A Case of Segmental Hypoganglionosis of the Colon

Running title: Segmental Hypoganglionosis of the Colon

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Abstract
A 64-year-old female was admitted to the hospital with constant abdominal pain. She had been previously hospitalized five times in 2 years with similar symptoms. Computed tomography revealed dilatation and fecal impaction from the ileum to the transverse colon. A barium enema and simultaneous ileus tube radiography demonstrated a segment of narrow descending-sigmoid colon. Colonoscopy did not show any mucosal change. These symptoms did not improve with conservative therapy when a descending and sigmoid colectomy was performed. In terms of histology, there was a disappearance of ganglion cells, and axon of Meissner’s plexuses was present along with a decrease in the number of Auerbach’s plexuses. The definite diagnosis given was segmental hypoganglionosis (SH) of the colon. The postoperative course was uneventful, and the functional result was positive following 1 year postoperatively. SH is extremely rare; however, surgical intervention is expected to be of benefit. Therefore, it is important to keep SH in mind when treating patients with chronic obstruction in the left side of the colon as it can cause SH.

Key words: colectomy, colon, dilatation
Introduction

Segmental hypoganglionosis (SH) is a rare condition, and one of the main symptoms of SH is chronic intermittent obstruction caused by a partial expansion failure of the intestine, wherein neural plexuses and ganglion cells are decreased in the submucosal or intramucosal layers\textsuperscript{1,2}. SH may be considered as a subtype of colonic pseudo-obstruction or similar disease of adult Hirschsprung’s disease, but it is still controversial. A definite diagnosis is only possible by histochemical characteristics from a full-thickness biopsy; therefore, it can be difficult to diagnose this condition preoperatively. This study reports a surgical case of SH in which the patient suffered from recurrent obstruction symptoms for a long period of time.

Case report

A 64-year-old woman was admitted to the hospital for severe abdominal pain and lack of defecation over the past few days. She had been prone to constipation for several years and occasionally used laxatives. She has been previously admitted five times with similar symptoms in the past 2 years. Her medical and family histories were unremarkable. A physical examination showed gross abdominal distention, moderate tenderness in the epigastrium, and no rebound tenderness. Bowel sounds were active and showed no increase. Laboratory evaluation including a white blood cell count and C-reactive protein were normal. An abdominal X-ray showed the niveau of the ileum and colon dilatation across the entire abdomen. Abdominal computed tomography (CT) revealed dilatation with feces present from the ileum to the transverse colon. The dilated transverse colon was elongated, but there was no significant obstruction and no suspected sign of tumor lesion (Fig. 1). Colonoscopy demonstrated a narrow segment in the descending colon and sigmoid colon with intact mucosa (Fig. 2). An ileus tube radiography and
Barium enema were simultaneously performed, which revealed a narrow segment in the descending colon and sigmoid colon with spastic change and diverticula and a dilated colon and ileum above the stricture (Fig. 3). A conservative therapy of fasting and ileus tube radiography was effective; however, a surgery was proposed owing to the patient’s recurrent symptoms. An informed-consent was acquired from the woman and her family. Upon surgery, a significantly dilated and redundant ascending and transverse colon were found (Fig. 4). The descending and sigmoid colon were both spastic and hard. Additionally, the diameter of the intestine was remarkably small and had diverticulitis. This area was considered to be responsible for the disease, so it was decided that the lesion between the middle of the transverse colon and the sigmoid colon would be removed. We performed primary anastomosis by functional end-to-end anastomosis. Due to the considerable risk of leakage with dilated intestine, we added buried suture to staple line and performed the decompression treatment by ileus tube radiography in the perioperative period to further prevent the anastomotic leakage. The transverse colon was markedly dilatated to 14 cm in diameter, while the descending colon was 4.5 cm, and there was no presence of a tumor lesion in the mucosa (Fig 5a). Histologically, the ganglion cells and fibers were not observed in Meissner’s plexuses, and the number of Auerbach’s plexuses was decreased with degenerative tendency of the ganglion cells in the narrow segment (Fig. 5b-e). A definite diagnosis of SH in the colon was made. The postoperative period was uneventful, and the patient was discharged 14 days postoperatively. Follow-up information was obtained 1 year postoperatively in the outpatient clinic, and the patient was well and had normal continence.

[Insert Figures 1–5 here]
Discussion

Segmental hypoganglionosis has been reported in cases with segmental dilation failure, diminution of ganglion cells, and degeneration of the Auerbach’s or Meissner’s plexuses in the segment with poor dilation on histopathological findings. Currently, there is no established theory explaining the cause behind this pathology. Degeneration and disappearance of myenteric neurons secondary to anoxemia, inflammation, and/or viral infections of the bowel wall are involved in this pathology.

Intramural neurons of the intestinal tract develop from vagus nerves in the early fetal stage, in which neuroblasts migrate down the gastrointestinal tract sequentially in a rostral to caudal manner, as proposed by the craniocaudal migration theory. Abnormal development during this stage can cause esophageal achalasia, which is characterized by abnormalities of gangliocytes in the lower esophagus, while congenital absence of neurons of the intestinal wall continuously from the rectum is understood to constitute Hirschsprung’s disease.

SH is acquired, occurs subacutely, and is relatively common in adults. Lesions are observed in the segment between the descending colon and sigmoid colon. Mecholyl, a cholinergic agent, was previously used for diagnostic tests by provoking a hyper-reaction to the autonomic drug at the segment with neural defect, but is no longer in use due to causing adverse reactions in the circulatory system. Specific markers such as the radiopaque marker may be useful for assessing the transition time for the functional evaluation. The diagnosis of SH is only possible through histochemical examination of a full-thickness biopsy. The histopathological characteristics include a significant reduction in the number of ganglion cells, thickened muscularis mucosae, and muscularis propria layers. More recently, S-100 and peripherin were validated as valuable
tools for the diagnosis of SH\textsuperscript{8}. The number of C-KIT immunoreactive cells or 171B5 (a novel marker of synapses) immunoreactive synapses were reduced in the muscle layers of the bowel affected by Allied Hirschsprung’s disease\textsuperscript{9}. Since the infiltration of T lymphocytes can lead to the death of neurons, this can cause a reduction in e-kit signaling\textsuperscript{10}. As a diagnostic image, double-contrast barium enema and CT images reveal a caliber change compared with the dilated proximal colonic segment to narrow distal segment.

Surgery is considered the definitive treatment method for SH\textsuperscript{11}. The stricture site alone may be resected\textsuperscript{7,12}, but some cases may require subtotal proctocolectomy for marked dilation or when an extensive resection is deemed necessary to remove the dilated portion. An inadequately selected resection site can result in anastomotic stricture.

Recurrent bowel obstruction occurs due to various diseases\textsuperscript{13}. Dudley et al. described a clinicopathology of chronic functional obstruction without organic obstruction as chronic intestinal pseudo-obstruction (CIP)\textsuperscript{14}. CIP can be classified according to the affected areas; CIP limited to the colon is defined as a colonic pseudo-obstruction (CPO)\textsuperscript{15}. Primary CPOs are caused by digestive tract lesions, secondary CPO by systemic disease or drugs, and idiopathic CPO by unknown causes. Primary CPO comprises Hirschsprung’s disease and Allied disorders of Hirschsprung’s disease, including SH\textsuperscript{1,6}. Secondary CPO has been drawing recent attention in studies investigating the involvement of viral infections, such as in the study by Debinski et al. who tested for the presence of EBV and CMV in CPO using nested polymerase chain reaction\textsuperscript{16}.

Hirschsprung’s disease is marked by dysperistalsis and absent anorectal reflex originating in aganglionosis of the distal enteric tract and can result in impaired passage of intestinal contents, delayed meconium passing, and megacolon. The majority is congenital, but it has also been reported to develop in adults after a chronic course\textsuperscript{17}. In recent years, there has been a group of
diseases in which symptoms and test findings are similar to Hirschsprung’s disease despite the presence of normal ganglion cells in the rectum, which has been termed as Allied Hirschsprung’s diseases in Japan\textsuperscript{18}. The majority of patients develop diseases of this group in childhood, but onset can also occur in adulthood for some patients, and SH is one such disease.

Several studies in the literature related to SH were reviewed. It was found that 17 cases were reported in Japan. The age of the patients ranged from 31 to 72 years, with males predominating over females with a 11:5 ratio. The site of the disease was localized from transverse to descending colon in all of the cases. All patients were treated surgically, and with the exception of two patients who underwent subtotal colectomy, surgery involved resection of the affected segment in the colon. However, there is no consensus on how the extent of this resection should be determined.

Due to the lack of clear diagnostic criteria for SH, the patient was diagnosed by general assessment of symptomatic course, laboratory findings, and diagnostic surgical pathology. Preoperatively, SH was not expected as the primary disease. The stricture site was determined to be the extent of resection based on intraoperative findings suggesting the pathology of subobstruction due to stagnation and volvulus on the rostral side of the narrowed enteric tract. The anal side of the tract was long; thus, it was reconstructed by a functional end-to-end anastomosis, which resulted in an improvement of defecation symptoms without postoperative stricture of the anastomotic site. The functional end-to-end anastomosis is a useful method because of the low frequency of bleeding, stenosis, and anastomotic leakage\textsuperscript{19}; on the contrary, blind loop syndrome is a unique complication of functional anastomosis. For this disease, in the intestinal tract with neural abnormality, the anastomosis method requires more attention and follow-up, and it is necessary to devise the obtuse angle of the intestinal tract. The extent of resection was deemed adequate; however, histopathological findings showed degeneration of ganglion cells on the anal
margin, and the healthy segment was not included. There are similar cases in which only the dilated segment was resected because preoperatively SH was not considered to be the cause. This also included cases where the main lesion was not completely resected, resulting in postoperative recurrent stricture, and cases in which the anal margin included the lesion, causing anastomotic stricture to occur. Quick pathological diagnosis was difficult because the ganglion cells were scattered and the examination of ganglion cells in the long axis of the intestine was necessary. We thus secured a centimeter margin from the stricture site. Detailed pathological examinations of the resected specimen are necessary for assessing neural abnormality in SH; thus, it is important to pay attention to the clinical features such as the recurrent bowel obstruction without organic obstruction and laboratory findings, and list SH as a differential diagnosis preoperatively and to plan therapeutic strategies accordingly. Future cases such as these should be investigated for establishing diagnostic criteria for SH.

We reported a case of SH in which surgical treatment after a long period of suffering allowed for histopathological diagnosis.

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Conflict of Interest:

The authors declare that there are no conflict of interest.
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**Figure legends**

Fig 1. Abdominal computed tomography (CT)

Abdominal CT scan revealed dilatation and elongation of ascending to transverse colon. Residue build-up and dilation of the ileum was also observed.

Fig 2. Lower gastrointestinal endoscopy findings

Colonoscopy showed a narrow segment in the descending colon and sigmoid colon with intact mucosa.

Fig 3. Ileus tube radiography and barium enema.

Ileus tube radiography revealed no obstructive lesion in the ileum or in the dilated ascending colon. 

a. In the barium enema study, the transition zone of dilated transverse to narrow descending colon was remarkably recognized.

b. The rectum was dilated by insufflation.

Fig 4. Surgical findings of the patient

The surgery revealed that the descending and sigmoid colon were narrow with spastic change and diverticula. The ascending and transverse colon were redundant and dilated.

Fig 5.

a. Macroscopic appearance of the marked caliber change and intact mucosa.

b and c. Histopathological findings of the yellow square area of segmental hypoganglionosis in Fig. 5a.

d and e. Histopathological findings of the green square area of the normal area in Fig. 5a.
The number of ganglion cells (triangle marks) in the present case were reduced compared with that in the normal area (b, d: Hematoxylin and Eosin stain; c, e: S-100 stain).
Figures

Fig 1.
Fig 2.
Fig 3.
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Fig 5.