A Rare Case of Adult-Onset Rectosigmoid Hypoganglionosis

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient:	**Male, 20**
Final Diagnosis:	**Rectosigmoid hypoganglionosis**
Symptoms:	**Severe abdominal pain • obstipation • vomiting • shortness of breath • palpitations**
Medication:	**—**
Clinical Procedure:	**Hartmann's procedure**
Specialty:	**Surgery**

**Objective:** Congenital defects/diseases

Background: Intestinal hypoganglionosis is very rare and accounts for 3% to 5% of all classified congenital intestinal innervation disorders. Isolated hypoganglionosis of the colon is a particularly rare form of the disease, and differential diagnosis includes association with Hirschsprung's disease and chronic intestinal pseudo-obstruction (CIPO) related to visceral myopathies. Most cases are diagnosed at an early age or in childhood with only a few cases reported in adults.

Case Report: We report a case of isolated hypoganglionosis of the rectum and sigmoid presenting as an emergency with acute intestinal obstruction in a 20-year-old male patient. A history of chronic constipation was reported since childhood, but this condition had never been investigated. A preoperative CT scan showed a megasigmoid and megarectum. A Hartmann's procedure was performed. The patient made a slow recovery and was discharged on the 12th postoperative day in good condition. Histology showed features consistent with isolated hypoganglionosis, and a full thickness rectal biopsies taken 2 months later confirmed the diagnosis.

Conclusions: Isolated hypoganglionosis in an adult is very rare, and a high index of suspicion is warranted in young patients with a history of chronic constipation to avoid delayed presentation as an emergency.

MeSH Keywords: Adult • Delayed Diagnosis • Hirschsprung Disease

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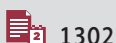
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Background

Intestinal innervation disorders represent a cluster of malformations of the intestinal nervous system and include intestinal neuronal dysplasia, Hirschsprung's disease, hypoganglionosis, and ganglioneuromatosis [1–3]. Although these subtypes have distinct histopathological features, clinical manifestations are similar with chronic constipation or pseudo-obstruction being the most common presenting symptoms [1,2]. Differential diagnosis includes chronic intestinal pseudo-obstruction (CIPO) that can be associated with visceral myopathies and mutations of the ACTG2 gene involved in myenteric contractility [4]. Hypoganglionosis is divided into 2 types: the isolated and Hirschsprung-associated form [5]. Isolated hypoganglionosis is rare, representing 3% to 5% of all congenital intestinal neurological diseases [6]. The histopathological features include hypertrophy of the muscularis mucosae, decrease in the activity of acetylcholinesterase in the lamina propria, and significant reduction in the number of myenteric ganglia. Diagnosis and ability to differentiate between different patterns of innervation is based on histopathology and immuno-histochemical markers [5,6]. The disease most commonly present in infancy or childhood with only a few cases reported in adults mainly diagnosed after elective surgery for intractable constipation or pseudo-obstruction [7,8]. The authors report a case of isolated hypoganglionosis in an adult presenting as an emergency; we also provide a review the literature.

Case Report

A 20-year-old male Saudi patient presented to the Emergency Department complaining of severe abdominal pain, obstipation, vomiting, shortness of breath, and palpitations. Past history revealed intermittent constipation since early childhood that had never been investigated and self-treatment with on and off use of laxatives. No symptoms of urinary dysfunction or infections were reported. He had no co-morbidities and was not on any medication. Family history was unremarkable. On examination, the patient was tachycardic (heart rate, 140 beats per minute), hypertensive (blood pressure, 146/92 mmHg), and tachypneic (respiratory rate, 23 breaths per minute). The abdomen was grossly distended with rebound tenderness and bowel sounds were scant. Fluid resuscitation and oxygen administration were initiated. A nasogastric tube and urinary catheter were inserted. Blood tests revealed a leukocyte count of 12 900 cells/µL and blood gas levels showed mild respiratory alkalosis. Acute x-ray series showed large-bowel dilatation with multiple air-fluid levels (Figure 1). A computed tomography (CT) scan of the abdomen and pelvis revealed gross dilatation of the sigmoid and rectum with a diameter up to 20 cm with a functional obstruction at the level of the lower rectum. No wall thickening, peri-colonic stranding, pneumatosis, or pneumoperitoneum
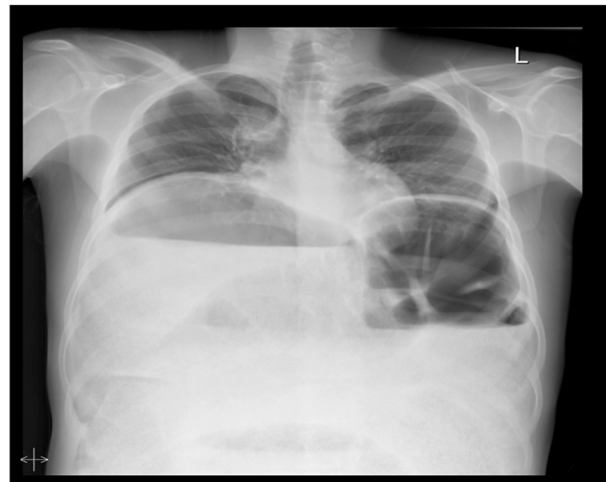

Figure 1. Acute x-ray series: The large bowel is dilated and filled with fecal matter, and multiple air-fluid levels are noted.

Figure 2. Preoperative computed tomography scan (sagittal view): Gross dilatation of the sigmoid and rectum.

were noted. There was significant stool volume throughout. The small bowel and urinary bladder were displaced by the distended colon to the right, with the liver and gallbladder being displaced posteriorly (Figure 2). An emergency laparotomy was performed, and this revealed a redundant megasigmoid and rectum (Figure 3). A rigid sigmoidoscopy was carried out and showed only fecal impaction with no evidence of obstructing lesions. A Hartmann's procedure was performed. The patient made a slow but uneventful recovery and was discharged on the 12th postoperative day. Histopathological examination of the resected specimen showed features consistent with hypoganglionosis. The ganglion cells were reduced but normal with no signs of degeneration or gliosis (Figure 4A–4C). The
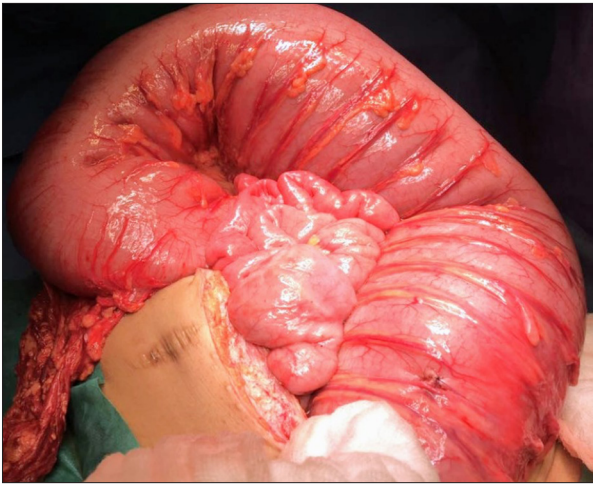
Figure 3. Intraoperative findings: The sigmoid and rectum measure approximately 20 cm in diameter.

muscularis mucosa was unremarkable with absence of atrophy, vacuolar degeneration, fibrosis, and normal collagenous network raising no suspicion of myopathy (Figure 4D). The proximal resection margin showed normal ganglia distribution. At 2 months from the surgery, full thickness rectal biopsies were taken under general anesthesia just above the dentate line for further characterization of the innervation disorder. Histology of the rectal specimen confirmed the diagnosis of hypoganglionosis with no evidence of agangliosis. The patient was reluctant to undergo definitive surgery and at 1-year follow-up had no complaints with a perfectly functioning colostomy.

Discussion

The most common intestinal innervation disorder is Hirschsprung's disease with a reported prevalence of 1: 5000
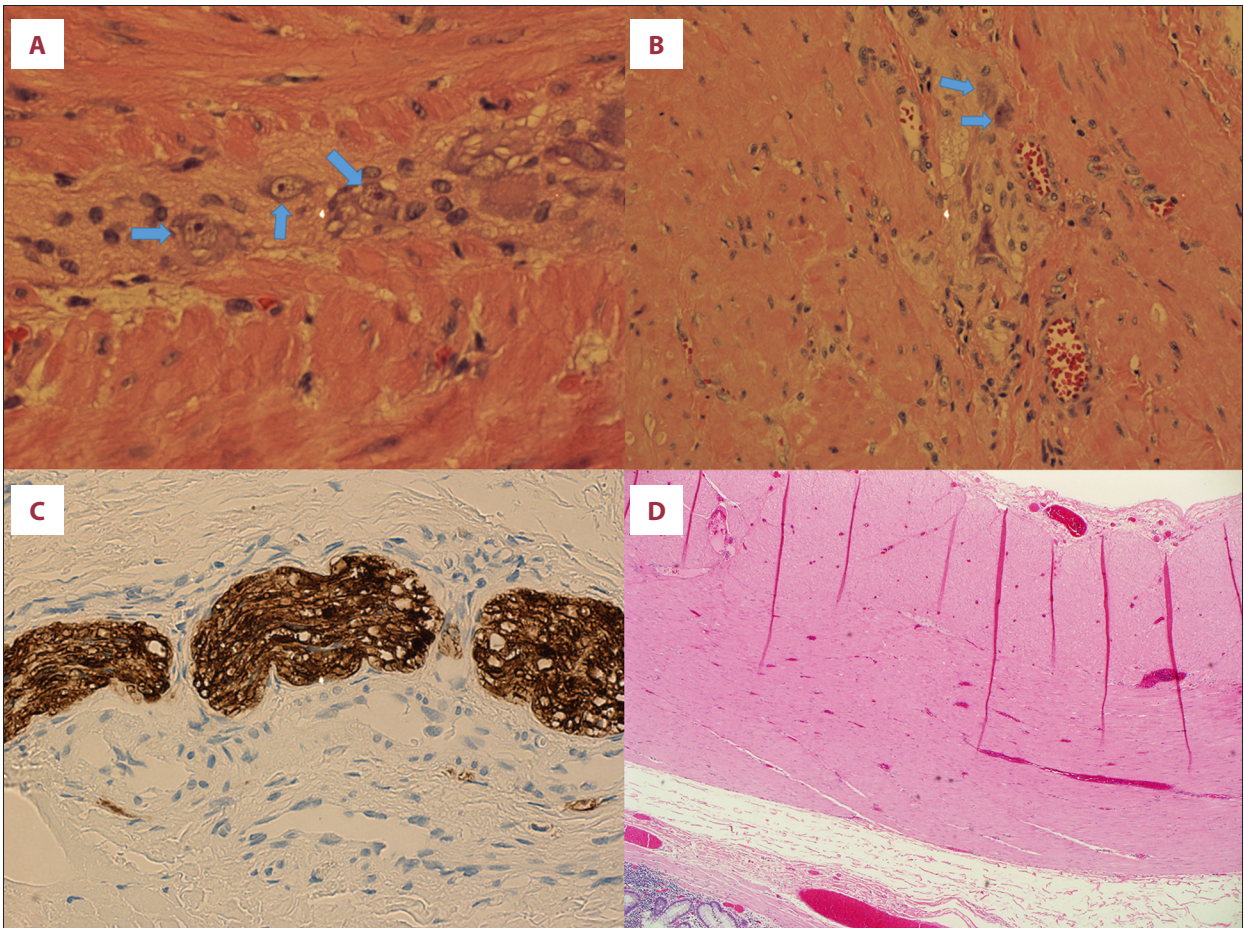

Figure 4. Histology findings: (**A**) Sigmoid colon: reduced number of ganglion cells (arrows) (hematoxylin and eosin staining, magnification 20×). (**B**) Proximal resection margin showing ganglion cells (arrows) (hematoxylin and eosin staining, magnification 40×). (**C**) Immunohistochemical staining (S100) showing hypertrophied nerve bundles. (**D**) Full-thickness bowel section showing unremarkable muscularis propria.

and a female to male ratio of 1: 4 [9]. The disease is characterized by the congenital absence of ganglion cells in the submucosal and myenteric neural plexuses of the rectal wall with variable extension proximally. Etiology is represented by impaired craniocaudal migration of neuroblasts during the first 3 months of gestation [10,11]. The transition of the distal aganglionic segment to the proximal normal bowel may be characterized by a segment of hypoganglionosis with maintained but reduced number of ganglia [11,12]. A number of ganglia less than 10 mm is generally considered diagnostic for hypoganglionosis [13]. Isolated hypoganglionosis not related to Hirschsprung's disease is a distinct and rare disorder. In this variety, the submucosal nerve plexus is normal while a significant reduction in the myenteric ganglia is noted. Other features include hypertrophy of the muscularis mucosae and decreased acetylcholinesterase activity in the lamina propria [5,6]. In congenital hypoganglionosis, the number and size of ganglion cells is reduced at birth, and although their size increases with time, their number does not change. On the other hand, acquired hypoganglionosis is of late onset and characterized by a degeneration of ganglion cells and histological findings of gliosis [13]. Histological examination of full-thickness rectal biopsies is the gold standard for diagnosis. Hematoxylin and eosin stain is most commonly used and allows for diagnosis in most cases. However, morphologic immaturity and small size of ganglion cells with irregular distribution in the submucosa may limit identification with high expertise needed. Also, acetylcholinesterase staining is technically demanding and not universally available [14]. More recently peripherin, S-100, and Calretinin immunohistochemistry have been shown to be a valuable tool to aid diagnosis [14–16]. Hypoganglionosis should be distinguished by cases of CIPO related to visceral myopathy that can be associated with mutations of the ACTG2 gene mutations involved in muscle contractility. In these cases, a family history is often positive, functional dysfunction of other organs is common as well as pathological features of the muscularis propria including vacuolization and fibrosis [4]. A recent review of the literature identified 92 patients with a diagnosis of isolated hypoganglionosis (69 males and 23 females with a mean age of 4.85 years) [6]. Symptoms at presentation included chronic constipation or pseudo-obstruction. Only 70% of these patients had surgical intervention at the time of presentation and

of these 80% had definitive surgery with pull-through procedures and 16% stoma formation. The overall mortality was 8%. A recent nationwide study in Japan reported 109 cases of isolated hypoganglionosis and provided detailed information on 90 patients (34 males and 56 females) with 19 being excluded from the study for diagnostic doubt or incomplete descriptions [17]. The diagnosis was made in the neonatal period in all patients. Almost all patients were initially treated with formation of stoma. Creation of a jejunostomy was significantly associated with a lower mortality. The overall mortality rate was 22%. A study from South Korea reported 24 cases of adult presentation of hypoganglionosis in patients who had undergone surgery for intractable constipation or chronic pseudo-obstruction. The mean age was 40 years [8]. There are only 5 other cases in the literature with adult presentation of hypoganglionosis as an emergency [7,18–21]. Paucity and intermittence of symptoms had allowed for a late diagnosis and ultimate acute presentation. Three of these case presented with toxic megacolon, 1 with phytobezoar obstruction and 1 with sigmoid volvulus. In our case, the initial sigmoid resection had shown hypoganglionosis with normal proximal resection margin. Subsequent rectal biopsies excluded agangliosis and confirmed hypoganglionosis. A functional obstruction seen on preoperative CT scan is a common finding in these patients and usually associated with a greater reduction of ganglion cells at the level of the transition zone [8].

Conclusions

Isolated hypoganglionosis is very rare and a high index of suspicion is required in young patients with prior history of chronic constipation to avoid delayed diagnosis and emergency presentation. Histopathology and immunohistochemistry allow differentiation among the various patterns of innervation disorders. Acute presentation with need of emergency surgery is rare and treatment should be limited to colonic resection with subsequent definitive treatment of the rectal disease.

Conflicts of interest

None.

References:

1. Montedonico S, Cáceres P, Muñoz N et al: Histochemical staining for intestinal dysganglionosis: Over 30 years experiencewith more than 1,500 biopsies. Pediatr Surg Int, 2011; 27: 479–86

2. Knowles CH, De Giorgio R, Kapur RP et al: The London Classification of gastrointestinal neuromuscular pathology: Report on behalf of the Gastro 2009 International Working Group. Gut, 2010; 59: 882–87

3. Schäppi MG, Staiano A, Milla PJ et al: A practical guide for the diagnosis of primary enteric nervous system disorders. J Pediatr Gastroenterol Nutr, 2013; 57: 677–86

4. Milunsky A, Baldwin C, Zhang X et al: Diagnosis of chronic intestinal pseudo-obstruction and megacystis by sequencing the ACTG2 gene. J Pediatr Gastroenterol Nutr, 2017; 65: 384–87

5. Kobayashi H, Yamataka A, Lane GJ, Miyano T: Pathophysiology of hypoganglionosis. J Pediatr Gastroenterol Nutr, 2002; 34: 231–35

6. Dingemann J, Puri P: Isolated hypoganglionosis: Systematic review of a rare intestinal innervation defect. Pediatr Surg Int, 2010; 26: 1111–15

7. Qadir I, Salick MM, Barakzai A, Zafar H: Isolated adult hypoganglionosis presenting as sigmoid volvulus: A case report. J Med Case Rep, 2011; 5: 445

8. Do MY, Myung SJ, Park HJ et al: Novel classification and pathogenetic analysis of hypoganglionosis and adult-onset Hirschsprung's disease. Dig Dis Sci, 2011; 56: 1818–27

9. Amiel J, Lyonnet S: Hirschsprung disease, associated syndromes, and genetics: A review. J Med Genet, 2001; 38: 729–39

10. Badner JA, Sieber WK, Garver KL, Chakravarti A: A genetic study of Hirschsprung disease. Am J Hum Genet, 1990; 46: 568–80

11. Puri P, Gosemann JH: Variants of Hirschsprungdisease. Semin Pediatr Surg, 2012; 21: 310–18

12. Zhang HY, Feng JX, Huang L et al: Diagnosis and surgical treatment of isolated hypoganglionosis. World J Pediatr, 2008; 4: 295–300

13. Taguchi T, Masumoto K, Ieiri S et al: New classification of hypoganglionosis: Congenital and acquired hypoganglionosis. J Pediatr Surg, 2006; 41: 2046–51

14. Holland SK, Hessler RB, Reid-Nicholson MD et al: Utilization of peripherin and S-100 immunohistochemistry in the diagnosis of Hirschsprung disease. Mod Pathol, 2010; 23: 1173–79

15. de Arruda Lourenção PL, Takegawa BK, Ortolan EV et al: A useful panel for the diagnosis of Hirschsprung disease in rectal biopsies: Calretinin immunostaining and acetylcholinesterase histochesmistry. Ann Diagn Pathol, 2013; 17: 352–56

16. Montedonico S, Piotrowska AP, Rolle U, Puri P: Histochemical staining of rectal suction biopsies as the first investigation in patients with chronic constipation. Pediatr Surg Int, 2008; 24: 785–92

17. Watanabe Y, Kanamori Y, Uchida K, Taguchi T: Isolated hypoganglionosis: Results of a nationwide survey in Japan. Pediatr Surg Int, 2013; 29: 1127–30

18. Pescatori M, Hattana C, Castiglioni GC: Adult megacolon due to total hypoganglionosis. Br J Surg, 1986; 73: 765

19. KahramancaŞ, Özgehan G, Celep BR et al: Isolated adult hypoganglionosis resulting in toxic megacolon: A case report. Kafkas J Med Sci, 2014; 4: 36–39

20. Ito T, Kimura T, Yagami T et al: Megacolon in an adult case of hypoganglionosis, a pseudo-Hirschsprung's disease: An autopsy study. Intern Med, 2008; 47: 421–25

21. Karpagam B, Vinayagam S, Kishore J, Samuel J: Isolated adult hypoganglionosis presenting as sigmoid phytobezoar: A case report. Dig Dis Sci, 2011; 56: 1818–27