

Crohn's Disease of the Foregut



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KEYWORDS

• Crohn's disease • Esophagus • Gastric • Foregut

KEY POINTS

- Crohn's disease of the foregut is underrecognized.
- The most common location of Crohn's disease in the proximal intestine is in the gastric antrum.
- Surgical management of esophageal Crohn's disease is reserved for complications such as strictures or fistulas.
- The most common indication for surgical management of gastroduodenal Crohn's disease is obstruction.
- The surgical options are gastric bypass or strictureplasty with or without concomitant vagotomy.

INTRODUCTION

In 1932, New York physicians Crohn, Ginzburg, and Oppenheimer published the seminal work describing the small bowel inflammatory process that would carry the eponymous name of its first author.¹ At that time, the disease was believed to be limited to the terminal portion of the small intestine. The authors and others quickly realized that the disease could be more extensively distributed, however. Two years after this initial publication, Crohn asserted that the disease "could involve other segments than the terminal ileum"² and he thereby favored the term regional ileitis. That same year, also in New York, the first operation for Crohn's disease involving the foregut likely occurred when Eggers performed an esophagectomy with plastic tube reconstruction for a young man with a benign esophageal stricture.³

Although the understanding of Crohn's disease has grown greatly since its first description, the experience with foregut disease remains sparse. It is now well-recognized that Crohn's disease can affect any part of the intestinal tract from the mouth to the anus. The recognition and documentation of foregut Crohn's disease remains underappreciated, however. The exact incidence of proximal intestinal Crohn's is difficult to define and the preponderance of the literature centers around

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case reports and small case series. Estimates of foregut Crohn's disease range between 1% and 13% in patients with documented ileocolic disease.⁴ The diagnosis is often made only in patients who have significant symptoms from their upper intestinal disease. Patients that have documented proximal Crohn's disease typically have evidence of the disease in their distal small intestine or colon.^{4,5} However, finding the evidence of proximal Crohn's disease often depends on how diligently it is sought.

In 1975, an extensive experience involving more than 8000 cases of regional enteritis was presented. There were no patients demonstrating any involvement of the proximal intestinal tract.⁶ Korelitz and associates⁷ performed one of the first series specifically looking for evidence of Crohn's disease in the proximal intestine. This evaluation of 45 patients with Crohn's disease distally was performed and histologic lesions were found in almost one-half of the patients, and 24% were diagnostic for Crohn's. An even larger evaluation involving 225 patients suffering from Crohn's disease of the lower gastrointestinal tract was also performed. The authors performed an upper endoscopic examination and found 49% of patients demonstrated evidence of gastric Crohn's disease, whereas 34% had evidence of disease in the duodenum.⁸ In another study, Alcantara and colleagues⁹ found that 56% of Crohn's disease patients demonstrated upper endoscopic abnormalities. Again, the most frequently affected site was the gastric antrum, followed by the duodenum. In the largest study to date, Oberhuber and coworkers¹⁰ performed a retrospective study of 792 patients with known distal disease. Crohn's disease was identified histologically in the antrum and body in 40% of patients and was found in the duodenum or duodenal bulb in 13% of patients.¹⁰ Clearly, the incidence of foregut Crohn's disease is greater than previously documented and finding it requires only seeking it in patients already diagnosed with the disease distally.

Granulomas, considered to be pathognomonic for the diagnosis of Crohn's disease, are frequently unseen. Despite a diagnosis of Crohn's in the distal bowel, granulomas are seen in only 20% to 30% of grossly abnormal tissue biopsies.^{8,9,11} Although they are more commonly found in grossly abnormal lesions, they can be detected in more than 10% of grossly normal tissue as well.⁹

Despite being more common than previously recognized, symptomatic proximal disease is indeed rare. Even patients with concomitant disease tend to seek medical care for their lower intestinal symptoms.¹² It remains imperative that physicians who treat patients with Crohn's disease remain vigilant for the possibility of foregut Crohn's and query for any upper intestinal complaints and perform an upper intestinal investigation if the clinical scenario presents itself.

ESOPHAGEAL CROHN'S DISEASE

First described by Franklin and Taylor in 1950,¹³ Crohn's disease of the esophagus is the least common location for the disease in the intestinal tract. A 1983 review of the English-language literature to that point revealed reports of only 20 patients with Crohn's disease of the esophagus.¹⁴ Several large reports have confirmed the scarcity of the condition. One study documents only 9 cases among 500 patients followed long term with Crohn's disease,¹⁵ and a review of a 20-year experience at the Mayo Clinic showed only 20 patients (0.2%) identified as having esophageal involvement.¹⁶ The majority of patients in these reports, however, came to medical attention owing to the severity of their condition. These patients were treated for the painful dysphagia, esophageal strictures, or fistulas associated with advanced, aggressive Crohn's disease. Indeed, 1 study group showed that more than 30% of the patients in their study had disease so severe that it required esophagectomy.¹⁴

This summary does not represent adequately all patients with esophageal involvement of Crohn's disease.

A higher incidence of esophageal disease has been noted in the pediatric population. One study documented a higher incidence in children with Crohn's disease who underwent upper endoscopy with biopsy.¹⁷ A higher involvement was also documented when all children with Crohn's disease underwent upper endoscopy. Their findings demonstrated esophagitis or esophageal ulcers in 44% of their patients.¹⁸ It is more likely that these findings stem from a more diligent search in the pediatric population than a higher prevalence, however. When adults with Crohn's disease underwent upper endoscopy, endoscopic lesions in the esophagus were observed in 15%.⁸ The incidence of esophageal Crohn's disease clearly lags behind that found in the lower intestine but it is not as rare as once believed.

Signs and Symptoms

It must be emphasized that any patient with an existing diagnosis of Crohn's disease warrants the performance of an upper endoscopy with biopsy for even minor upper intestinal complaints. Most patients are asymptomatic, with only 33% of patients with documented esophageal disease having any esophageal complaints in 1 study.¹⁹ When present, these symptoms can be difficult to differentiate from more common intestinal complaints such as gastritis or gastroesophageal reflux disease. Patients often complain of vague abdominal discomfort or heartburn. More advanced disease is heralded by dysphagia, nausea, vomiting, or odynophagia.^{19,20} The radiographic or endoscopic findings of esophageal Crohn's disease mirror those of colonic disease. On endoscopic examination, inflammation or linear ulceration consistent with esophagitis is seen in 75% to 85% of patients.^{15,16} More advanced disease shows aphthous ulcerations, mucosal nodularity or the typical cobblestone appearance in 30% to 40%. The histology typically shows inflammation, whereas granuloma formation is seldom identified.

The acute inflammatory process can progress to chronic fibrosis and stenosis and can lead to the development of an esophageal stricture.²¹ Patients typically present with progressive dysphagia, odynophagia, or worsening reflux symptoms. Symptoms can progress to nausea and emesis with resultant weight loss. These patients are best evaluated with an esophagram in conjunction with upper endoscopy and biopsy, and the differentiation from malignancy can understandably be difficult. As with Crohn's disease found elsewhere in the gastrointestinal tract, fistula formation can occur. The most common location for a fistula is between the esophagus and the tracheobronchial tree, but can occur between any structure in the mediastinum or abdomen as well. Patients present similarly to and often have a coexisting esophageal stricture present. Epigastric or chest pain, dysphagia, weight loss, and odynophagia²² are the most common complaints. A fistula can also present as recurrent pneumonia without concomitant esophageal complaints. Recurrent lower lobe pneumonia, pneumonitis, or abscess in patients with Crohn's disease should be considered signs of fistula formation and warrant evaluation of the esophagus with radiography and endoscopy.

Treatment

As with Crohn's disease in any anatomic location, medical management is the first line of therapy. Owing to the rarity of symptomatic presentation, and the fact that most cases presented the literature are severe, there is a dearth of literature regarding the medical management of esophageal Crohn's disease, and no randomized studies exist. The treatment that is defined is of variable efficacy. Successful medical therapy

with symptom resolution has been reported with corticosteroids and acid suppression alone. Recurrent esophageal dilatations have been reported to control symptoms of esophageal stricture.²³ The largest published series consists of only 14 patients with Crohn's disease of the esophagus. All of the patients had concurrent evidence of Crohn's disease elsewhere and more than one-half experienced "complete healing" of their esophageal lesions when treated with corticosteroids after 2 to 4 weeks.²⁴ Several other treatment modalities have been reported in case reports. Topical steroid application with swallowed aerosolized budesonide has been reported as successful,²⁵ as has granulocyte/monocyte adsorption²⁶ and infliximab administration.²⁷ In an attempt to coalesce sparse data, the European consensus guidelines recommend that esophageal Crohn's disease is best managed with a proton pump inhibitor, systemic corticosteroids, and thiopurines or methotrexate.²⁸ The surgical management of these patients is limited typically to management of complications, such as persistent stricture or fistula formation.

Strictures

The treatment of intestinal strictures with endoscopic dilation is well documented. Although the occurrence of an esophageal stricture secondary to Crohn's disease is uncommon, numerous authors have reported an experience with the procedure.^{23,29} These strictures often require multiple dilations and the recurrent stricture rate is high. The practitioner should always be cognizant of the fact that, although the surgical therapy required is typically an esophagectomy, there are reports of undiagnosed malignancy lurking within these strictures.³⁰

Fistulas

The literature dealing with esophageal fistula from Crohn's disease involves case reports, with fewer than 20 described in the English literature.³¹⁻³³ These reports document fistula formation between the pleural cavity, bronchus, esophageal wall, as well as the stomach. Although there have been reports of successful fistula closure using liquid polymer sealant,³⁴ as well as using intravenous infliximab,³⁵ the majority of these require surgical repair. Esophagectomy with gastric pull-through and primary anastomosis offers definitive treatment of both the fistula and any resultant infectious complications and should be considered the standard for symptomatic fistula patients.

GASTRODUODENAL CROHN'S DISEASE

Gastroduodenal Crohn's disease is encountered more frequently than esophageal disease, but as with all foregut Crohn's disease the likelihood of finding it depends on how diligently it is sought. In the 1970s, Nugent and associates³⁶ published the largest series of patients to that time, documenting an incidence of gastroduodenal Crohn's of around 2%. At that time, slightly more than 150 total cases had been reported in the literature. These numbers remained consistent with later reports.³⁷ As with esophageal disease, a slightly greater incidence is documented in the pediatric population. Griffiths found an incidence of around 5%, but again only patients with suggestive symptoms were evaluated.³⁸

These studies center on patients being evaluated for upper intestinal complaints. When all patients with lower intestinal Crohn's disease are subjected to esophagogastroduodenoscopy, much higher rates are encountered. In 1 such study, investigators found almost one-half of their patients with Crohn's demonstrated gastric lesions consistent with the disease whereas one-third had duodenal evidence of the disease.⁸ In another evaluation, 10% of patients with distal Crohn's were found to harbor

Helicobacter pylori, but 32% of patients had evidence of *H pylori*-negative gastritis. The inflammation present closely resembled the inflammatory changes seen in Crohn's disease.³⁹ Clearly, as with esophageal Crohn's, the incidence of the disease depends on if whether is sought, because the majority of patients lack significant symptomology.

Signs and Symptoms

Although the majority of patients are asymptomatic, patients who do have symptoms of upper intestinal disease most commonly complain of upper abdominal pain. Nausea and emesis are the second most common complaints. Significant weight loss, and occasionally upper gastrointestinal bleeding or fever, have also been reported. Pancreatitis secondary to duodenal scarring has also been cited rarely.^{40,41} In the pediatric population, the most common presenting symptom is weight loss, followed by epigastric pain and recurrent vomiting. Hematemesis and melena are noted to occur less commonly than in the adult population.³⁸ It should be emphasized, however, that even when upper intestinal disease is documented, the majority of patients remain more symptomatic from their lower intestinal disease.⁴²

Endoscopic Findings

There should be a low threshold for performing upper endoscopy on any patient with Crohn's disease with any upper tract complaint. Endoscopy allows better visualization of mucosal defects for biopsy and allows monitoring of any therapeutic effect. Endoscopic biopsy is an invaluable tool for the diagnosis of gastroduodenal Crohn's disease. The mucosal lesions found at endoscopy are heterogeneous, but irregularly shaped ulcers and erosions are typical for gastroduodenal Crohn's disease.³⁷ The most common endoscopic findings in the upper intestine are similar to those encountered distally. These findings include mucosal nodularity or a cobblestone appearance of the mucosa. Aphthous or linear ulcerations, thickening or narrowing of the antrum, and duodenal strictures are also encountered.⁴³ Diffuse granularity, nodularity, and ulceration can be accompanied by the lack of distensibility of the involved area with insufflation.³⁶ Notching in the duodenal folds has been reported to be a strong indication for Crohn's disease.⁴⁴ Biopsies should be taken from endoscopically normal mucosa as well as grossly abnormal tissue.⁴⁵ Although the presence of the granulomas is conclusive for the diagnosis, these are identified in fewer than 33% of patients in most series. Confirmed Crohn's disease of the gastrointestinal tract or the presence of radiographic or endoscopic findings of diffuse inflammation involving the stomach or duodenum is consistent with a diagnosis of Crohn's disease, and more than 90% of patients have endoscopic abnormalities.⁴⁶

Treatment

Even patients with symptomatic foregut disease will likely be amenable to medical management and are not likely to require surgical intervention for their foregut disease. For patients who do require surgical evaluation, most operative interventions are required for complications stemming from their disease. The most common indications for surgical therapy are in patients suffering from unrelenting duodenal obstruction secondary to strictures. Patients may also rarely come to surgery for fistulous disease or even less commonly for malignancy arising in the chronic inflammation.

Medical Management

There are no controlled, prospective studies evaluating the management of gastroduodenal Crohn's disease. Because the majority of patients already have documented,

concomitant distal disease at the time of diagnosis, these patients are commonly already receiving medical management when the upper tract disease is diagnosed.^{47,48} These patients do not need to have their medical management adjusted from those patients only with disease involving only the distal intestine.³⁸ Several experts recommend intense acid suppression with a proton pump inhibitor. Peptic ulcer disease and *H pylori* infection should be excluded and, if present, treated. Occasionally, this treatment alone is sufficient to allow healing of the gastroduodenal Crohn's disease.⁴⁹ Historically, the primary treatment recommendation was for systemic corticosteroids coupled with acid suppression.^{49,50} In addition, there are reports of successful management with sucralfate, 6-mercaptopurine,⁵¹ azathioprine, and H2 receptor antagonists used as adjunct therapy.⁵² The role of infliximab remains to be defined. To reiterate, the European consensus guidelines recommend a proton pump inhibitor, systemic corticosteroids, and thiopurines or methotrexate for the management of upper intestinal Crohn's disease.²⁸

Endoscopic Management

Strictures are the most common indication for intervention in patients with gastroduodenal Crohn's disease. Short pyloric or duodenal strictures are typically well-suited for endoscopic balloon dilation. Numerous reports of balloon dilation have been made, with a low risk of perforation of 1% to 2%, yet often repeated endoscopic dilation is required⁵³ to completely treat strictures. In 1 series, 5 patients with obstructive gastroduodenal Crohn's disease were treated with endoscopic balloon dilation. Each of the initial dilations was successful but 3 of the 5 patients had recurrent symptoms that required repeat dilations every 3 to 4 months. All 5 patients avoided surgery over a mean follow-up interval of 4 years with concomitant use of either a proton pump inhibitor or a histamine-2 receptor blocker.⁵⁴ In the largest study involving Crohn's strictures—the majority in the lower intestine—Singh and associates⁵⁵ performed 29 dilations with a mean follow-up period of 18 months. Technical success was achieved in 28 of 29 stricture dilations. The recurrence rate was noted to be lower when steroid injections were performed concurrently with the dilation. Three perforations, all in the colon, occurred for a complication rate of 10%, and there were no mortalities.⁵⁵

Surgical Management

The most common indication for surgical intervention in patients with gastroduodenal disease is also duodenal obstruction. The most common symptoms of duodenal obstruction are nausea and emesis, occasionally coupled with refractory ulcer-type abdominal pain. Additional indications for surgery include massive or persistent upper gastrointestinal hemorrhage, and less commonly fistula formation or the development of malignancy in the setting of the chronic inflammation.

Duodenal Obstruction

Surgical options for managing gastroduodenal Crohn's disease include bypass surgery, typically with either gastrojejunostomy or gastroduodenostomy reconstruction. These procedures can be performed either with or without a concurrent vagotomy. The other commonly used surgical procedure is a stricturoplasty, performed similarly to that performed elsewhere in the intestine. Most patients either remain asymptomatic or are adequately managed medically and the requirement to perform these procedures is rare. As a result, there are no randomized trials comparing results and the literature stems primarily from case series based on single-institution experiences.

In 1983, 1 assessment of the long-term follow-up of patients treated surgically was performed. Ross and coworkers⁵⁶ evaluated 10 patients with Crohn's disease who

had been managed surgically at the Cleveland Clinic and had a follow-up of on average 14 years. Eight of the patients had a gastrojejunostomy performed, 3 with concomitant vagotomy. They found that 7 of the patients required reoperation for recurrent duodenal Crohn's disease. The indications for subsequent operations were marginal ulceration, recurrent obstruction, or duodenal fistula. Their conclusions were that vagotomy should be part of the operative management of these patients.⁵⁷ The following year, Murray and associates⁵⁸ published the Lahey clinic experience of 25 patients who required an operation for duodenal Crohn's disease. Duodenal obstruction was the indication for operation in 22 of these patients, and duodenoenteric fistula was the cause for the other 3. After a median follow-up of 12 years, one-third of the patients required reoperation for duodenal disease. Marginal ulceration and recurrent gastroduodenal obstruction again were the primary reasons for reoperation. The addition of vagotomy was not noted to protect against subsequent marginal ulceration, yet the absence of appreciable morbidity associated with vagotomy and the high incidence of marginal ulcers reported with gastroenterostomy led the authors to recommend vagotomy at the primary operation for duodenal Crohn's disease.⁵⁸

The largest series was reported by Nugent and Roy,⁴⁶ who documented 33 patients who required surgery. Again, the most common indication for surgery was for gastroduodenal obstruction. Reoperation was required in only 8 patients; however, 7 of these patients also had a vagotomy performed. Based on their findings that vagotomy did not mitigate the presence of marginal ulceration or the need for reoperation, these authors thought that their results did not support the routine use of vagotomy when a bypass procedure is performed.⁴⁶ Poggioli and colleagues⁵⁹ added their results of 8 surgical patients spanning a 15-year period. Three patients had surgery for a duodenal fistula, and 5 had evidence of duodenal obstruction. Of the patients with obstruction, 3 were treated with strictureplasty and 2 with duodenojejunostomy.⁵⁹ One of the strictureplasty patients required revision and was treated with a subsequent gastroduodenal resection.

Worsey and associates⁶⁰ updated the Cleveland Clinic experience after adopting strictureplasty as the primary procedure. They documented a total cohort of 34 patients requiring surgery. The authors performed intestinal bypass in 21 patients, whereas strictureplasty was favored in 13. Vagotomy was performed concurrently with 16 of 21 bypasses and 7 of 13 strictureplasty procedures. Although follow-up was shorter, strictureplasty was felt to be a safe and effective operation for duodenal Crohn's disease and no additional benefit could be seen with the addition of vagotomy.⁶⁰ Yamamoto and coworkers⁶¹ added their strictureplasty experience with an additional 13 patients spanning a 20-year period. Ten patients underwent strictureplasty as the primary procedure, and in 3 strictureplasty was performed as a revision. Symptoms of obstruction persisted in 4 patients after strictureplasty with 1 requiring revision to a gastrojejunostomy. Six patients developed recurrent stricture, and 5 required repeat strictureplasty and the other patient underwent duodenojejunostomy. Overall 9 of 13 patients required additional surgery after the strictureplasty.⁶¹

Shapiro and associates⁶² have documented the most recent experience with the surgical management of gastroduodenal Crohn's disease. Thirty patients required surgical intervention over a 10-year period. Four patients underwent operation for fistulas, and 26 underwent surgery for obstructive symptoms. The operations performed were 11 open bypasses, 13 laparoscopic bypasses, and 2 strictureplasty procedures. Only 1 vagotomy was done. Patients resumed oral diet and were discharged sooner after laparoscopic bypass, compared with the open procedure. Two patients experienced disease recurrence, requiring revision 1 in each of the open and laparoscopic groups. Despite not using vagotomy frequently, the authors did not notice an increased incidence of gastroduodenal ulcers in their patients.^{62,63}

It is apparent that there are insufficient data to definitively favor 1 operative technique over another. Strictureplasty is a viable treatment option for this patient population, but does seem to have a higher recurrence rate than intestinal bypass. Intestinal bypass can be safely performed laparoscopically with a more rapid return of diet and a faster discharge from the hospital. Owing to a lack of clear benefit, the routine use of vagotomy in a patient population that is already prone to disabling diarrhea should be questioned.

Fistulas

The surgical management of duodenal fistulas from Crohn's disease does not share the operative dilemmas that those of duodenal obstruction carry. Although there are reports of isolated fistulous disease arising in the stomach with no evidence of disease elsewhere,⁶⁴ fistula formation typically originates in the colon or small intestine in areas of active Crohn's disease and forms a fistulous connection to the stomach or duodenum. The fistula most commonly involves an ileocolic anastomosis that is positioned adjacent to the duodenum.^{65,66} Surgical management consists of resection of the source of the fistula with primary closure of the duodenum.⁵⁹ If a large duodenal defect exists, then a duodenojejunostomy is recommended, provided there is no evidence of jejunal Crohn's disease.⁶⁶ Prevention should be stressed, and any ileocolonic anastomosis should be positioned away from the stomach or duodenum or protected with omentum in an attempt to prevent fistulization.

Malignancy

Malignant degeneration is possible in upper tract Crohn's disease, as it is in inflammatory bowel disease elsewhere. There are reports of malignant degeneration and malignancy may not be clearly identified preoperatively.^{67,68} Resection may be the most prudent course for disease that fails other management.

SUMMARY

Proximal intestinal Crohn's disease is likely more common than previously recognized, and the incidence of diagnosis depends on the diligence with which it is sought. The majority of patients with proximal Crohn's disease has concurrent disease distally or will likely develop it in the future. Patients that have demonstrated colonic or ileocolic disease that complain of upper abdominal complaints such as pain, gastric reflux, or dysphagia should be evaluated with an upper endoscopy and biopsy. The most common surgical indication for gastroduodenal disease is for obstructive symptoms. These patients are adequately served with strictureplasty, but have a higher recurrence rate than with intestinal bypass procedures that can safely be performed laparoscopically. There is no definitive benefit to adding vagotomy in these patients. Fistulas most commonly originate in the colon or distal small intestine and are best prevented or treated with resection and duodenal or gastric closure.

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