, eosinophilic infiltration of the gastrointestinal tract is frequently confined to specific layers of the gut wall. This article reports a severe case of EG that involved multiple layers of the gastrointestinal tract (both mucosal and subserosal) as well as several organs, making this particular presentation unusual. This article also reviews the clinical features, diagnosis, and management of EG.

CASE PRESENTATION

Initial Presentation and History

A 20-year-old Hispanic man in apparent good health presented to the emergency department with a 6-week history of a burning sensation in the upper abdomen, nausea, and loose nonbloody stools. He denied vomiting, fever, joint pains, gastrointestinal bleeding, weight loss, or other symptoms. Two weeks prior to presentation, the patient began to notice gradual swelling of his abdomen. The only history of travel outside the United States occurred 2 months previously when he traveled to Mexico. Past medical history revealed no previous hospitalizations or history of asthma, allergic rhinitis, atopic dermatitis, food allergy, or similar symptoms in the past.

Physical Examination

Initial physical examination revealed a well-appearing young man who appeared comfortable but voiced concern about his abdominal distention. The patient was afebrile, with nonicteric conjunctivae, no lymphadenopathy, and a normal cardiopulmonary examination.

His abdomen was moderately distended, with moderate ascites confirmed by a positive fluid wave. He had no peritoneal signs and no focal areas of tenderness to deep palpation. Extremity examination revealed no edema or any joint tenderness or swelling. The remainder of the physical examination was unremarkable.

Laboratory and Imaging Studies

The patient's complete blood count revealed an elevated white blood cell (WBC) count of 21,000/ μ L (normal, 4500–11,000/ μ L) with marked eosinophilia of 66% and an absolute eosinophil count of 14,000/ μ L (normal, 0%–1% and < 350/ μ L, respectively). Peripheral blood smear revealed marked mature eosinophilia, and liver function tests revealed decreased total protein (5.8 g/dL [normal, 6.0–8.0 g/dL]) and decreased albumin (3.1 g/dL [normal, 3.5–5.0 g/dL]). Diagnostic paracentesis was performed, and the patient was administered empiric intravenous ceftriaxone due to concern for possible spontaneous bacterial peritonitis. Fluid obtained from the paracentesis was yellow in color with a WBC count of 31,200/ μ L, a red blood cell count of 6750/ μ L, markedly elevated eosinophils (93%), and decreased polymorphonuclear neutrophils (2%), lymphocytes (3%), and histiocytes (2%). Analysis of the paracentesis fluid revealed a lactate dehydrogenase level of 171 U/L, protein level of

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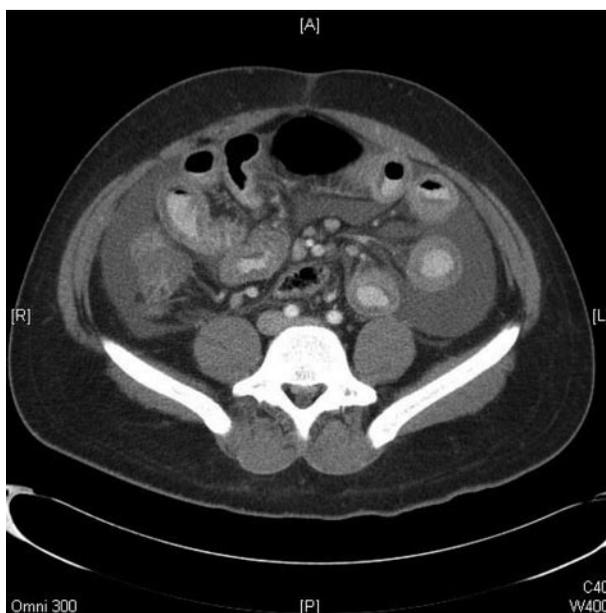


Figure 1. Computed tomography scan of abdomen demonstrating diffuse thickening of the entire small bowel and ascites.

4.3 g/dL, and glucose level of 70 mg/dL. The fluid was negative for malignant cells or acid-fast bacilli. Once spontaneous bacterial peritonitis was ruled out, ceftriaxone was discontinued and the patient was managed conservatively with medications as needed for nausea. Computed tomography (CT) imaging of his abdomen was performed with and without intravenous contrast and demonstrated a moderate amount of ascites and diffuse concentric bowel wall thickening involving the entire small bowel, with the large bowel largely unaffected (**Figure 1**). No obstruction was seen on the CT scan, and the other intra-abdominal organs were felt to be unremarkable in appearance.

Consultation and Diagnosis

Gastroenterology was consulted given the CT findings. The patient then underwent esophagogastroduodenoscopy (EGD) and colonoscopy, both with multiple biopsies. EGD revealed a normal esophagus and proximal stomach as well as raised erythematous patches of mucosa predominantly in the distal gastric antrum and the proximal duodenum without frank ulceration or mucosal breaks (**Figure 2**). The colonoscopy revealed a diffusely inflamed and erythematous terminal ileum, a patulous, inflamed ileocecal valve, and right-sided colonic mucosal erythematous patches similar to that seen in the stomach and duodenum (**Figure 3**). Esophageal biopsy results were unremarkable. Evaluation of gastric, small bowel, and large



Figure 2. Endoscopic appearance of the stomach. Note diffuse, raised erythematous patches of mucosa predominantly seen in the gastric antrum without frank ulceration or mucosal breaks.

bowel biopsy specimens revealed diffuse infiltration of eosinophils and multifocal chronic inflammatory infiltrates in the antrum, duodenal bulb, terminal ileum, and colon (**Figure 4**). Biopsy specimens were negative for fungi or parasites. Four stool cultures were completed over 3 days and were negative for ova or parasites. Given the history, physical examination, laboratory, imaging, endoscopy, and pathologic findings, the patient was diagnosed with severe EG.

Management

Oral prednisone 40 mg daily for 2 weeks was initiated, to be followed by a rapid taper over 2 weeks. The patient's nausea resolved once he was placed on nothing-by-mouth status and prednisone was instituted. Diet was slowly reintroduced over several days from clear fluids through regular food without recurrence of nausea. The patient felt less fatigued over several days and was discharged on hospital day 6 with instructions to follow-up at the family medicine clinic. Despite his initial improvement, his abdominal distension did not change during his hospitalization.

The patient was seen at the family medicine clinic 4 weeks after discharge, coincident with the completion of his steroid taper. He reported complete resolution of his abdominal distention and abdominal burning. Likewise, his stools were normal in caliber and consistency and he remained free of nausea. His physical examination was normal, showing neither evidence of ascites nor abdominal tenderness. Complete blood count with differential obtained at this time showed 6400 WBCs/ μ L, with 53% neutrophils, 32% lymphocytes, 8% monocytes,

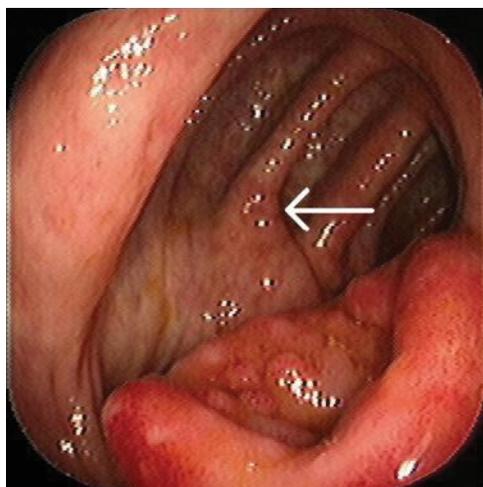


Figure 3. Endoscopic appearance of the cecum. Note inflamed, patulous ileocecal valve in foreground and patchy erythema on cecal mucosa (arrow).

1% basophils, and 6% eosinophils (absolute eosinophil count, 384/ μ L). Total protein was 6.7 g/dL with serum albumin of 4.2 g/dL. Repeat CT of the abdomen with and without contrast showed resolution of the ascites, although the patient did have some residual small bowel wall thickening. He has done well for 1 year thereafter and has remained asymptomatic.

EOSINOPHILIC GASTROENTERITIS

Clinical Features and Diagnosis

EG is a rare condition of unknown etiology characterized by peripheral eosinophilia, eosinophilic infiltration of the gastrointestinal tract, and gastrointestinal symptomatology.^{1,2} It is generally classified according to the layers of the gastrointestinal tract that are involved. EG was subdivided into predominant mucosal layer disease, predominant muscle layer disease, and predominant subserosal disease by Klein and colleagues in 1970.³ The frequency of involvement of each layer varies, but retrospective studies show that mucosal EG is most common (25%–60%), followed by muscular layer EG (13%–37%) and subserosal EG (13%–40%).^{4–6} EG can have a varying clinical presentation depending on the layer that is involved.⁷ Mucosal involvement may result in abdominal pain, nausea, vomiting, diarrhea, weight loss, anemia, protein-losing enteropathy, and intestinal perforation. Patients with muscular layer disease generally have obstructive symptoms. Subserosal eosinophilic infiltration may result in the development of eosinophilic ascites.¹ The case patient had features of both mucosal and subserosal EG, which is highly unusual.

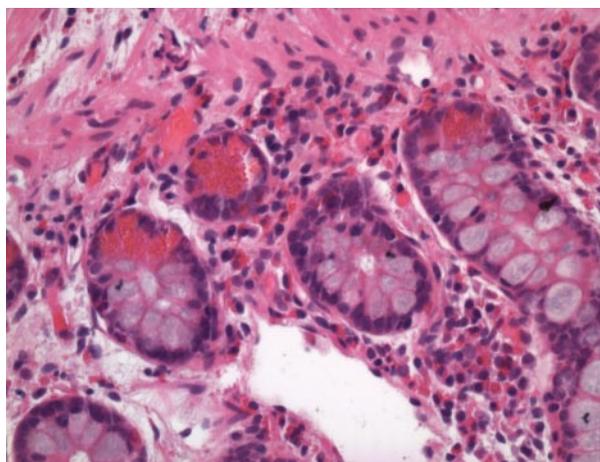


Figure 4. Specimen from the terminal ileum showing moderate to severe eosinophilic infiltrate in the lamina propria consistent with eosinophilic gastroenteritis (hematoxylin and eosin, 400x).

Common presenting symptoms of EG include episodic abdominal pain (77%–100%), diarrhea (42%–62.5%), vomiting (33%–62.5%), and nausea (50%–67%).^{4,5,8,9} The stomach was the most common site of involvement (43%), although 36% of patients were found to have 2 or more sites of disease at the time of presentation.⁸ Ultrasound and CT scans may reveal the characteristic thickening of the intestinal wall.^{4,10,11} The most common CT finding is nodular and irregular fold thickening in the distal stomach and proximal small bowel; it is this characteristic involvement of only the gastric antrum and proximal small bowel that suggests the diagnosis of EG.¹⁰ The gold standard for diagnosis, usually demonstrated on endoscopic biopsies, is prominent tissue eosinophilia consisting of more than 20 eosinophils per high-power field on microscopic examination.^{1,2,7,12} The diagnosis can sometimes be obscured by the patchy nature of the disease. In some cases, full-thickness biopsies are required to arrive at a definitive diagnosis.²

In the case patient, the presenting symptoms were abdominal distention as well as upper abdominal pain, nausea, vomiting, and diarrhea. The biopsies from his EGD and colonoscopy revealed marked eosinophilia, which was also found in his ascitic fluid. CT imaging showed extensive small bowel involvement, with bowel wall thickening from the level of the antrum to the cecum and the large bowel seemingly spared, although colonoscopy ultimately demonstrated mucosal changes in the proximal colon. As mentioned, the case patient demonstrated symptoms of both subserosal and mucosal involvement, which is an unusual and rare presentation.^{1,13} There have been several case reports of EG presenting with eosinophilic ascites and peripheral

eosinophilia. Full-thickness biopsies from the gastrointestinal tract of these patients revealed intense eosinophilic infiltration involving both muscular and serosal layers and extending from the stomach to the ileum.¹⁴ Patients with uncomplicated ascites should undergo a paracentesis for diagnosis. Paracentesis often reveals exudative fluid rich in eosinophils, as was seen in the case patient.^{15,16}

In EG, eosinophilic intestinal inflammation also occurs secondarily in the gastrointestinal tract in inflammatory bowel disease, autoimmune diseases, reactions to medications, infections, and hypereosinophilia syndrome (HES) and after solid organ transplantation.¹⁷ EG may be confused with irritable bowel syndrome or dyspepsia and, rarely, mimics pancreatitis or appendicitis.⁷ The differential diagnosis for patients with presenting complaints similar to the case patient's would include parasitic infections (which could also elevate the peripheral blood eosinophil count) as well as inflammatory bowel disease (which could produce both small and large bowel wall thickening on CT scan). Crohn's disease could produce small and large bowel wall changes, while ulcerative colitis would produce predominately large bowel findings on imaging studies. Ascites would be uncommon with either Crohn's disease or ulcerative colitis. Idiopathic HES is a condition of sustained hypereosinophilia that affects multiple organs including the lung, skin, blood vessels, and nervous system. HES can produce gastrointestinal symptoms through thrombosis and should be considered in patients with abdominal pain and hypereosinophilia. Lastly, a variety of medications and malignancies can produce eosinophilia and abdominal pain as side effects.

Treatment

Most patients will improve with administration of oral steroids regardless of the intestinal layer involved.^{4,5,8,14–16,18,19} Short courses of corticosteroids are the mainstay of treatment, although some patients with relapsing disease require long-term low-dose steroids.⁵ Up to 90% of patients with EG reported rapid clinical improvement with institution of steroid therapy.⁸ Patients with mild and sporadic symptoms can be managed with reassurance and expectant observation.^{1,12} Patients with disabling symptoms can be effectively treated with corticosteroids after other systemic disorders associated with peripheral eosinophilia have been excluded.¹

Data on steroid-sparing treatment regimens for EG are limited but encouraging. Sodium cromoglycate, a mast cell stabilizing agent, has been used in case reports to treat EG with good results.^{20,21} Specific

food allergies have been implicated in some patients (eg, milk, fish) and can be treated with modified or simplified diets.²² Reports of favorable responses to leukotriene inhibitors in patients with EG have been published.²³ Promising new drugs for EG also include suplaxast tosilate, a selective Th2 cytokine inhibitor with inhibitory effects on allergy-induced eosinophilic infiltration and IgE production.⁷ Questions regarding the natural history of EG; optimal duration of therapy; safer steroid-sparing long-term therapeutic agents; and the means of reliable and noninvasive follow-up require further investigation.¹⁷

CONCLUSION

This article presents the case of a young man who developed symptoms of both mucosal and serosal EG with striking laboratory, imaging, and pathologic features. His extensive small bowel involvement was quite impressive, and is unusual. EG should be suspected in a patient with abdominal pain and nausea presenting with ascites and peripheral eosinophilia. This case underscores the well-documented dramatic response of even severe EG to systemic steroid therapy with the complete resolution of the patient's ascites and serum eosinophilia, emphasizing the need for accurate diagnosis. **HP**

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