

Case Report

Evanescent eosinophilic gastritis in recurrent *Helicobacter pylori* infection

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Abstract

Eosinophilic gastroenteritis is characterized histologically by eosinophilic infiltration of the gut wall and clinically manifests by gastrointestinal (GI) symptoms. A high index of suspicion is required for the early diagnosis of this uncommon disease in patients who have concomitant GI symptoms and peripheral eosinophilia. This unusual case who initially had duodenal ulcer with duodenal stenosis, responded to *Helicobacter pylori* treatment and dilatation. He was symptom free for 2 years. Subsequently, developed evanescent eosinophilic gastritis and recurrent *H. pylori* infection with refractory prepyloric ulceration, but no duodenal stenosis. Eosinophilic gastritis and *H. pylori* infection initially responded to treatment, but subsequently the patient developed nonhealing prepyloric ulcer and refractory *H. pylori* infection and had persistent symptoms; all these necessitated surgical intervention consisting of antrectomy with gastrojejunostomy.

Key words

Antrectomy, duodenal stenosis, duodenal ulcer, eosinophilic gastroenteritis, *H. pylori*, refractory *H. pylori* infection

Introduction

Helicobacter pylori play a role in the pathogenesis of a number of diseases ranging from asymptomatic gastritis to gastric cancer and is one of the main causes of gastroduodenal diseases, such as chronic gastritis and peptic ulcer. Inflammatory response is pivotal in the epithelial dysfunction and mucosal injury caused by *H. pylori*. It leads to increased production of many mucosal proinflammatory and immunoregulatory cytokines.^[1,2] Eosinophils are involved in a broad range of diseases such as allergic, inflammatory, and malignant disorders.^[3-5] They are present only in small numbers in healthy gut mucosa. Eosinophilic gastroenteritis is characterized by eosinophilic infiltration of the gastric and intestinal mucosa and peripheral

eosinophilia. Clinical presentations widely vary depending on the site, extent, and depth of bowel wall involvement depends on the region of the GI tract involved and the depth of bowel wall involvement and usually runs a chronic relapsing course.

Case Report

A 42-year-old man presented with a 2-month history of epigastric burning pain and occasional postprandial vomiting. There was no history of nonsteroidal anti-inflammatory drug (NSAID) ingestion. His past medical history was insignificant. He did not smoke or drink alcohol. Physical examination revealed only mild diffuse epigastric tenderness. Laboratory evaluation revealed hemoglobin level of 10.8 g/dl, white blood cells count of 9,600 cells/mm³ (normal 4,000-10,000) with an eosinophilic count of 288 cells/mm³ (normal 0-800), and a normal platelet count (187,000/mm³). The upper gastrointestinal (GI) endoscopy showed a clean-based ulcer 1 × 1 cm at the junction of first and second part of the duodenum with narrowing at the junction of first and second part of the duodenum, but the endoscope was negotiable across the narrowing. Rapid urease test for *H. pylori* was positive. Patient was given triple drug therapy consisting of pantoprazole, amoxicillin, and

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clarithromycin for *H. pylori* for 14 days. He presented 2 months later with epigastric pain and postprandial vomiting. Repeat upper GI endoscopy showed narrowing at the junction of first and second part of the duodenum and scope could not be negotiated across it. Duodenal dilatation was done with Through-The-Scope (TTS) balloon. Rapid urease test for *H. pylori* was negative. After dilatation, the patient remained asymptomatic for 2 years. Two years later he presented with severe epigastric pain. At this point of time, upper GI endoscopy showed prepyloric clean-based ulcer 1 × 1 cm with positive rapid urease test. Antral biopsies showed inflammatory infiltrate with 30 eosinophils per high power field [Figures 1 and 2]. Complete blood count showed total leukocyte count 14,500/mm³ with 28% eosinophil count. Patient was started on triple drug therapy consisting of pantoprazole, amoxicillin, and clarithromycin for *H. pylori*. Patient remained symptomatic and repeat endoscopy 2 months later showed persistent prepyloric ulcer with no sign of healing. Repeat rapid urease test was still positive. Biopsies were taken from the antrum as well as from the ulcer margin. Complete blood count showed hemoglobin 11.2 g/dl and total leukocyte count 9,500/mm³ with 3% eosinophils. Antral biopsies showed few polymorphonuclear cells with no eosinophils and the biopsies from the ulcer margin were negative for the malignancy. This time the patient was put on quadruple therapy for *H. pylori* for 10 days consisting of bismuth subsalicylate, metronidazole, tetracycline, and pantoprazole. One month later, upper GI endoscopy showed no change in the size of the prepyloric ulcer with positive rapid urease test. He was now put on rescue treatment for *H. pylori* consisting of levofloxacin, amoxicillin, and pantoprazole for 10 days. On follow-up endoscopy, ulcer in the prepyloric site was persistent with no sign of healing and positive rapid urease test. As patient had persistent symptoms with nonhealing prepyloric ulcer and refractory *H. pylori* infection, therefore, a decision for surgical management was taken. Patient underwent antrectomy with gastrojejunostomy. Surgical biopsy specimen [Figure 3] showed fibrosis with few inflammatory infiltrates and the presence of *H. pylori*. On follow-up, the patient is asymptomatic with weight gain. Although no confirmed association between *H. pylori* gastritis and eosinophilic gastroenteritis can be documented in the literature, our case shows that *H. pylori* may play a pathogenic role in the development of blood eosinophilia and eosinophilic gastroenteritis.

Discussion

H. pylori is the most common bacterial infection worldwide. It is estimated that 60% of the world's population is infected by this microorganism. *H. pylori* is generally acquired in childhood and causes lifelong chronic gastritis unless initial acute gastritis is adequately managed.^[6] Antral biopsies of individuals infected with *H. pylori* show focal epithelial cell damage as well as an inflammatory infiltrate in the lamina propria. This infiltrate consists of polymorphonuclear leukocytes, eosinophils, and mononuclear cells.^[7] Inflammatory response is pivotal in the epithelial dysfunction and mucosal injury caused by *H. pylori*.

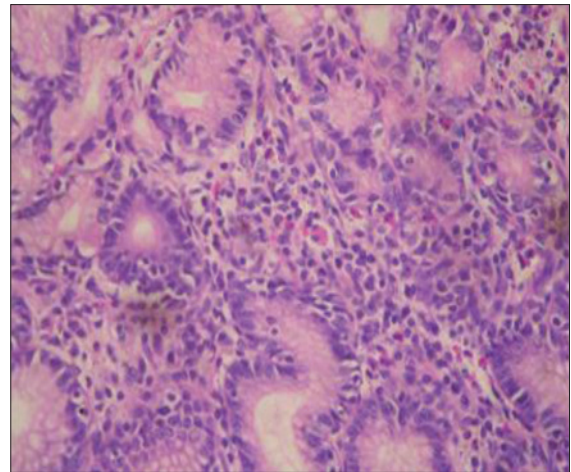


Figure 1: Gastric biopsy showing eosinophilic infiltrates (low power view, ×20)

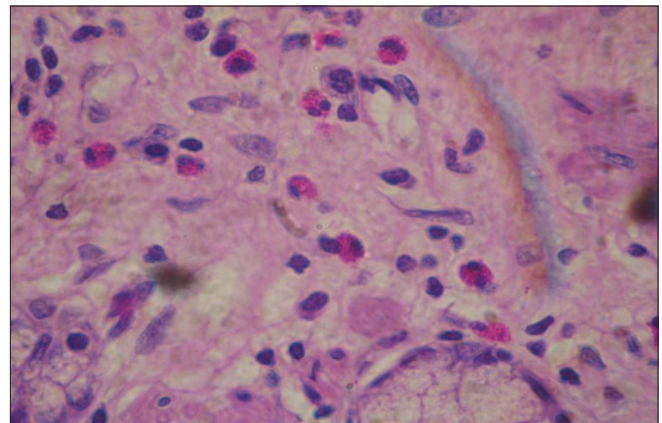


Figure 2: Gastric biopsy showing eosinophilic infiltrates (high power view, ×400)

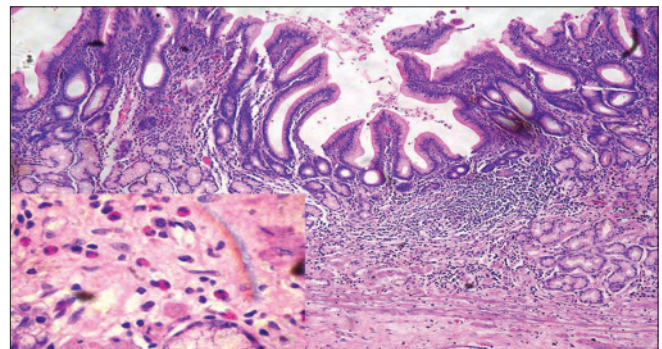


Figure 3: Surgical gastric biopsy showing inflammatory cells

It stimulates the release of a variety of inflammatory mediators both directly by bacterial products such as vacuolating cytotoxin, lipopolysaccharide, neutrophil-activating factor and porins, and indirectly as a result of interaction with gastric epithelial cells.^[8] The role of eosinophils in the pathogenesis of *H. pylori*-associated gastritis and ulcer is not clearly explained. Eosinophilic gastroenteritis is a rare and heterogeneous condition characterized by patchy or diffuse eosinophilic infiltration of GI tissue, first described by Kaijser in 1937.^[9]

Presentation may vary depending on location as well as depth and extent of bowel wall involvement and usually runs a chronic relapsing course. It can be classified into mucosal, muscular, and serosal types, based on the depth of involvement.^[10] Any part of the GI tract can be affected, and isolated biliary tract involvement has also been reported. The stomach is the organ most commonly affected, followed by the small intestine and the colon.^[11,12] Patients with predominantly mucosal disease present with diarrhea, abdominal pain, vomiting, and nutritional deficiency (i.e., iron deficiency anemia). Those with predominantly muscular involvement present with symptoms of gastric outlet obstruction or intestinal obstruction. Patients with involvement of serosal and subserosal layers present with eosinophilic ascites.^[13]

Association of *H. pylori* with eosinophilic gastroenteritis has been reported in the literature, but there have been few case reports only. Papadopoulos *et al.*, reported a case of symptomatic eosinophilic gastritis that responded well to anti-*H. pylori* treatment.^[14] A similar association was also reported by Kawaguchi *et al.*^[15] Other authors reported the relationship between eosinophilic gastroenteritis and *H. pylori* gastritis as causal factor rather than a coincidence.^[16]

Recurrence of *H. pylori* after a successful eradication is rare in developed countries, but is more frequent in developing countries.^[17] In most cases recrudescence (re-colonization of the same strain) rather than reinfection (colonization with a new strain) is considered more likely to be responsible.^[18] Recrudescence is a clinical problem as a result of treatment failure. Recrudescence is most likely to occur during the 1st year after eradication, while reinfection may account for recurrence after a year from the eradication therapy. Heavy contamination of the environment and sources such as in drinking water, institutionalized patients, medical personnel, or family members, may be the source of reinfection, especially in developing countries.^[19] In our case, patient was negative for *H. pylori* and had responded to duodenal dilation, which was carried out as he had duodenal stenosis. He had gained weight. He returned after 2 years with recurrent dyspeptic symptoms and had positive rapid urease test for *H. pylori*, so it was likely to be reinfection rather than recrudescence.

Refractory gastric ulcers are those with no healing despite 12 weeks of full-dose H₂-receptor antagonists or 8 weeks of proton pump inhibitor (PPI) therapy.^[20] Eradication of *H. pylori* infection is confirmed after the completion of therapy using noninvasive testing such as the urea breath test, 4-8 weeks after the completion of therapy.^[21] In our case, patient had persistent *H. pylori* infection after initial treatment with triple regimen of pantoprazole, amoxicillin, and clarithromycin, so patient was put on quadruple therapy for *H. pylori* for 10 days consisting bismuth subsalicylate, metronidazole, tetracycline, and pantoprazole. *H. pylori* infection was persistent after quadruple therapy as well, so rescue treatment with levofloxacin, amoxicillin, and pantoprazole was given, but it also failed to eradicate *H. pylori*.

Prevalence of *H. pylori* resistance to clarithromycin ranges from close to nil to 20 to 25%. The essential risk factor for clarithromycin resistance is a previous consumption of macrolides.^[22,23] Prevalence of *H. pylori* resistance to metronidazole ranges from 20 to 40% in the United States.^[22,23] In developing countries, the prevalence is much higher (50-80%).^[24] Prevalence of *H. pylori* resistance to amoxicillin is very low (1%), as is the prevalence of *H. pylori* resistance to tetracycline, except in a few countries like South Korea. In contrast, fluoroquinolones, which have shown an increasing consumption over the past few years, have a higher prevalence of 20% in adults in Portugal. A secondary resistance rate of 9% has been found in Germany.^[25]

While eosinophils are part of the inflammatory reaction in acute *H. pylori* gastritis, the role of the eosinophil in the pathogenesis of chronic gastritis is unknown. In a study that evaluated eosinophil infiltration and degranulation in association with chronic gastritis and *H. pylori* infection, it was found that the severity of chronic gastritis was significantly correlated with the eosinophil score. Eosinophil degranulation did not appear to be greater at or near sites of bacterial colonization in the *H. pylori* gastritis specimens. The results suggest that eosinophil infiltration and degranulation may be associated with *H. pylori* gastritis.^[26] The patient underwent surgery in view of refractory *H. pylori* infection and nonhealing prepyloric ulcer. Antrectomy with gastrojejunostomy was performed. The postoperative specimen from antrum also showed *H. pylori* and a nonmalignant prepyloric ulcer. Patient is on regular follow-up and is doing well.

Conclusion

There have been few case reports on association between *H. pylori* gastritis and eosinophilic gastroenteritis; however, our case shows that *H. pylori* may play a pathogenic role in the development of blood eosinophilia and eosinophilic gastroenteritis.

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