A Man With Diarrhea And Achalasia

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A 78 y/o male with an extensive history of CAD s/p multiple MIs and CABG surgery, presents with two and one half weeks of diarrhea. About 9 weeks prior, he had been diagnosed with achalasia, and was treated with a botulinum toxin injection, with resolution of his symptoms of dysphagia. He was also hospitalized a month ago after experiencing chest pain, and subsequently ruled in for a small non-ST elevation MI. He underwent coronary catheterization at that time, and was found to have severe multivessel disease unamenable to PTCA or bypass surgery. Now, he presents with progressively frequent "brown watery" diarrhea for the past couple of weeks, reporting up to 20 episodes a day, occurring also at night and causing episodes of fecal incontinence. He denies blood in his stools, or recent antibiotic use. Diarrhea is associated with abdominal cramping, and is not relieved with Lomotil taken every 8 hours. During this period, the patient also notes several episodes of non-bloody, non-bilious emesis, the last occurring one day ago, with an inability to tolerate po intake and a 10 lb weight loss over the two weeks. He denies recurrent dysphagia, fevers or chills, recent travel, heat intolerance, or palpitations. He had a routine screening colonoscopy 6 years ago that was reportedly 'normal'.

Past medical history includes multivessel coronary artery disease status post 3 vessel bypass surgery in 1998, chronic renal insufficiency with a baseline Cr of 1.7, and newly diagnosed achalasia.

His present medications include lisinopril, diltiazem, metoprolol, isosorbide mononitrate, aspirin, atorvastatin, clopidogrel, pantoprazole, and sublingual nitroglycerine as needed He has no known drug allergies or food intolerances.

Family history is significant for a father who died of an unspecified ileitis, and a paternal uncle with Crohn's disease. The patient smoked 5-6 cigars a day for 45 years. He lives with his wife at home and often babysits his healthy 5 y/o grandson.

Vital signs include a temperature of 97.9 degrees, respirations 12 per minute, 99% saturation on room air, supine BP 90/50 and HR 68, and standing BP 80/50 and HR 68,. Physical examination reveals a thin male in no acute distress. Dry mucus membranes are noted, with flat neck veins, a normal cardiac exam, and lungs clear to auscultation. He has normoactive bowel sounds, a non-tender, non-distended abdomen without organomegaly. On rectal exam, he was found to have heme negative brown stool in the vault with good rectal tone. There was no evidence of peripheral edema and he was neurologically intact.

Laboratory tests obtained on admission are shown in tables 1 and 2.

Table 1. **Admission Hematology Labs**

White cells (per mm3)	11,300
Differential count (%)	
Neutrophils	54
Lymphocytes	17
Monocytes	6
Eosinophils	22 (0-6)
Basophils	1
Hemoglobin (g/dL)	14
Hematocrit (%)	40.8
Platelet (B/L)	193
ESR (mm/hr)	17 (0-15)
PTT (sec)	29
INR	1.13
PT (sec)	14.4

Table 2. **Admission Blood Chemistry**

Sodium (mmol/L)	133
Potassium (mmol/L)	4.6
Chloride (mmol/L)	101
Bicarbinate (mmol/L)	22
BUN (mg/dL)	60
Creatinine (mg/dL)	3.5
Total protein (g/dL)	5.8(6.0-8.5)
Albumin (g/dL)	4.5
Total bilirubin (mg/dL)	1.0
Direct bilirubin (mg/dL)	0.3
Alk Phos (IU/L)	104
AST (IU/L)	20
ALT (IU/L)	27

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Table 3. **Stool Studies**

Sodium (mmol/L)	88 (135-146)
Potassium (mmol/L)	42.2(3.5-5.0)
Chloride (mmol/L)	77(98-109)
C.diff	Negative x3 sets
Fecal leukocytes	Negative x2
Stool ova and parasite	Negative x2
Stool giardia antigen	negative

Hospital Course

Given the patient's recent hospitalization, he was initially started on oral metronidazole for the possibility of Clostridum difficile colitis, and rehydrated. Creatinine corrected to baseline over the next several days. Stool studies were performed, with results detailed in table 3.

Metronidazole and loperamide resulted in significant improvement of diarrhea, with bowel movements decreased to 6 episodes daily. When metronidazole was discontinued after negative C diff specimens, the patient again clinically worsened. A diagnostic flexible sigmoidoscopy was performed, which was essentially normal. Upper endoscopy for evaluation of the small bowel was then done, which showed the esophagus was mildly dilated, consistent with the patient's history of achalasia. Nonerosive gastritis was also visualized. Multiple biopsies were taken of antrum and duodenum. Pathology several days later revealed eosinophilic infiltration consistent with a diagnosis of eosinophilic gastroenteritis. H pylori stains were negative.

The patient was subsequently started on oral prednisone, with rapid resolution of both his diarrhea and peripheral eosinophilia.

Discussion

Eosinophilic gastroenteritis is an uncommon disease characterized by eosinophilic infiltration of the gastrointestinal tract. Diagnosis of eosinophilic gastroenteritis requires the following criteria: (i) presence of gastrointestinal symptoms, (ii) eosinophilic infiltration of one or more areas of the GI tract on biopsy, (iii) organs outside the GI tract must be free of eosinophilic infiltration, and (iv) parasitic infestation must be absent.[1] A slight male predominance has been reported, with patients typically presenting in the third through fifth decades of life.[1] Though any segment of the gastrointestinal tract may be affected, the stomach or small bowel are most commonly involved.[1,2]

Eosinophilic gastroenteritis is classified according to the layer of bowel wall affected.[3] Patients with mucosal layer disease present with protein-losing enteropathy, fecal blood loss, and malabsorption. Muscle layer disease may lead to obstruction, while subserosal involvement leads to eosinophilic ascites.[3] However, clinical and pathologic features may overlap, with involvement of multiple layers of the gut wall.[2] In one series, abdominal pain was the most frequently recorded symptom (100%), followed by diarrhea (62.5%), vomiting (62.5%), and nausea (50%).[3] Of note, as seen in our reported patient, isolated esophageal involvement may cause a variety of manometric abnormalities, including achalasia.4 About half of patients have a personal or family history of allergic disease, and half report a history of food intolerance or allergy.[2]

Peripheral eosinophilia is found in about 80% of patients, though the presence of peripheral eosinophilia is not a diagnostic criterion.[1,2] Iron deficiency anemia can develop.[1] The serum albumin level may be low in 20-30% of cases, mostly with mucosal disease.[1] The erythrocyte sedimentation rate may be normal to moderately elevated.[1]

Stool studies should be done to exclude parasitic infestation. Charcot-Leyden crystals may be seen on a stool wet mount examination.[2] Though stool may be positive for occult blood, this finding is variable.[2] The radiographic changes found in eosinophilic gastroenteritis are nonspecific, and in at least 40% of cases, are completely absent.[5]

Endoscopic findings also vary, including prominent mucosal folds, hyperemia, ulceration, or nodularity.[6] The distribution of disease tends to be patchy, and for this reason, multiple biopsies (at least six) should be taken, if eosinophilic gastroenteritis is suspected.[1]

Histologically, eosinophilic gastroenteritis is characterized by an inflammatory cell infiltrate comprised almost entirely of eosinophils.[7] It should be noted, however, that eosinophilic infiltration is the most consistent histologic finding found on biopsy in gastroesophageal reflux as well.[8] In cases where there is a question whether eosinophilic infiltration represents eosinophilic esophagitis or gastroesophageal reflux,the location may be a clue, with more proximal locations favoring eosinophilic esophagitis.[2] Table 4 outlines some of the important clinical and laboratory features of eosinophilic gastroenteritis.

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Table 4. **Features Consistent with Eosinophilic Gastroenteritis**

Mucosal layer disease
Pain, nausea, vomiting, diarrhea, weight loss
Iron deficiency anemia
Malabsorption
Protein-losing enteropathy
Muscle layer disease
Obstruction
Subserosal layer disease
Eosinophilic ascites
Peripheral eosinophilia 80%
Eosinophilic infiltration of GI tract on biopsy
Low serum albumin 20-30%
ESR normal to moderately increased
Negative stool studies for parasites
Stool positive for occult blood (variable)
Charcot-Leyden crystals on stool exam (unknown frequency)

Parasitic infections are characteristically associated with peripheral eosinophilia and should be ruled out. The hookworm A. caninum as well as the pinworm Enterobius vermicularis may cause eosinophilic colitis.[2] Giardia lamblia can be associated with jejunal infiltration with eosinophils, though peripheral eosinophilia is usually absent.[2] The consumption of raw fish may lead to infection with Anisakis.[2] Other parasites which may be considered include T. stercoralis, Trichinella spiralis, and Schistosomiasis.

Various drugs including azathioprine, gemfibrozil, carbamazepine or clofazimine may cause diarrhea and peripheral eosinophilia.[2] Vasculitic disorders may mimic eosinophilic gastroenteritis, including Churg-Strauss syndrome, typically seen in patients with a history of asthma, and polyarteritis nodosa, typified by peripheral eosinophilia in association with multisystem involvement including the kidney, lung, nervous system or skin.[2]

Other diagnostic considerations may include Crohn's disease, cancer, and hypereosinophilic syndrome. Histologic features should clearly separate Crohn's disease from eosinophilic gastroenteritis.[2] Gastric infiltration of eosinophilis may be striking in gastric adenocarcinoma, though peripheral eosinophilia is unusual.[2] In hypereosinophilic syndrome, persistent peripheral eosinophilia is associated with infiltration of multiple organs including bone marrow, heart, lung liver, spleen kidneys, skin, and central nervous system.[2] Table 4 outlines other disoders which may mimic eosinophilic gastroenteritis

Table 4. **Differential Diagnosis for Eosinophilic Gastroenteritis**

Parasitic infections
Vasculities
Inflammatory bowel disease
Hypereosinophilic syndrome
Drugs
Cancer (specifically gastric adenocarcinoma)

Steroids are the mainstay of therapy for eosinophilic gastroenteritis, and clinical response is usually dramatic.[1] In approximately 50% of cases, low dose prednisone therapy may be required to maintain remission.[2] Other therapies, including sodium cromoglycate, have been reported to be effective.[2] In patients who have traveled to, or live in areas that put them at high risk for parasitic infection, a trial of antimicrobial therapy such as mebendazole may be considered, prior to initiating steroids, since parasitic infection may be difficult to rule out.[2] Once recognizably diagnosed, eosinophilic gastroenteritis has a good prognosis without associated risk of cancer.[1]

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