A Puzzling Case of Refractory Constipation in a Young Adult. Diagnostic Approach and Treatment Outcomes

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Abstract
A 19-year-old male had a several-year history of chronic constipation, which had been refractory to all forms of medical therapy. The persistent condition had prompted frequent ER visits for disimpaction. Lower GI bleeding with severe iron deficiency anemia required up to two blood transfusions per month. When this patient was referred to our Gastroenterology Motility Center, idiopathic-slow colonic transit was documented. Colonoscopy showed erythematous friable colonic mucosa due to the chronicity and severity of his disease. Surgical biopsies were negative for adult Hirschprung’s disease. Subtotal colectomy with colorectal anastomosis was performed. Histopathology revealed some degree of muscular fibrosis and scattered Interstitial Cajal Cells (ICC), which play a major role in normal colonic motility. This patient is now one year post-surgery, and has returned to a more normal quality of life.

Introduction
Constipation is characterized by unsatisfactory defecation that results from difficult stool passage (straining, hard stools), infrequent stools or both. The standard definition is less than three bowel movements per week. It has been reported that 99% of U.K. population has a stool frequency between three bowel movements per week to three per day. Constipation affects between 2 to 27% with an approximate mean of 15% of the population. Constipation is more common in women than men, non-white than white, children than adult and elderly than younger adults.

Constipation is most often mild and intermittent, but in some cases it becomes chronic, consuming and debilitating. Etiologically, chronic constipation can be approached in the following ways: neurogenic forms are divided into peripheral (e.g.: diabetes, Hirschsprung disease, Chagas) and central (e.g.: multiple sclerosis and spinal cord injury). Systemic disorders (e.g.: systemic sclerosis, hypokalemia, hypothyroidism) or idiopathic. Idiopathic chronic constipation can be subdivided into slow transit or normal transit with accompanying dyssynergic defecation.

This review focuses on a Case Report about a young male with chronic constipation with reoccurring fecal impaction and incontinence spanning 18 years, eventually surgically managed definitively to provide a marked improvement in his quality of life.

Case Presentation
A 19-year-old male with a protracted history of iron deficiency and chronic constipation since he was two years old, had eventually been referred to the GI motility center. He recounted an average one bowel movement producing “very hard, pebble-like black stools” per week since childhood. Over the years, polyethylene glycol, bisacodyl, magnesium citrate, senna and other over-the-counter laxatives had been tried in addition to prescription medications including lubiprostone and linaclotide. His constipation required multiple emergency department visits and hospital admissions each year for stool disimpaction (Figure 1). In recent years, the patient has developed overflow fecal incontinence necessitating adult diapers for constant dark fecal leakage.

Fig 1. Chest X-Ray showing a distended splenic flexure and transverse colon elevating the left hemidiaphragm.

During the two years prior to his referral to the GI motility center, the patient developed severe iron deficiency anemia, with hemoglobin as low as 3g/dl., requiring blood transfusions one to two times per month. Diagnostic work-up for celiac disease was negative. Iron studies and bone marrow biopsy with flow cytometry ruled out hematopoietic defects. Following positive
A Puzzling Case of Refractory Constipation in a Young Adult.
Diagnostic Approach and Treatment Outcomes
(Continued)

fetal occult blood tests, iron deficiency anemia was attributed to occult fecal blood loss. Hematochezia had not been previously reported. A pediatric gastroenterologist subsequently identified the source of bleeding as well documented slow colonic transit. The patient was hospitalized for one week to evacuate the colon in order to proceed with the colonoscopy. Despite being on liquid diet and laxatives for one week, the colonoscopy was incomplete due to continued presence of mucky stool coating the dilated colon. Due to residual fecal matter, the proximal transverse colon was the farthest region that could be adequately visualized. The mucosa was erythematous and friable. Colonic transit testing demonstrated slow-transit constipation with retention of 20% of radiopaque markers after 5 days.

Then, the patient was referred to the GI motility center to consider the possibility of adult Hirschsprung’s disease. There, a barium enema was performed that showed a markedly dilated sigmoid colon measuring 20 cm with a narrowed rectosigmoid transition area (Figure 2). Those findings were suggestive of with an aganglionic zone. A subsequent anorectal manometry study revealed that rectal sensation was markedly impaired, with threshold up to 100cc of balloon inflation (normal is 20-25cc), incomplete anal canal relaxation during Valsalva maneuver but normal internal and external anal sphincter pressure. Relaxation of the internal anal sphincter during balloon distention in the rectum was equivocal.

The next step was a subtotal colectomy to create an ileo-rectal anastomosis approximately 20cm from the anus while maintaining the diverting ileostomy. Biopsies from the resected colon revealed acute inflammation of the mucosa with crypt abscesses consistent with the working hypothesis that the ulceration, bleeding and infection could be attributed to a possible “decubitus colitis” from the constant pressure of fecal impaction, explaining the anemia. Mild to moderate collagen fibrosis was also present within the muscularis propria. Ganglion cells were detected throughout the colon using S-100 and CD56 immunostain with positive calretinin immunostain ruling out aganglionosis (Figure 3). There were scattered interstitial cells of Cajal (ICC) stained with C-KIT immunostain. There are no defined numbers of ICC in the muscularis propria patients with idiopathic slow transit chronic constipation compared to a normal colon. The ICCs in this patient were very scattered and interpreted as reduced in number in the muscularis propria of the colon muscle tissue (Figure 4).

Fig 2. Barium enema showed an extremely dilated sigmoid colon, and fecal material was noted to be present at 20 cm proximal to the anus.

Based on the strong diagnostic probability of adult Hirschsprung’s disease, rectal biopsies were obtained, however, the presence of ganglion cells in submucosal and myenteric plexus excluded the diagnosis of Hirschsprung’s disease. In review of the extensive workup of his refractory constipation, there was a joint decision by Departments of Gastroenterology and General Surgery that surgery was warranted to address the working diagnosis of “idiopathic constipation”. The surgical team performed a decompression ileostomy and a rectal biopsy. Terminal ileum biopsy showed normal small bowel mucosa with ganglion cells. The rectal biopsy again showed presence of ganglion cells with a swollen axonal appearance and chronic inflammation in the myenteric plexus, definitively excluding Hirschsprung’s disease. Six months after the diverting ileostomy, the patient was reporting substantial symptom relief.

Six months later with continued excellent symptomatic progress, the ileostomy was taken down at the time of a third surgery. One year after the last surgery the patient had appropriately gained

Continued on page 10
A Puzzling Case of Refractory Constipation in a Young Adult.
Diagnostic Approach and Treatment Outcomes
(Continued)

Figure 4. Myenteric plexus and ganglion cells of the colon muscle were stained by S100 and found to be intact with only mild swelling ruling out adult Hirschsprung’s disease.

body weight, had no recurrence of constipation, nor has he required any blood transfusion. This patient’s life is much better after surgery. He is a college student, and is able to have a normal high quality life.

Discussion
Most patients define constipation based on the number of bowel movements per week. In addition, symptoms include hard stools with a presence of ≤ 2 on the Bristol stool scale, infrequent stools, necessity for excessive straining and sense of incomplete bowel evacuation with unsuccessful defecation.8,9 Physical inactivity, depression, low income and history of sexual abuse are known risk factors for chronic constipation.10 Changes in diet, fiber intake, and physical activity can reduce the symptoms but many patients with severe cases seek specialist attention.11

Rome III Criteria for chronic constipation are ≥ 12 week/months (not necessarily consecutive weeks) of at least two of the following symptoms:
• Straining during >25% of bowel movements
• Lumpy or hard stools for >25% of bowel movements
• Sensation of incomplete evacuation for >25% of bowel movements
• Manual maneuver to facilitate >75% of bowel movements (e.g., digital evacuation)
• <3 bowel movements per week
• Insufficient criteria for irritable bowel syndrome met.

Several mechanisms may explain chronic constipation in a patient. Idiopathic constipation can be classified into three categories: normal-transit constipation, slow-transit constipation, and dyssynergic rectal evacuation.12

Normal-transit constipation
Normal-transit constipation, also known as functional constipation, is the most common cause of chronic constipation, accounting up to 59% of the cases. Patients believe they are constipated because they have difficulty passing stools on a regular basis.13 This type of constipation usually resolves with conservative therapy.

Defecatory disorders
This dysfunction is commonly due to anismus (dysfunction of anal sphincter) also termed pelvic floor dysfunction. It can be identified clinically or with ano-rectal motility test and defecography. Patients may have a medical history of sexual or physical abuse. Up to 30% of the patients with “idiopathic” constipation have this dysfunction which can co-exist with normal transit constipation.

Slow-transit constipation
In 1969, Hinton et al described a new method of measuring total intestinal transit with the use of radiopaque markers called Sitz marker study. Normal subjects were able to pass 80% of the radiopaque marker within 5 days. Subjects who retained more than 20% of the markers at 5 days were categorized as idiopathic slow-transit constipation.14,15 Slow transit constipation occurs most commonly in women who have infrequent bowel movements (as few as 1 per week) and often poorly responsive to laxatives and fiber. Associated symptoms such as abdominal pain, bloating, malaise, nausea and anorectal symptoms are indicative of delayed rectal expulsion.11

Slow-transit constipation is a clinical syndrome attributable to ineffective colonic propulsion with delayed emptying of the proximal colon and fewer high-amplitude peristaltic contractions after meals,2 yet none of these abnormalities is pathognomonic for the disorder.16 Anorectal and defecatory studies can identify patients with dyssynergic defecation, based on an increase in external sphincter pressures during attempted expulsion of a 60mm water balloon. This test may be used as an office-based screening method.17 Patient with slow transit constipation may or may not have an accompanying dyssynergic disorder.17

Histopathological studies in patients with slow transit constipation have shown alterations in the myenteric plexus,18 decreased-neurofilaments in the myenteric plexus and variable alterations in nerves containing vasoactive intestinal peptide and substance P, and inhibitory transmitters like vasoactive intestinal peptide and nitric oxide.19 Furthermore, significantly fewer nerve fiber and interstitial cells of Cajal (ICC) in the sigmoid colon in slow-transit constipation have been reported. Those can be detected using antibodies directed against gene product 9.5 and c-kit.10 ICC play an important role in intestinal motility. The interstitial cells of Cajal generate the electrical slow waves in the smooth muscle that determine the rate of bowel contractions than can occur. They also play a role in signaling between the nerve and the smooth muscle.16,19,20 Our patient had a reduction in ICC number as well as degrees of moderate fibrosis on the smooth muscle. We believe these factors, probably present since birth, contributed to his persistent refractory condition. The anemia was secondary to a form of “decubitus colitis” due to chronically impacted stool evoking inflammation and bleeding of colonic mucosa.

Surgery
Surgery is last line of treatment, only recommended for patients with refractory constipation after all medical therapies have failed and have no treatable defecatory disorder. Appropriate candidates
A Puzzling Case of Refractory Constipation in a Young Adult.
Diagnostic Approach and Treatment Outcomes
(Continued)

for surgery have slow-transit constipation with colonic stasis. Colectomy and ilorectal anastomosis is the treatment of choice. The most common complications after surgery are frequent bowel movements and incontinence. There are reports that diarrhea and incontinence improve after the first year. A complete workup for slow transit defecation including rectal manometry and defecography studies had the best outcomes with a satisfaction rate of 89%, compared to patients without a complete workup and a premature decision to operate with ~80% satisfaction rate. About 90 per cent of patients with proven slow transit constipation have favorable outcomes.

Conclusion
Idiopathic slow transit constipation beginning in infancy will often resolve with laxatives. Refractory cases where Hirschsprung’s disease has been excluded will require surgery, which provides access to a tissue diagnosis by examining the colonic smooth muscle and can result in a successful outcome.

References


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