

ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Disease

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Gastroduodenal and Jejunoileal Crohn's Disease



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G&H How common are gastroduodenal and jejunoileal Crohn's disease among the various types of Crohn's disease?

BC Crohn's disease can occur anywhere from the mouth to the anus. Approximately one-third of patients have colonic disease, another third have ileal or isolated small-bowel disease, and another third have ileocolonic disease. A smaller percentage of patients with Crohn's disease (5%-15%) have proximal disease in the gastroduodenum, esophagus, or mouth, and even fewer have purely jejunal Crohn's disease. Gastroduodenal Crohn's disease (also known as Crohn's disease with upper gastrointestinal [GI] tract involvement) may be underdiagnosed, as the majority of patients are asymptomatic or have dyspepsia symptoms not typically associated with Crohn's disease. Gastroduodenal Crohn's disease is more often diagnosed in pediatric patients, in whom upper endoscopy is more commonly part of the diagnostic assessment, than in adult patients with Crohn's disease.

G&H What are the main symptoms and clinical presentations of gastroduodenal and jejunoileal Crohn's disease?

BC As mentioned, many patients with gastroduodenal Crohn's disease are asymptomatic, which is likely part of the reason it may be underdiagnosed. Physicians may not know to look for it. The most common symptom associated with gastroduodenal Crohn's disease is postprandial dyspepsia, so the disease can present similarly to peptic ulcer disease. Patients may also have nausea, anorexia, diarrhea, or weight loss. In severe cases, gastroduodenal Crohn's disease may present with gastric outlet

obstruction, in which patients cannot keep food down. They may have postprandial vomiting, weight loss, and symptoms of early satiety because of the blockage. In rare cases, patients may present with hematemesis. Even more

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rarely, presentations from duodenal involvement could include pancreatitis or some type of biliary obstruction from compression on the biliary tree.

Patients with jejunoileal Crohn's disease present with more stricturing disease than, for example, patients with ileocolonic Crohn's disease. The underlying mechanism of this fibrostenotic phenotype is incompletely understood. Classic symptoms of stricture include abdominal pain, nausea, and, in severe cases, vomiting. It can also present with constipation or diarrhea.

G&H What are the typical clinical outcomes of these types of Crohn's disease?

BC Gastroduodenal Crohn's disease has been associated with worse clinical outcomes than other phenotypes of Crohn's disease. Patients with jejunoileal Crohn's disease also tend to have a more severe disease course, particularly those with significant stricturing disease. Effective treatment of stricturing disease with antifibrotic therapies remains one of the biggest unmet needs in Crohn's disease. The Stenosis Therapy and Antifibrotic Research consortium is leading the effort to identify important biomarkers and define endpoints for clinical trials of Crohn's disease to bring effective antifibrotic therapies to patients.

G&H What modalities can be used to diagnose gastroduodenal and jejunoileal Crohn's disease?

BC The challenge with diagnosing gastroduodenal or jejunoileal Crohn's disease is that physicians may not be able to reach the disease using their usual endoscopic techniques. Colonoscopy often does not reach proximal ileal or jejunal Crohn's disease, and standard upper endoscopy may not reach distal duodenal disease. Thus, physicians are more reliant on imaging modalities for diagnosis. The key modalities currently being used are computed tomography (CT) enterography and magnetic resonance imaging (MRI) enterography, which can visualize the mid–small bowel. These modalities can also help diagnose stricturing disease as well as penetrating complications or fistulas that may be associated with small bowel disease.

Physicians can also utilize capsule endoscopy to diagnose inflammation in the mid–small bowel. Capsule endoscopy may be even better than CT or MRI at picking up mucosal disease. However, if there is suspicion of a stricture, it is important to be careful when deploying a capsule owing to the risk of capsule retention. Physicians may give patients a patency capsule first to make sure that they will not have any difficulties passing the actual capsule. In addition, there has been research looking at intestinal ultrasound to help with diagnosis. However, ultrasound is operator-dependent, and the sensitivity may be less for diagnosis of disease proximal to the terminal ileum.

Another diagnostic challenge with jejunoileal disease is that it is difficult to obtain biopsies, which is usually done with upper endoscopy or colonoscopy. If inflammation is identified on CT/MRI or capsule endoscopy, it is still important to try to obtain a tissue diagnosis. It may be necessary to work with an advanced endoscopist to perform balloon enteroscopy to reach that area.

As for gastroduodenal Crohn's disease, upper endoscopy is the gold standard for diagnosis. However, patients are often asymptomatic, so physicians may not think to

perform an upper endoscopy when trying to establish the diagnosis. In pediatrics, where there is a higher incidence of gastroduodenal Crohn's disease, physicians tend to perform upper endoscopy as part of their initial workup for Crohn's disease. That is less commonly done in adult patients. Generally speaking, if I have a patient with a new diagnosis of Crohn's disease, I perform both colonoscopy and enterography (CT or MRI). If the patient has upper GI abnormalities on enterography or any type of upper GI tract symptoms—such as nausea, dyspepsia, or even gastroesophageal reflux disease—I may perform an upper endoscopy as well to see whether there is any evidence of gastroduodenal Crohn's disease.

G&H What other conditions should be excluded when establishing a diagnosis?

BC One potential mimic for jejunoileal Crohn's disease in particular is tuberculosis. One of the ways to differentiate the conditions is to consider the clinical symptoms. Fevers, night sweats, and pulmonary manifestations may suggest tuberculosis. Also, if the patient is from an area where tuberculosis is endemic, that may be a clue that the patient has tuberculosis. In contrast, the presence of GI symptoms such as diarrhea and extraintestinal symptoms suggests Crohn's disease. Likewise, perianal manifestations are more commonly associated with Crohn's disease. Diagnostic testing will also help differentiate Crohn's disease from tuberculosis. For example, some features on CT imaging, such as asymmetric thickening of the wall and suspicious necrotic lymph nodes, may signal tuberculosis. Other findings that favor Crohn's disease include anorectal involvement, ulcerations, and a cobblestone appearance (which is caused by chronic inflammation). Both tuberculosis and Crohn's disease can be associated with granulomas on histopathology, but Crohn's disease has a lower prevalence of confluent granulomas with caseating necrosis. Physicians have to check for latent tuberculosis as part of their prelaboratory workup before starting biologics, particularly anti-tumor necrosis factor (TNF) biologics. Thus, physicians are often looking to see whether there has been exposure to tuberculosis.

Small intestinal adenocarcinoma is another rare diagnosis that should be considered, particularly in patients with obstructive symptoms and weight loss. Adenocarcinoma has been associated with Crohn's disease, even though it is rare.

In the case of gastroduodenal Crohn's disease, the differential diagnosis is wide and should also include peptic ulcer disease, Zollinger-Ellison syndrome, celiac disease, autoimmune enteritis, Whipple disease, sarcoidosis, and infectious causes, among others.

G&H Have there been any studies on the treatment of Crohn's disease specifically with gastroduodenal or jejunoileal involvement?

BC Because gastroduodenal and jejunoileal Crohn's disease are less common than other types of Crohn's disease, especially in adults, there have been no treatment studies specifically for these phenotypes. Crohn's disease clinical trials may include some patients who have gastroduodenal Crohn's disease, but those patients are usually few in number. Part of the issue is that the endpoints for clinical trials are dependent on colonoscopy. If it is not possible to reach the disease via colonoscopy, then the patient is often excluded, or his or her gastroduodenal and jejunoileal Crohn's disease may not be part of the endpoint assessment. Thus, data on the treatment of these patients are limited to case reports and real-world experiences.

I generally treat gastroduodenal and jejunoileal Crohn's disease the same as lower GI tract Crohn's disease. I use the same medications, and I try to treat patients aggressively, early in the disease course with the most-effective therapies. I may alter which agent I choose based on other phenotypic characteristics, for example, fistulizing disease or perianal disease. However, no study has found that one mechanism of action is superior to another.

Physicians try to manage gastroduodenal Crohn's disease medically as much as possible but strictures prove challenging, as the approved therapies appear to be less effective. I attempt to manage strictures endoscopically because the surgical options are associated with higher morbidity. Balloon dilation can be performed safely in strictures, whether they are located in the mid–small intestine or in the gastroduodenum. Recent systematic reviews and meta-analyses of real-world experiences show that balloon dilation has similar complication rates for upper GI tract strictures and lower GI tract strictures. However, if the strictures are long, significant proximal dilation associated with them is seen on imaging, or the patient has ongoing obstructive symptoms, surgical management may still be necessary.

G&H How effective is treatment for gastroduodenal and jejunoileal Crohn's disease?

BC Severe stricturing disease is difficult to treat in general. None of the therapies currently available are ideal. As far as inflammatory disease of the gastroduodenum is concerned, it is possible to achieve good response to medical therapy. Because gastroduodenal and jejunoileal Crohn's disease in particular tend to have more severe disease courses with worse clinical outcomes than other

phenotypes of Crohn's disease, I am fairly aggressive in my management and try to optimize biologic therapies. If I start an anti-TNF therapy, I usually do so in combination with a thiopurine because evidence has shown that combination therapy is the best strategy when using an anti-TNF agent. I use a treat-to-target approach and monitor response to therapy with biomarkers, endoscopy, and imaging with dosing adjustments as needed. It is important to optimize therapy soon after diagnosis, as early control of inflammation may yield a better chance of preventing long-term bowel damage as well as other complications.

G&H What other complications can occur?

BC Patients with multifocal stricturing disease in the mid–small bowel can develop malnutrition. If patients require multiple resections because of mid–small bowel disease, they can develop short-gut complications. Thus, it is important to identify these patients early and treat them aggressively to control their disease. In pediatrics,

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there is evidence for using enteral nutrition to help control inflammation, particularly if patients have upper GI tract strictures. Not as much evidence is available for adults, partly because of treatment nonadherence. As more is learned about the microbiome and more palatable dietary treatments are developed, dietary strategies may be utilized more in adults with severe gastroduodenal and jejunoileal phenotypes of Crohn's disease.

There has also been research in the surgical field on bowel-sparing surgery using strictureplasties to help prevent short-gut complications in patients with significant small bowel Crohn's disease. This strategy avoids large resections of the small bowel in patients who have complicated mid–small bowel disease to try to preserve the bowel as much as possible for nutritional purposes.

G&H How should patients with these types of Crohn's disease be monitored?

BC With any monitoring strategy, it is important to select the modality that will best examine the area of concern. For example, if the patient's inflammation is in the jejunum and there is no inflammation in the lower GI tract, repeat colonoscopies will not help. Therefore, my general approach for monitoring is to identify where the disease is active when first diagnosing the patient and then to select the monitoring modality that best assesses that area. In the case of isolated small bowel disease, this may be done best with inflammatory biomarkers and cross-sectional imaging such as CT or MRI enterography. However, if the active disease is reachable by upper endoscopy or colonoscopy, I will also use that to monitor response to therapy.

G&H Do you have any other advice for managing these patients?

BC It is important to listen to the patient and obtain a good history. Gastroduodenal Crohn's disease can be missed, and it is important to perform a complete assessment to identify the entire distribution of disease. If the patient is experiencing any symptoms that may indicate gastroduodenal Crohn's disease such as dyspepsia or nausea, an upper GI assessment should be considered.

Physicians may feel a bit uncomfortable when managing patients with gastroduodenal and jejunoileal Crohn's disease because there is less evidence to guide management, and their disease course tends to be more severe. I think the key is for physicians to act as they would with lower GI tract Crohn's disease in terms of using advanced therapies early in the disease course, monitoring response to therapy, and making adjustments when not achieving therapeutic targets. This is most critical when dealing with any severe phenotype of Crohn's disease.

Disclosures

Dr Cohen has no relevant conflicts of interest to disclose.

Suggested Reading

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