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Isolated Severe Stricturing Duodenal Crohn Disease in a Pediatric Patient

Keren L. Appel, Linda Wang, Dong Xi, and Vrinda Bhardwaj

Crohn's disease (CD), a subentity of inflammatory bowel disease (IBD), is a chronic relapsing/remitting disorder characterized by segmental and transmural intestinal inflammation affecting the entirety of the gastrointestinal (GI) tract from mouth to anus. Patients most typically present with abdominal pain, bloody diarrhea, fatigue, anemia, weight loss, and/or extra-intestinal manifestations. However, gastroduodenal CD may present with symptoms of epigastric pain, dyspepsia, early satiety, anorexia, nausea, vomiting, and weight loss.

The first report of duodenal involvement of CD was described by Gottlieb and Alpert in 1937,[1] and later Ross[2] reported gastric CD in 1949. Recent reports suggest that upper GI tract (esophageal, gastric, and/or duodenal) involvement occurs in 0.5–4.0% of symptomatic adults with CD, with the majority having concomitant terminal ileal and colonic disease.[3] This incidence may be underestimated because upper endoscopy is not routinely performed in the initial evaluation of adult CD as in the pediatric population.[4]

Isolated gastric CD accounts for less than 0.07% of adult CD patients and is even rarer in the pediatric population.[5] Isolated duodenal CD is limited to a few cases in the adult literature.[6,7] A recent pediatric study also identified 2 incident cases of stricturing duodenal CD which partially responded to intensive medical therapy and ultimately required laparoscopic gastroduodenostomy.[8] Duodenal CD typically manifests as single, short segment duodenal strictures surrounded by nodular and ulcerated mucosa, rather than a fistulizing or perforating phenotype.[9] Patients are usually asymptomatic and diagnosed incidentally following cross-sectional imaging and/or esophagogastroduodenoscopy. Symptomatic cases, clinically manifesting as small bowel obstruction, are associated with a worse prognosis and more severe disease course.[9,10] We present a case of pediatric CD with rare isolated duodenal involvement resulting in severe stricturing.

CASE REPORT

A 12-year-old African American female with iron deficiency anemia presented with 2 months of weight loss, decreased appetite, abdominal pain, and bilious emesis. Physical examination revealed generalized abdominal tenderness and epigastric fullness. Laboratory evaluation was notable for thrombocytosis and elevated serum inflammatory markers. Initially, an upper GI series showed severe gastric distension and gastric outlet obstruction (Fig. 1A). Subsequent magnetic resonance enterography demonstrated marked distension of the stomach, first and second portions of the duodenum, with a decompressed third portion (Fig. 1B and C). The remainder of the visualized small and large bowel was normal. At first, only upper endoscopy was performed, given the presenting symptom of emesis without diarrhea or hematochezia, and revealed complete obstruction at the second portion of the duodenum (Fig. 2A). Biopsies showed chronic gastritis and mildly active duodenitis with chronicity proximal to the stricture. There was no evidence of granulomas, viral inclusions, or malignancy.

She subsequently underwent laparotomy guided by endoscopy to resect a long-segment stricture of the third and fourth portions of the duodenum with duodenojejunostomy. Gross nodularity was noted on the serosal aspect at the level of the ligament of Treitz. Pathology of the resected bowel demonstrated chronic lymphocytic inflammation and multiple granulomas were seen on a seromuscular biopsy of the proximal jejunum (Fig. 2B and C). Testing for both chronic granulomatous disease and tuberculosis was negative. Postoperatively, she received total parenteral nutrition and required nasogastric tube decompression for high-volume output.

Additional investigation was aimed to identify the etiology of her severe duodenal inflammation and stricturing. Fecal calprotectin was normal at 40.7 mg/kg. Repeat endoscopy after surgery showed duodenitis with increased eosinophils (40 per high-power field) and several nonbleeding duodenal ulcers (Fig. 3A). The anastomotic site had chronic active duodenitis with full-thickness ulceration (Fig. 3B). The colon and terminal ileum were endoscopically and histologically normal (Fig. 3C and D). *Helicobacter pylori*, viral, and fungal stains were negative. Further evaluation including anti-nuclear antibody, myeloperoxidase antibody, cytoplasmic and perinuclear anti-cytoplasmic antibodies, and radioallergosorbent testing were also negative. An IBD diagnostic panel was positive for anti-*Saccharomyces cerevisiae* IgA and IgG antibodies, consistent with CD. She also had elevated tissue transglutaminase (TTG) IgA antibody (41 U/mL), deamidated gliadin IgA antibody (134 U/mL), and antiendomysial IgA antibody titer (1:5) in the setting of a normal total IgA level.

Three months later, she returned with bilious emesis and malnutrition requiring total parenteral nutrition. She was given intravenous steroids, started infliximab (10 mg/kg at weeks 0, 2, and 6), and discharged on a soft mechanical diet. Prior to her first maintenance infliximab dose, she had recurrent bilious emesis (drug level of 18 µg/mL and no detectable antibodies). Repeat magnetic resonance enterography showed a dilated proximal duodenum and stomach with an anastomotic site stricture, requiring multiple endoscopic balloon dilations without improvement. A 15-mm lumen-apposing metal stent (LAMS) was deployed over a guidewire across the 10-mm stricture to help alleviate the obstruction and dilate it over 2 months.

During that time, she significantly improved and advanced to a regular diet. She continued to receive a proton-pump inhibitor,

Received June 3, 2020; accepted July 14, 2020.
From the Division of Gastroenterology, Hepatology, and Nutrition, Children's Hospital Los Angeles (CHLA), Los Angeles, California.
Address correspondence and reprint requests to Keren L. Appel, MD, Division of Gastroenterology, Children's Hospital Los Angeles, 4650 Sunset Blvd, MS#78, Los Angeles, CA 90027 (e-mail: kdallal@gmail.com).
The authors report no conflicts of interest.

JPGN Reports (2020) 1:2(e003)
ISSN: 2691-171X
DOI: 10.1097/PG9.0000000000000003

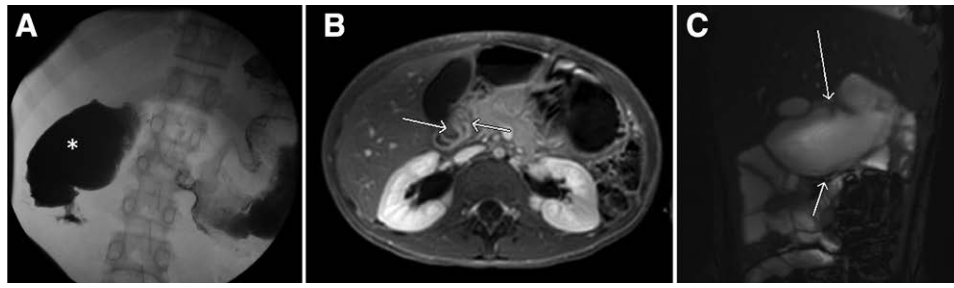

FIGURE 1. Initial radiologic findings. A) Upper gastrointestinal series showed gastric outlet obstruction with no contrast passing beyond a severely distended stomach. B) Magnetic resonance enterography with distal duodenal stricture and (C) marked distention of the stomach and first and second portions of the duodenum with a decompressed third portion.

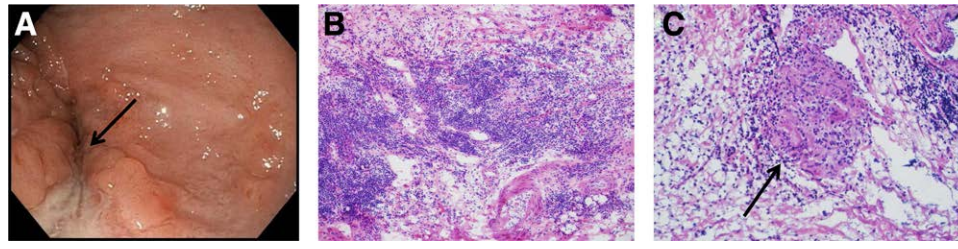

FIGURE 2. Initial endoscopic and surgical findings. A) Upper endoscopy revealed complete obstruction at the second portion of the duodenum. B) Seromuscular biopsy of the proximal jejunum showed prominent chronic lymphocytic inflammation and (C) rare ill-defined granulomas with foreign-body multinucleated giant cells (hematoxylin and eosin stain, 100×). No evidence of gram-positive or gram-negative bacteria, fungal elements, or acid fast bacilli.

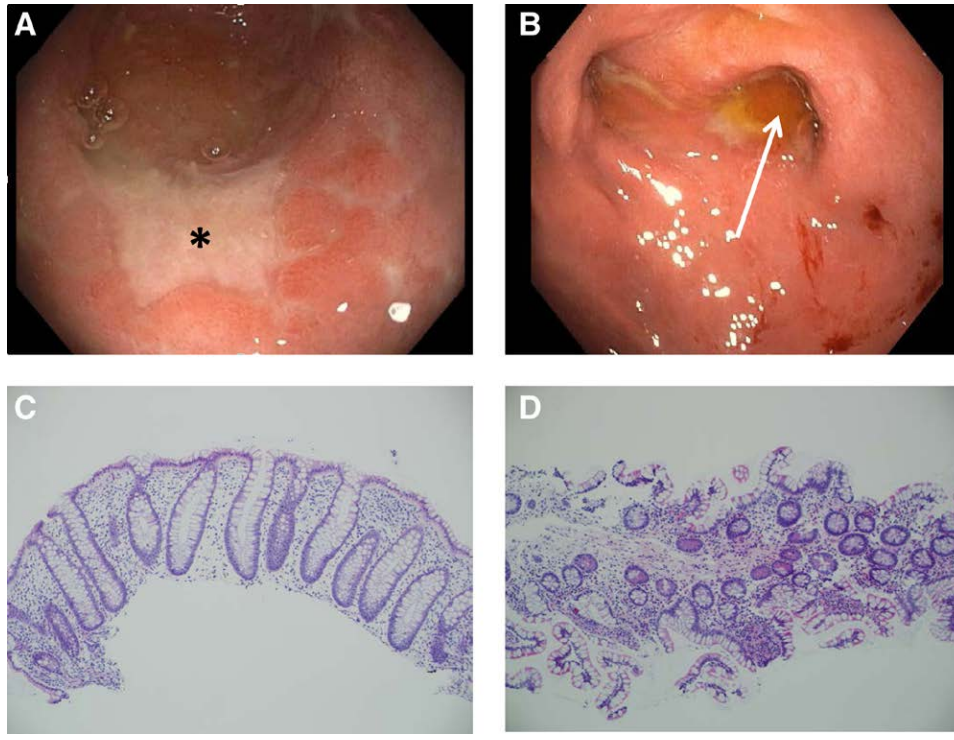

FIGURE 3. Interval endoscopy with recurrent duodenal stricturing. A) Endoscopy after surgery showed duodenitis with increased eosinophils (40 per high-power field) and several nonbleeding duodenal ulcers. B) Anastomotic site with chronic active duodenitis and full-thickness ulceration. The colon (C) and terminal ileum (D) were both endoscopically and histologically normal.

low-dose oral steroids, and infliximab (10 mg/kg every 4 weeks and later every 8 weeks) as maintenance therapy. Repeat endoscopy 18 months after initiation of infliximab showed complete visual improvement of the duodenal inflammation with biopsies revealing only a mild increase in intraepithelial lymphocytes in the duodenum and jejunum without villous atrophy. The colon was once again visually and histologically normal.

DISCUSSION

This case presented with a wide differential diagnosis that included *H. pylori*, celiac disease, eosinophilic GI disease, autoimmune disease, and GI tumors. Detection of noncaseating granulomas, only found with deeper seromuscular biopsy, ultimately helped diagnose CD. Interestingly, the patient's celiac markers were elevated. The prevalence of serologic celiac disease in patients with IBD has previously been described and is thought to relate to mucosal barrier defects.[11] Increased intestinal tight junction permeability may lead to increased antigen presentation and, therefore, generation of autoantibodies.[12] TTG can also be overexpressed in apoptotic tissue, such as mucosal lesions due to chronic bowel inflammation.[13] Other studies have also described false-positive anti-TTG antibodies as a phenomenon of autoimmunity.[14] Celiac markers, repeated after initiation of IBD therapy, had normalized without gluten restriction. Moreover, the classical features of celiac disease were never present on duodenal biopsies.

The treatment of this patient's stricturing CD involved a multifaceted approach including early surgical intervention, total parenteral nutrition, prolonged steroids, anti-tumor necrosis factor (TNF) therapy, and endoscopic dilations. The effectiveness of infliximab in isolated gastroduodenal CD is limited to a few adult case reports with unknown long-term outcomes.[15,16] In a prospective study, 19 of 119 adults with CD had upper GI tract involvement, and of those 11 were treated with anti-TNF therapy (10 with infliximab and 1 with adalimumab). After 12 weeks, 8 of the 11 patients had significant macroscopic improvement and 7 had significant histologic improvement of their upper GI disease.[17] Here we discuss a pediatric case where infliximab was used to maintain long-term disease remission.

Management of stricturing disease typically also involves a combination of surgical resection and endoscopic balloon dilation to relieve obstruction while maximizing bowel conservation. Indications for surgery include failure of medical management with intractable pain, bleeding, perforation, and fistulous disease.[18] Endoscopic dilation has been noted to have 87% short-term clinical efficacy with major complications arising in 2.9% of procedures. With a 2-year follow-up period, 70.5% of patients had recurrence of symptoms, 59.6% required redilation, and 30.8% required surgical intervention. Patients with small bowel disease had a higher risk for symptom recurrence and repetitive dilations.[19]

In this case, a LAMS was used when the patient's anastomotic duodenal stricture did not respond to dilation alone. LAMS was initially developed to drain peripancreatic fluid collections by creating a cyst-gastrostomy, but they have also been used to stent short luminal strictures.[20] The distal flange was deployed downstream to the stricture under fluoroscopic guidance, and the stent's proximal end was then deployed under both fluoroscopic and endoscopic guidance. The stents are fully covered to prevent tissue ingrowth and therefore have decreased stent migration risk and are endoscopically removable with a snare or forceps. LAMS has been used to stent esophageal and duodenal strictures in adults[21]; however, their use in pediatrics is rare.

In conclusion, it is atypical to have isolated duodenal CD present as early gastric outlet obstruction. This case emphasizes that a high index of suspicion is necessary to diagnose isolated duodenal CD. It also highlights the many therapeutic challenges we faced, requiring a multidisciplinary approach involving anti-TNF, surgical, and advanced endoscopic treatments. We discuss the novel use of LAMS as an adjunct therapy to alleviate obstructive symptoms.

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