Megacolon in an Adult Case of Hypoganglionosis, a Pseudo-Hirschsprung’s Disease: An Autopsy Study

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Abstract

We report an autopsied 20-year-old man case of intestinal necrosis associated with megacolon from hypoganglionosis, a pseudo-Hirschsprung’s disease. The patient had suffered from severe constipation since two years of age, and presented abdominal distention from age ten. Autopsy revealed marked dilatation and necrosis of the entire large intestine. Although ganglion cells in the intestinal plexus were found throughout the large intestine, their number was reduced to 12-20% of that in the normal control. In pseudo-Hirschsprung’s disease, there are occasional cases where an acute abdomen first presents itself in adulthood after running its course as chronic constipation.

Key words: megacolon, pseudo-Hirschsprung’s disease, hypoganglionosis, adult, autopsy


Introduction

Pseudo-Hirschsprung’s disease is characterized by gastrointestinal motility disorders that closely resemble Hirschsprung’s disease despite the presence of intramural ganglion cells throughout the large intestine. Usually, symptoms of chronic ileus present in the newborn period (1-4). The term “pseudo-Hirschsprung’s disease” is a collective term comprising different disease entities, including immature enteric intramural neuronal cells (5), declines in the number of intramural neuronal cells (hypoganglionosis) (6), neuronal intestinal dysplasia (7), chronic idiopathic intestinal pseudo-obstruction syndrome (8) and megacystis-microcolon-intestinal hypoperistalsis syndrome (9, 10). Here, we report an autopsy case of hypoganglionosis in an adult patient who was in cardiac arrest on admission.

Case Report

A 20-year-old man in cardiac arrest was admitted to our hospital. His mother provided the following medical history. The patient had suffered from severe constipation since two years of age, and presented abdominal distention from age ten. A private clinic took an X-ray and diagnosed the child’s condition as chronic refractory constipation. The use of large amounts of laxatives only produced small amounts of watery stools at a time, and at one point the patient refused to attend school, concerned about this condition. After entering high school, the patient always used laxatives and sometimes complained about his abdominal distension. There was no family history of the disease.

On the first day of the illness, the mother found the patient face down on the bathroom floor. There were no early signs such as complaints of abdominal pain. The mother called the ambulance, during which time the patient lost...
consciousness. When the emergency team arrived at his house, he was in cardiac arrest. Cardiopulmonary resuscitation (CPR) was performed in the ambulance while transferring the patient to the hospital.

CPR was performed in the emergency room, which managed to restore spontaneous circulation and respiration. Vital signs upon recovery of circulation were consciousness of Glasgow Coma Scale E1 V1 M4, spontaneous respiratory rate 19 breaths per minute, heart rate 88 beats per minute regular rhythm, blood pressure 50/20 mmHg, and axillary temperature 36.0°C. Physical findings on examination were height 165 cm, weight 80 kg, no head wounds, no conjunctival anemia or jaundice, normal pupil reaction to light, no chest murmur or rales, severe distention of the abdomen with hard abdominal walls, no lower-limb edema, and no abnormal neurological findings. Two to three kilograms of muddy stools were extracted from the anus, followed by hematochezia. There was neither ischemic change nor arrhythmia on electrocardiograph.

Blood testing and urinalysis results were as follows: White blood cells 37,600 per mm³, hemoglobin 10.8 g/dl, hematocrit 38.0 percent, total proteins 7.2 g/dl, blood urea nitrogen 27.9 mg/dl, creatinine 1.3 mg/dl, aspartate aminotransferase 118 mg/dl, alanine aminotransferase 46 IU/l, γ-glutamyl transpeptidase 16 IU/l, lactate dehydrogenase 705 IU/l, potassium 4.9 mEq/l, c-reactive protein <0.3 mg/dl and glucose 218 mg/dl, troponin T (-), urinary proteins (-), urinary sugars (-), urinary occult blood (-), urinary acetone (-). Arterial blood gas (FiO₂ 100%) analysis demonstrated pH 6.89, PaCO₂ 40.6 mmHg, PaO₂ 85.1 mmHg, HCO₃⁻ 7.7 mmol/L, BE -24.4 mmol/L, clearly indicating metabolic acidosis. There was a rapid progression of anemia after two-and-a-half hours: hemoglobin 6.9 g/dl and hematocrit 23.4 percent. The patient’s general condition did not allow for emergency surgery, and the patient was not able to recover from shock during this time and died the following day, on the second day of his illness.

Autopsy restricted to abdominal organs was performed one hour after death. Macroscopically, marked dilatation of the entire large intestine and ileum was found (Figs. 1, 2). Intestinal walls were thinned in the ascending to descending colon, and thickened in the sigmoid colon and rectum. A large volume of muddy stools and some hematochezia were present in the intestinal canal. In the ascending to descending colon, necrosis was evident in the mucosa, submucosa, and muscularis propia (MP) was noted. Neutrophil infiltration and hemorrhage was found in the mucosa, submucosa, muscularis propia, and subserosa (bottom) (Hematoxylin and Eosin staining, ×40).
portion of ileum also showed mild necrotic changes. The stomach, duodenum and jejunum were intact.

Histologically, ganglion cells in the intestinal plexus were found throughout the large intestine. However, the number of ganglion cells in this case was reduced compared with the control cases. The control cases used in this study were autopsy cases without intestinal disorders (n=5, age 24 to 67). In the sigmoid colon and rectum, we counted the number of ganglion cells of myenteric or submucosal plexus per 3 cm in length on histological sections. The number of ganglion cells of myenteric plexus was 16 to 27 in this case and 135 +/- 20 (mean +/- S.D.) in the controls. The number of ganglion cells of submucosal plexus was 17 to 23 in this case and 144 +/- 25 in the controls. In the myenteric and submucosal plexuses of the sigmoid colon and rectum of this patient, the number of ganglion cells was approximately 12-20% of that in the control cases (Figs. 4, 5). We performed silver staining, and the results confirmed the observations by Hematoxylin and Eosin staining. In the ascending to descending colon, since necrosis was extensive but some areas showed relatively preserved histology, such areas were used for evaluation of the ganglions. Because even in these areas the mucosal and submucosal layers showed marked necrotic changes, we were able to evaluate only the myenteric plexus. A decreased number of ganglion cells was noted in the myenteric plexus of the ascending, transverse, and descending colons. From these observations, it was strongly suggested that hypoganglionosis existed in the entire length of the large intestine diffusely. Heterotopic ganglion cells, which were abnormally placed in the muscularis mucosae or within the muscle bundle of the muscularis propria, were sometimes seen (Fig. 6). Isolated ganglion cells were also observed in the submucosal plexus (Fig. 7). In the submucosa of the normal control cases, one ganglion usually consists of more than one ganglion cells grouped together; in this case, isolated ganglion cells were frequently found. Regarding the nerves, aganglionic segment, hyperplasia nor narrow segment was identified. There was no abnormality which appeared to be responsible for his cardiac arrest in brain at suboccipital puncture. These autopsy findings indicated that the patient died of severe intestinal necrosis associated with megacolon due to hypoganglionosis.
the present case; patients with pseudo-Hirschsprung’s disease undergo surgery during childhood.

Discussion

We diagnosed the cause of megacolon as hypoganglionosis based on the histopathological findings showing a significantly small number of intramural ganglion cells in the large intestine. There was no perforation of the gastrointestinal tract, however, we can assume that intra-intestinal pressure became abnormally high and effected necrosis in parts of the bowel probably by ischemia, which caused further bowel necrosis from shock. Hematochezia further aggravated the state of shock, creating a vicious cycle that lead to cardiac arrest.

Most patients with Hirschsprung’s disease and pseudo-Hirschprung’s disease undergo surgery during childhood. However, there have been several reports in Japan similar to the present case; patients with pseudo-Hirschprung’s disease (11-14) who are diagnosed with chronic refractory constipation as infants and present acute abdomen in adulthood. The present case was prescribed laxatives by his family physician who diagnosed the condition as chronic constipation persisting since early childhood. When chronic constipation does not improve after various differential diagnosis and conservative treatment, and when it is associated with abdominal distention and megacolon, diagnostic tests such as rectal biopsy should be considered in order.

Cases where chronic pseudoileus causes intestinal necrosis and then leads to sudden death have been rarely reported. In the past, Evans et al reported a case of acute chronic intestinal pseudo-obstruction as a cause of death (15), which is somewhat similar to the present case. In their case, a naturally healthy 21-year-old man developed chronic pseudoileus after developing postprandial emesis and constipation and died. Following the emergency abdominal surgery, the necrotic small bowel from the ligament of Treitz to the distal ileum was found without evidence of obstruction. As a result of a histopathological examination, the diagnosis was visceral myopathy. However, details related to the ganglia of the intestine were not discussed. The authors simply supposed that the cause of the death was hypotension and hypoxia due to decreased venous return in the setting of the massive abdominal distention.

The present patient suffered from chronic constipation for about 20 years but his condition never deteriorated until the emergency admission. It is a significant point how an exquisite balance of bowel movements could be sustained during this period. The decline in the number of intestinal ganglion cells to 12-20% of that in the normal control appeared to be the critical point for the onset of the disease. We hope that the accumulation of reports of this type of cases will become a useful reference for determining the timing of surgery in infants and deciding the appropriate operative procedures.

Conclusion

We reported an autopsied adult case of megacolon in hypoganglionosis, a pseudo-Hirschsprung’s disease, together with histopathological analysis.

References


