

Gastroduodenal Crohn's disease

COSTAS H. KEFALAS, MD

Crohn's disease is one of 2 archetypes of chronic idiopathic inflammatory bowel disease, the other being ulcerative colitis. Crohn's disease is defined by chronic inflammation that may involve any site of the gastrointestinal tract, from mouth to anus, most commonly the terminal ileum and proximal colon (1). Rarely, Crohn's disease may affect the stomach and duodenum. The unusual clinical features of gastroduodenal Crohn's disease and the various treatments available, including medical, endoscopic, and surgical, are discussed in this article.

BRIEF CASE REPORT

A 43-year-old white man had been diagnosed with ileocolonic Crohn's disease 23 years earlier and had undergone a proctocolectomy with resection of 9 cm of distal ileum and creation of an ileostomy 8 years previously. He presented with a 2-month history of postprandial fullness, intermittent nausea and vomiting, usually later in the day, and midepigastric, crampy, nonradiating abdominal pain. He had normal ileostomy output and took no medicines. The results of the physical exam and laboratory tests were normal. An upper gastrointestinal and small bowel follow-through x-ray demonstrated antral narrowing with a pyloric stricture, duodenal narrowing in the second portion, and normal jejunum and ileum. Endoscopy revealed a normal esophagus; a distal stomach characterized by mucosal nodularity, scattered ulcerations, antral narrowing, and a pyloric stricture that was successfully dilated with a 54-French through-the-scope balloon; and a deformed, ulcerated duodenum. Biopsies revealed severe granulation tissue, with acute and chronic inflammation in the stomach and duodenum. No granulomas or *Helicobacter pylori* bacteria were detected. The patient was treated with prednisone 10 mg/day and a proton pump inhibitor. The patient's symptoms improved, and repeat endoscopy with biopsies 2 weeks later demonstrated improvement in gastric and duodenal inflammation.

DEFINITION/EPIDEMIOLOGY

The most well known criteria for the diagnosis of gastroduodenal Crohn's disease are those of Nugent and Roy, which include either 1) histologic finding of noncaseating granulomatous inflammation of the stomach or duodenum, with or without concomitant Crohn's disease in the remaining gastrointestinal tract, and the absence of other systemic granulomatous disorders; or 2) confirmed Crohn's disease of the gastrointestinal tract and radiographic or endoscopic findings of

diffuse inflammation of the stomach or duodenum consistent with Crohn's disease (2–6).

Clinically significant gastroduodenal disease occurs in 0.5% to 4% of all patients with Crohn's disease (6–9). Most patients have associated involvement of distal small or large intestine (5). One third of patients with gastroduodenal Crohn's disease do not have small or large bowel disease at the time of diagnosis but develop distal disease over time (1). Prospective studies of patients with intestinal Crohn's disease have identified upper gastrointestinal abnormalities through double-contrast radiography in 20% to 40%, through endoscopy in 20% to 30%, and through histology in 30% to 50% of patients (7, 10). Contiguous gastroduodenal involvement is the most common pattern, with about 60% of patients having diseased antrum, pylorus, and proximal duodenum (2, 3, 9). Gastroduodenal Crohn's disease is noted almost equally in men and women, with a 1.2:1 ratio (9, 11). The age of presentation varies, and cases are reported in both adults and children. The mean age of presentation is the third and fourth decades (9).

SYMPTOMS

Most patients with gastroduodenal Crohn's disease are asymptomatic from the gastroduodenal involvement (10). The most common symptom is epigastric abdominal pain, which is often postprandial in timing, nonradiating, and usually relieved by food and antacids (3, 7, 10). Pronounced, continuous abdominal pain associated with nausea and vomiting suggests gastric outlet obstruction due to gastroduodenal stricture formation (7). Other common symptoms include profound weight loss, nausea with or without vomiting, and anorexia (7, 10–12) (Table 1). Symptoms may be wrongly attributed to peptic ulcer disease or a side effect of drug therapy (i.e., 5-aminosalicylic acid, prednisone, 6-mercaptopurine, azathioprine, or metronidazole) (7). Gastrointestinal blood loss may be noted in gastroduodenal Crohn's disease, usually in the form of chronic anemia, although melena and hematemesis indicating acute hemorrhage may rarely occur (7, 10–12).

From the Division of Gastroenterology, Department of Internal Medicine, Baylor University Medical Center, Dallas, Texas.

Corresponding author: Costas H. Kefalas, MD, Division of Gastroenterology, Department of Internal Medicine, Baylor University Medical Center, 3500 Gaston Avenue, Dallas, Texas 75246 (e-mail: CHKefalas@worldnet.att.net).

Table 1. Symptoms encountered in gastroduodenal Crohn's disease

Common	Rare
Epigastric abdominal pain	Anemia
Nausea/vomiting	Malaise
Weight loss	Pyrosis
Early satiety	Diarrhea
Anorexia	Feculent vomiting (fistula)
Bloating	Hematemesis
Belching	Melena

Table 2. Radiographic features of gastroduodenal Crohn's disease

Mucosal nodularity ("cobblestoning")
Thickened folds
Ulcers
Strictures
Intramural fissures/sinuses
Hypoperistalsis
Poor gastric emptying
Small, contracted stomach
Lack of distensibility
"Ram's horn" sign
Pseudo-Billroth I configuration

DIAGNOSIS

The diagnosis of gastroduodenal Crohn's disease requires a high level of clinical suspicion for patients with Crohn's disease of the lower gastrointestinal tract and the use of imaging or endoscopic modalities to secure the diagnosis. The earliest radiographic sign in Crohn's disease is aphthous ulcers (13). The most common radiologic findings in gastroduodenal Crohn's disease are mucosal nodularity, or "cobblestoning," thickened folds, and ulcerations (7) (Table 2). A pseudo-Billroth I appearance of involved antrum and proximal duodenum has been described (4, 7). A rare but classic radiographic finding is the funnel-shaped deformity of diseased antrum and duodenal bulb, known as the "ram's horn" sign (5, 13) (Figure 1). Radiographic evaluation with double-contrast medium is the best modality to assess lesions that have formed stenoses or strictures, which are findings of advanced disease (4, 9, 12, 14, 15). A barium enema should be done when a gastrocolic fistula is suspected, as this has a higher sensitivity than upper gastrointestinal radiography (7).

Endoscopy with biopsy, ideal for surveying the mucosa, remains the gold standard in the diagnosis of gastroduodenal Crohn's disease and is most likely to identify early gastric and/or duodenal involvement (9, 10, 12, 15). Endoscopic findings include patchy erythema, mucosal friability, thickened folds, and ulcerations, both aphthous and linear (4, 5, 7, 10) (Table 3). Unlike peptic ulcers, those of gastroduodenal Crohn's disease are not usually circular but linear or serpiginous (12). Another common endoscopic feature, characteristic but not specific, is a nodular mucosa (cobblestoning) (4, 5, 10) (Figure 2). A linitis plastica

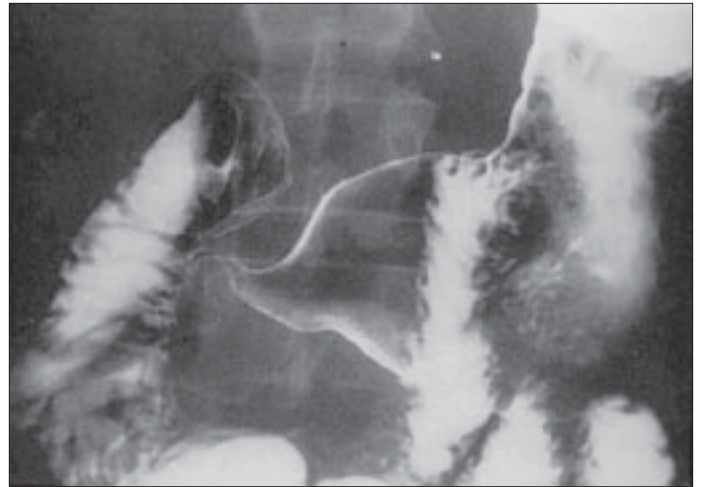


Figure 1. A double-contrast radiograph showing the "ram's horn" sign, a characteristic finding in gastroduodenal Crohn's disease. Reproduced with permission from reference 13.

Table 3. Endoscopic findings in gastroduodenal Crohn's disease

Edema
Erythema
Friability
Granularity
Erosions
Ulcers (aphthous/deep and linear/serpiginous)
Thickened folds
Mucosal nodularity ("cobblestoning")
Notching of Kerckring's folds
Luminal narrowing
Strictures
Fistulae
Pseudodiverticula
Lack of distensibility

appearance, with luminal narrowing and rigidity, and thickened folds suggest diffuse gastric involvement (16, 17). The differential diagnosis of the upper gastrointestinal tract endoscopic findings in Crohn's disease includes peptic ulcer disease, carcinoma, lymphoma, sarcoidosis, tuberculosis, eosinophilic gastroenteritis, Zollinger-Ellison syndrome, pancreatitis, and pancreatic cancer (7, 9).

The histologic findings of gastroduodenal Crohn's disease are often nonspecific and have a patchy distribution. To exclude other diagnoses, multiple biopsies should be taken from the stomach and duodenum. Noncaseating granulomas (Figure 3) are seen in 5% to 83% of gastroduodenal biopsies in Crohn's disease and therefore may not be present (4, 10). Granulomas can be seen in a number of other diseases, including *H. pylori* infection, peptic ulcer disease complications, gastric carcinoma, gastric lymphoma, sarcoidosis, tuberculosis, syphilis, hypertrophic gastropathy, eosinophilic gastritis, Wegener's granulomatosis, food and suture granulomas, histoplasmosis, Whipple's disease, and the controversial diagnosis of idiopathic isolated granulomatous gastritis,

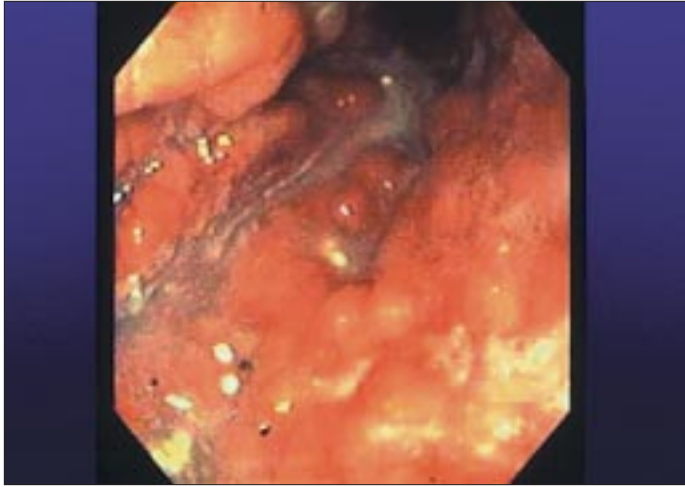


Figure 2. An endoscopic image of the antrum of a patient with gastroduodenal Crohn's disease showing mucosal nodularity ("cobblestoning"). Image courtesy of Daniel E. Polter, MD.

to name only a few (5, 10, 17). Therefore, the finding of granulomatous gastritis is not specific for Crohn's disease.

The most common pathologic finding encountered in gastric Crohn's disease is *H. pylori*-negative focal patchy gastritis, or focally enhanced gastritis, with or without granulomas, noted in 76% of patients with known Crohn's disease of the small and/or large intestine (5, 10, 18–20). Characterized by focal infiltration of lymphocytes and histiocytes, this focally enhanced gastritis has no correlation with clinical and laboratory findings (17). It should be noted that the prevalence of *H. pylori* in patients with Crohn's disease is similar to that in the general population (7). Additional histologic features include mucosal edema, acute or chronic inflammation, crypt abscesses, lymphoid aggregates, erosions, ulcers, abnormal villi, and fibrosis extending into the muscularis mucosa (17, 18).

TREATMENT

No controlled, prospective treatment studies have been reported for gastroduodenal Crohn's disease (7, 8). Most experts recommend intense acid suppression with a proton pump inhibitor. Peptic ulcer disease and *H. pylori* should be excluded and, if present, treated (7). Occasionally this treatment is sufficient to allow healing of the gastroduodenal Crohn's disease as well. Most of the time, additional treatment must be provided for Crohn's disease of the small bowel and colon, which often coexist (4, 6). Treatment should be based on symptom severity in individual patients (7). Initial treatment for active gastroduodenal Crohn's disease often involves corticosteroids along with a proton pump inhibitor (5, 8, 10, 22, 23). Not all studies demonstrated corticosteroid-induced remission in active disease, however (2, 3, 19, 22–24). 6-Mercaptopurine and azathioprine have been shown to maintain corticosteroid-induced remission and should be instituted early in the disease course (23–25). Aminosalicylic acid compounds are generally not beneficial in upper gastrointestinal Crohn's disease and may aggravate symptoms (23). The role of infliximab remains to be defined (7, 9, 10).

Strictures can complicate the course of gastroduodenal Crohn's disease. Short pyloric or duodenal strictures are ideal for endoscopic balloon dilation (7, 8). Successful endoscopic dilata-

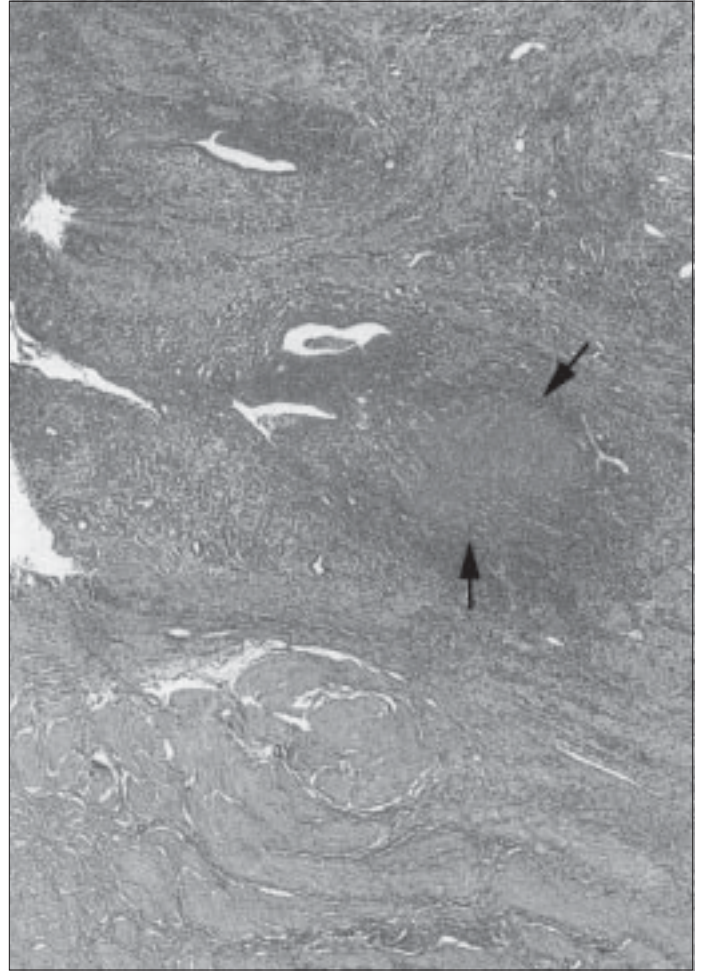


Figure 3. Specimen from a stomach biopsy demonstrating a noncaseating granuloma within the gastric mucosa and surrounding mononuclear cell infiltration in a patient with gastric Crohn's disease. Reproduced with permission from reference 17.

tion with a Rigiflex balloon (8 mm, Boston Scientific, Natick, Mass) or a Microvasive balloon (10 to 20 mm, Boston Scientific, Natick, Mass) has been described, with a risk of perforation of 1% to 2% (7, 26). Often, repeated endoscopic dilation is required to completely treat strictures (27, 28). In one series, 5 patients with obstructive gastroduodenal Crohn's disease were treated with endoscopic balloon dilation with an 18- to 20-mm balloon (26). Each of the initial dilations was successful; 3 of the 5 patients had recurrent symptoms that required repeat dilations every 3 to 4 months (26). All 5 patients avoided surgery during a mean follow-up interval of 4.2 years with concomitant use of either a proton pump inhibitor or histamine-2 receptor blocker (26).

One third of patients with gastroduodenal Crohn's disease do not respond to medical therapy alone and require surgery (29). Additional indications for surgery include massive, persistent upper gastrointestinal hemorrhage, gastric outlet obstruction, and fistula or abscess formation (2, 4, 5, 7, 8, 30). The most common indications for surgery are duodenal obstruction and refractory ulcer-type abdominal pain (9). Before surgical therapy is initiated, patients should undergo upper gastrointestinal tract endoscopy, small bowel radiography, and colonoscopy for assessment of the extent of Crohn's disease to allow optimal surgical planning (9).

Surgical options in gastroduodenal Crohn's disease include bypass surgery with gastrojejunostomy (with or without vagotomy), commonly to bypass a duodenal stricture, gastroduodenostomy, duodenojejunostomy, and stricturoplasty (5, 9, 10). Due to post-vagotomy diarrhea and marginal ulcers after bypass surgery, gastrojejunostomy with highly selective vagotomy, preserving autonomic innervation to the small bowel, should be regarded as the ideal surgical treatment of gastroduodenal Crohn's disease (29). Gastric emptying may be delayed postoperatively in up to 24% of patients undergoing bypass surgery, but this complication may be seen in patients treated with stricturoplasty as well (9, 31, 32). Other postoperative complications include anastomotic leak, enterocutaneous fistula, intraabdominal abscess, and stomal ulceration (33).

Certain patients with obstructive duodenal Crohn's disease may be candidates for duodenal stricturoplasty (10, 34), although repeat surgery rates tend to be higher in those patients treated with stricturoplasty than in those treated with bypass surgery (9, 31, 32). Two recent retrospective studies yielded opposing conclusions regarding the need for reoperation in patients who had undergone stricturoplasty as an alternative to bypass surgery; one study found that 9 of 13 patients required revision surgery for a complication or recurrent stricture (32), whereas the second study found this was needed in only 3 of 13 patients (31).

PROGNOSIS/COMPLICATIONS

The prognosis of gastroduodenal Crohn's disease is usually good, irrespective of type of therapy used (3, 6, 33). However, a number of complications may develop. Gastric outlet obstruction due to gastroduodenal stricture formation is the most common complication of gastroduodenal Crohn's disease (7). Fistula formation between the stomach or duodenum and colon or small intestine usually originates in the colon or small intestine in areas of active or inactive Crohn's disease (5). Gastrocolic fistula, usually from the transverse colon to the greater curvature of the stomach, is the most common fistula encountered, and 30% of patients with this fistula have the classic triad of diarrhea, feculent vomiting, and weight loss (4, 35). Also described are gastroileal, gastrosplenic, duodenocolic, duodenobiliary, duodenocutaneous, and duodenopancreatic fistulas (5–7, 12, 14). Surgery is the treatment of choice for fistulas. Unlike peptic ulcer disease, gastroduodenal Crohn's disease is not commonly associated with perforation and severe gastrointestinal hemorrhage, although these have been reported (2, 4, 6, 7). Pancreatitis is a rare complication of gastroduodenal Crohn's disease and may be related to reflux of duodenal contents into the pancreatic duct or to ampullary stenosis or obstruction from duodenal inflammation (4, 5, 7). Very rarely, malignant degeneration has been noted in the setting of long-standing duodenal Crohn's disease (4, 5, 7, 36–38).

CONCLUSION

Gastroduodenal involvement is a rare manifestation of Crohn's disease. In a patient with upper digestive tract symptoms and characteristic abnormalities documented on radiographic and endoscopic evaluation, the diagnosis can be made and appropriate treatment initiated.

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