

CASE REPORT

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Radiological Findings in Total Colon Aganglionosis and Allied Disorders

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Objective: The aim of this study was to review the radiological findings of three cases of total colon aganglionosis (TCA), hypoganglionosis, and immature ganglionosis, and to compare the differences in diagnosis and follow-up of these three disease entities.

Materials and Methods: Three neonates with neonatal onset of abdominal distension with vomiting were investigated, and the cases were diagnosed as TCA, hypoganglionosis, and immature ganglionosis, respectively. Radiological examination of each neonate was performed during the neonatal period and at follow-up.

Results: A plain abdominal radiograph showed massive abdominal bowel gas and multiple air-fluid levels in all cases. Barium enema findings including no transition zone, normal rectosigmoid index, reflux of barium into a dilated ileum, and retention of barium on delayed film were observed in all three cases. In aganglionosis and hypoganglionosis, a normal-sized colon, irregular contraction, shortening of the colon, and lack of redundancy were observed. In immature ganglionosis, microcolon was present but there was no shortening of the colon or loss of redundancy. Barium studies following ileostomy during childhood revealed no efficient peristalsis after the neonatal period in patients with aganglionosis and hypoganglionosis. Conversely, the patient with immature ganglionosis showed maturity of colonic function on barium studies after infancy.

Conclusion: The clinical and radiological findings of TCA and allied disorders are similar in neonates. Sequential contrast intestinal studies could reveal peristalsis of the colon wall, suggesting maturity of the ganglion cells.

Key words: colon, aganglionosis, hypoganglionosis, immature ganglionosis, contrast barium study

INTRODUCTION

HIRSCHSPRUNG'S DISEASE is a form of functional intestinal obstruction characterized by congenital absence of ganglion cells in the submucosal and intramuscular layers of the distal colon. The extent of bowel segments involved in this disease varies. Total colon aganglionosis (TCA) is a rare disorder, with an estimated incidence of 5-15% among cases of

Hirschsprung's disease.^{1,2} Functional obstruction of the colon may also be caused by paucity or immaturity of ganglion cells, defined as allied disorders of Hirschsprung's disease, or pseudo-Hirschsprung's disease.³

In this study, the radiological findings of three cases of TCA and allied disorders were reviewed and correlated with their pathological features.

Case 1: Total colon aganglionosis

A 3-day-old girl was admitted to hospital with vomiting of bilious material and massive abdominal distension. She had been born at full-term weighing 2,890 g. She had one brother and one sister, and had no significant family history. No meconium was discharged spontaneously. An AP upright radiograph showed dilated bowel loops with multiple air-fluid levels (Fig. 1A). A barium enema study revealed a normal-caliber colon with loss of normal redundancy involving the

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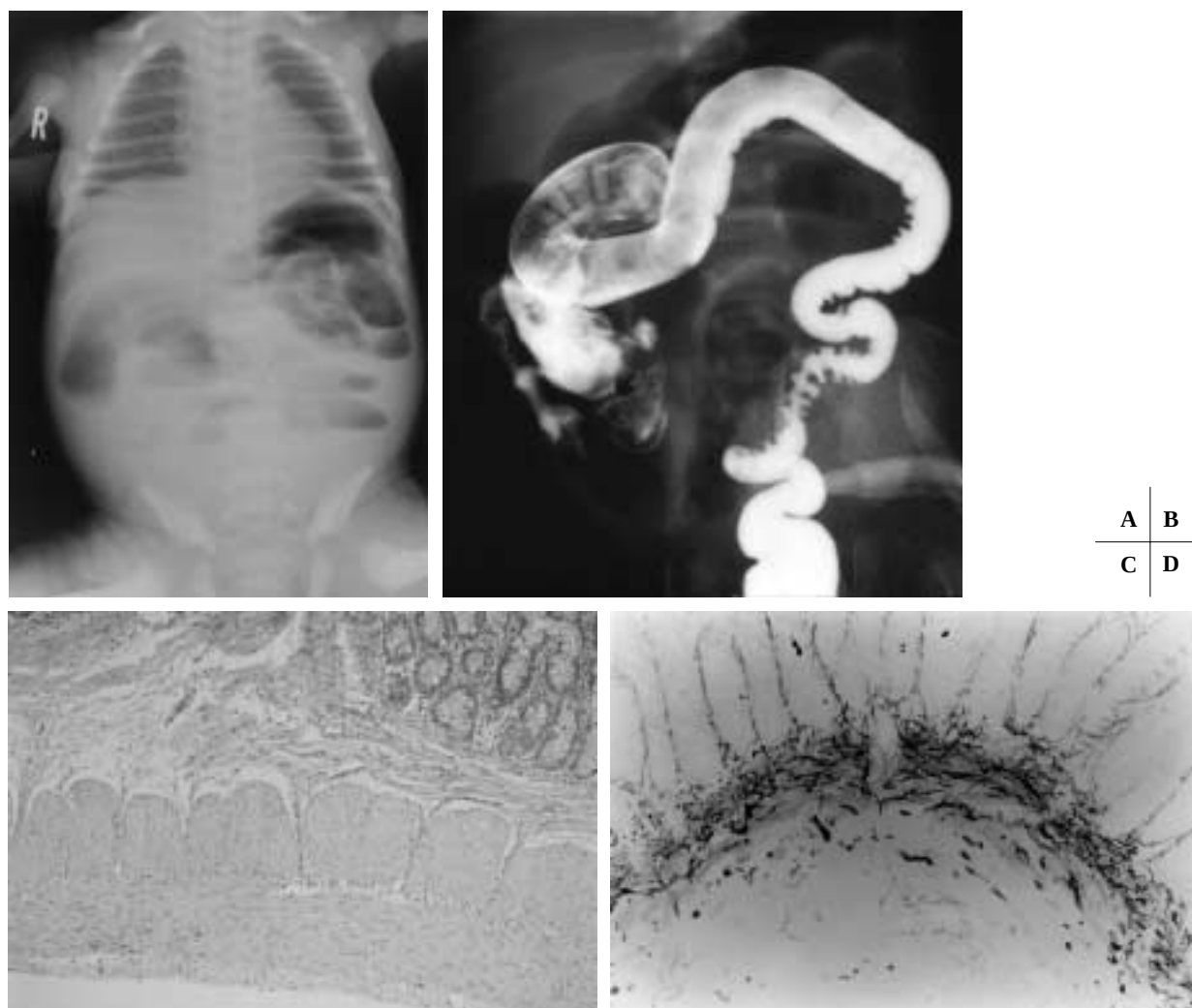


Fig. 1. Total aganglionosis. (A) AP upright radiograph shows dilated bowel loops with multiple air-fluid levels. (B) Barium enema study reveals small caliber colon with loss of normal redundancy of sigmoid colon, splenic, and hepatic flexures. A “saw-tooth” appearance of the sigmoid colon and reflux of barium into the dilated small bowel can also be observed. (C) Hematoxylin-eosin staining of the specimen demonstrates the absence of ganglion cells in the submucosal and intramuscular layer of the narrowed distal ileum (original magnification, $\times 100$). (D) Immunohistochemical stain for acetylcholinesterase demonstrates marked proliferation of neural fibers without a ganglion cell, consistent with aganglionosis (original magnification, $\times 100$).

entire colon. The sigmoid and descending colon had a serrated appearance with contour indentation. Reflux into the dilated small bowel was also noted (Fig. 1B). At laparotomy, the entire colon and the distal 5 cm of the ileum were narrowed in caliber. Ileostomy was performed 15 cm proximal to the narrowed segment. Hematoxylin-eosin staining of the specimens obtained from multiple biopsies of the colon and ileum, including dilated and non-dilated segments during laparotomy, demonstrated absence of ganglion cells in the submucosal and intramuscular layers of the narrowed distal ileum and ascending colon (Fig. 1C). However, there were normal ganglion cells in the biopsy specimen obtained from the ileum 20 cm proximal to the Bauchin valve. Histochemical staining for acetylcholinesterase showed pronounced proliferation of neural fibers in the

submucosal layer of the narrowed segments without ganglion cells (Fig. 1D). The final diagnosis was total colon aganglionosis. At the age of 9 months, a second operation was carried out involving resection of the proximal 20 cm of the ileum, right hemicolectomy using the resected ascending colon as a colonic patch graft in order to enhance water absorption from the colon, and formation of a new ileostomy. At the age of 1 year and 5 months, a barium enema examination from the anus revealed no movement of the barium column in the residual colon after 9 days. A residual barium column was seen in the left colon 18 days post-examination. At the age of 1 year and 7 months, resection of the residual colon, closure of the ileostomy, and anastomosis of the distal end of the ileum to the upper end of the rectum were performed. The patient has been readmitted many

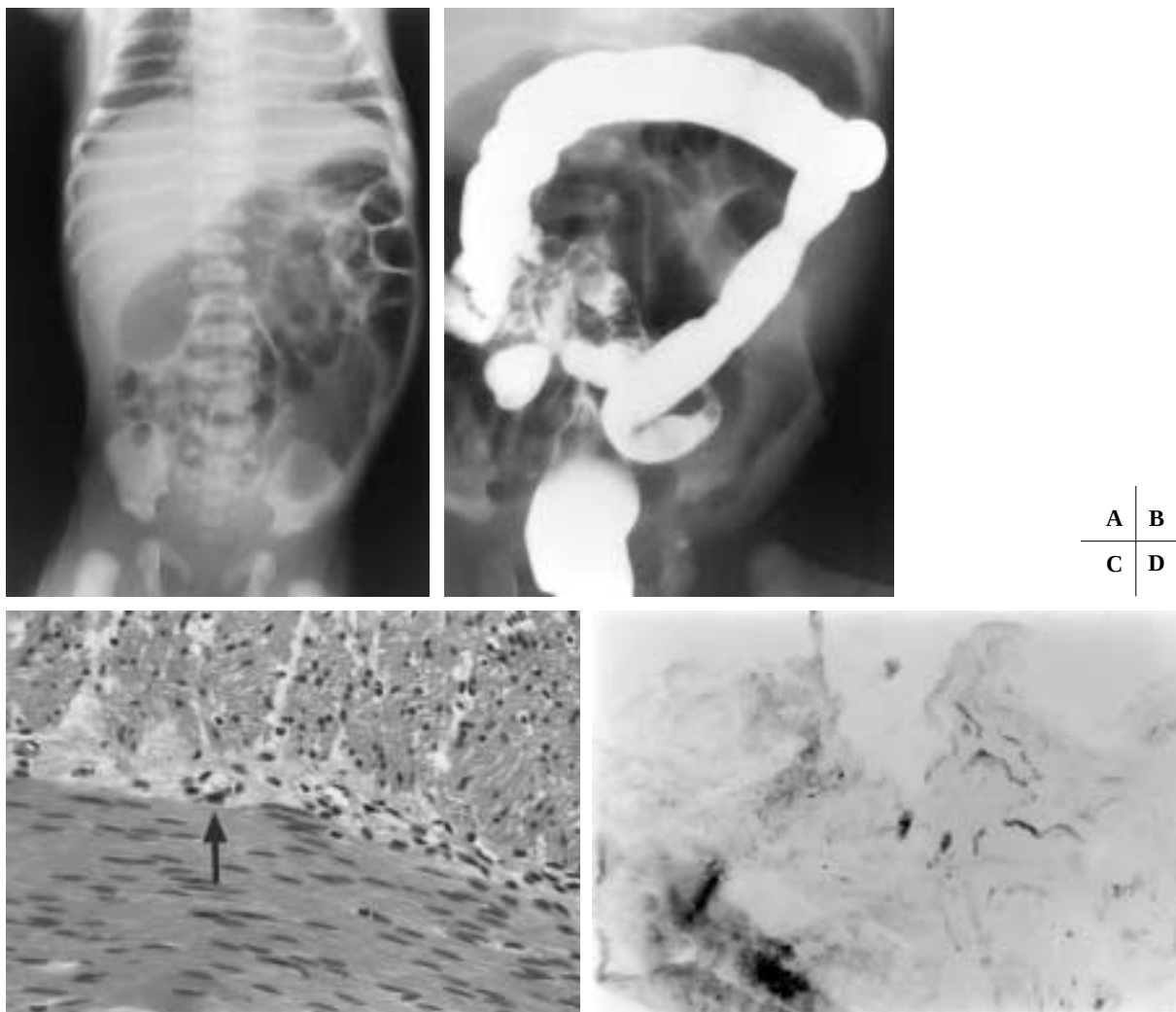


Fig. 2. Hypoganglionosis. (A) AP supine radiograph shows marked gaseous bowel distension. **(B)** Barium enema study reveals a relatively short colon with spasm of the sigmoid. Reflux of contrast into a dilated ileum and distension of the rectum can be observed. Marked dilation of the small bowel is also present. **(C)** Hematoxylin-eosin staining of the specimen demonstrates hypoplasia of the myenteric neural plexus and an oligoganglionic state (*arrow*) (original magnification, $\times 200$). **(D)** Immunohistochemical staining for acetylcholinesterase demonstrates no proliferation of neural fibers with a small ganglion cell, consistent with hypoganglionosis (original magnification, $\times 200$).

times since this operation with relapsing enteritis, but is now in good condition at the age of 8 years.

Case 2: Hypoganglionosis

A 2-day-old girl was transferred to the hospital due to persistent vomiting of bilious material and a markedly distended abdomen. She was a first baby and had been born after a full-term, normal pregnancy. She had no significant family history. Her body weight was 3,142 g at birth, and had decreased to 2,844 g on admission. No meconium was discharged after birth. A plain supine radiograph (Fig. 2A) demonstrated marked gaseous bowel dilation without evidence of intra-pelvic bowel gas. A barium enema revealed a relatively short colon with normal caliber, spasm at the sigmoid, appropriate rectosigmoid index, and dullness of hepatic flexure.

Reflux of contrast into the marked dilation of the small bowel loops was noted (Fig. 2B). At the age of 22 days, an ileostomy was made in the dilated bowel at a site 50 cm proximal to the ileum end. At the time of this operation, the entire colon and a portion of the distal ileum 5 cm in length were narrow in caliber, and the proximal small bowel was markedly distended. Histological sections (Fig. 2C) obtained from multiple biopsies of the colon and ileum during laparotomy showed hypoplasia of the myenteric plexus and a few immature ganglion cells at the submucosal and intramuscular layers of the narrowed segment. Immunohistochemical staining for acetylcholinesterase demonstrated no proliferation of neural fibers with small ganglion cells, consistent with hypoganglionosis (Fig. 2D). A follow-up barium study from the stoma at the

age of 1 year and 11 months revealed no movement of the barium column in the colon by the next day. At the age of 3 years, partial resection of the colon and anastomosis of the ileum to the descending colon were performed. Subsequently, weight gain was insufficient and parenteral alimentation had to be continued until the patient was transferred to another hospital at the age of 4 years.

Case 3: Immature ganglionosis

A 2-day-old girl was admitted to the hospital with severe abdominal distension and bilious vomiting. She was a first baby and had been born at full-term weighing 2,840 g. She had no significant family history. No spontaneous passage of meconium was noted, but a small amount of sesame-like substance was discharged artificially from the anus. Although a gastric tube was inserted on the day of birth, abdominal distension became more prominent. An AP supine radiograph showed massive gaseous distension of the bowel (Fig. 3A). A barium enema study revealed microcolon. Lack of spasm and contour irregularity at the colonic walls was noted, whereas no shortening of the colon was noted, and the length of the entire colon appeared to be normal (Fig. 3B). After 24 h, barium was still distributed throughout the colon. At laparotomy, the entire colon and the distal 20 cm of the ileum were narrowed in caliber, and the dilated proximal ileum was filled with a large amount of meconium. An ileostomy was made at a site 30 cm proximal from the terminal ileum. Histological examination showed that the ganglion cells were small in size but the number of ganglion cells in the intramuscular layer of the narrowed segment was not decreased (Fig. 3C). Immunohistochemical staining for acetylcholinesterase demonstrated no proliferation of neural fibers (Fig. 3D). This patient was diagnosed as having immature ganglionosis. At the age of 1 year and 4 months, a barium study from the ileal stoma was performed using a paste in which barium was mixed with carrot powder to mimic the consistency of feces. This showed absence of peristalsis. At the age of 1 year and 10 months, a similar barium paste study again revealed no effective peristalsis. After this examination, partial ileostomy and side-to-side ileocolostomy with a colonic patch graft were performed. Histological examination of this specimen revealed persistent immaturity of the ganglion cells. At the age of 2 years and 5 months, a barium study from the anus showed evacuation of the barium, indicating the presence of peristalsis. A subsequent barium paste enema study performed the next day demonstrated clearance of the barium paste, consistent with effective peristalsis. Six months later when the patient was 3 years and 1 month

old, a barium paste study from the anus showed complete evacuation of the paste (Fig. 3E, F). Closure of the ileostomy was then performed. A histological study of the biopsy specimen confirmed maturation of the ganglion cells. The patient subsequently presented with anemia and enteritis several times, and an ulcer on the ileal patch was detected. This portion was resected at the age of 5 years and 7 months. The patient is now 9 years old and in good condition.

DISCUSSION

TCA is defined as aganglionosis limited to the total colon and distal 30-50 cm of the terminal ileum, whereas extensive aganglionosis (EA) is defined as aganglionosis of the total colon with involvement of the more proximal small intestine beyond this point.⁴⁻⁸ Immunohistochemical studies for acetylcholinesterase have revealed marked proliferation of neural fibers in the submucosal layer of the narrowed segments without ganglion cells. A nationwide survey of TCA and EA was performed between 1988 and 1992 in Japan.⁷ This survey reported a frequency of TCA of 4.5% (50 cases) and a frequency of EA of 5.2% (57 cases) among 1,121 cases of aganglionosis, and a male-to-female ratio for all types of aganglionosis of 3.4:1, and for TCA and EA of 1.5:1.

Functional obstruction of the colon may be caused by paucity or immaturity of ganglion cells and is defined as an allied disorder of Hirschsprung's disease. Since the 1960s, many cases of allied disorders of Hirschsprung's disease or pseudo-Hirschsprung's disease have been reported in Japan.⁹⁻¹¹ These cases showed similar clinical and radiological findings to Hirschsprung's disease. However, the histological findings were different to those of congenital aganglionosis. There are two types of allied disorders of Hirschsprung's disease (Table 1): one with normal ganglion cells and one with abnormal ganglion cells. The former entity includes chronic idiopathic intestinal pseudo-obstruction and megacystis-microcolon-intestinal hypoperistalsis syndrome. The latter entity with abnormal ganglion cells includes hypoganglionosis, immature ganglionosis (immaturity of ganglia), hypogenesis of ganglia, and intestinal neuronal dysplasia. When normal ganglion cells are present in the submucosal and intramuscular layers but their population is decreased, the disease is referred to as hypoganglionosis. In this disease, immunohistochemical staining for acetylcholinesterase demonstrated no proliferation of neural fibers, in contrast to TCA. When the number of ganglion cells is normal but the ganglion cells are prominently immature, the disease is referred

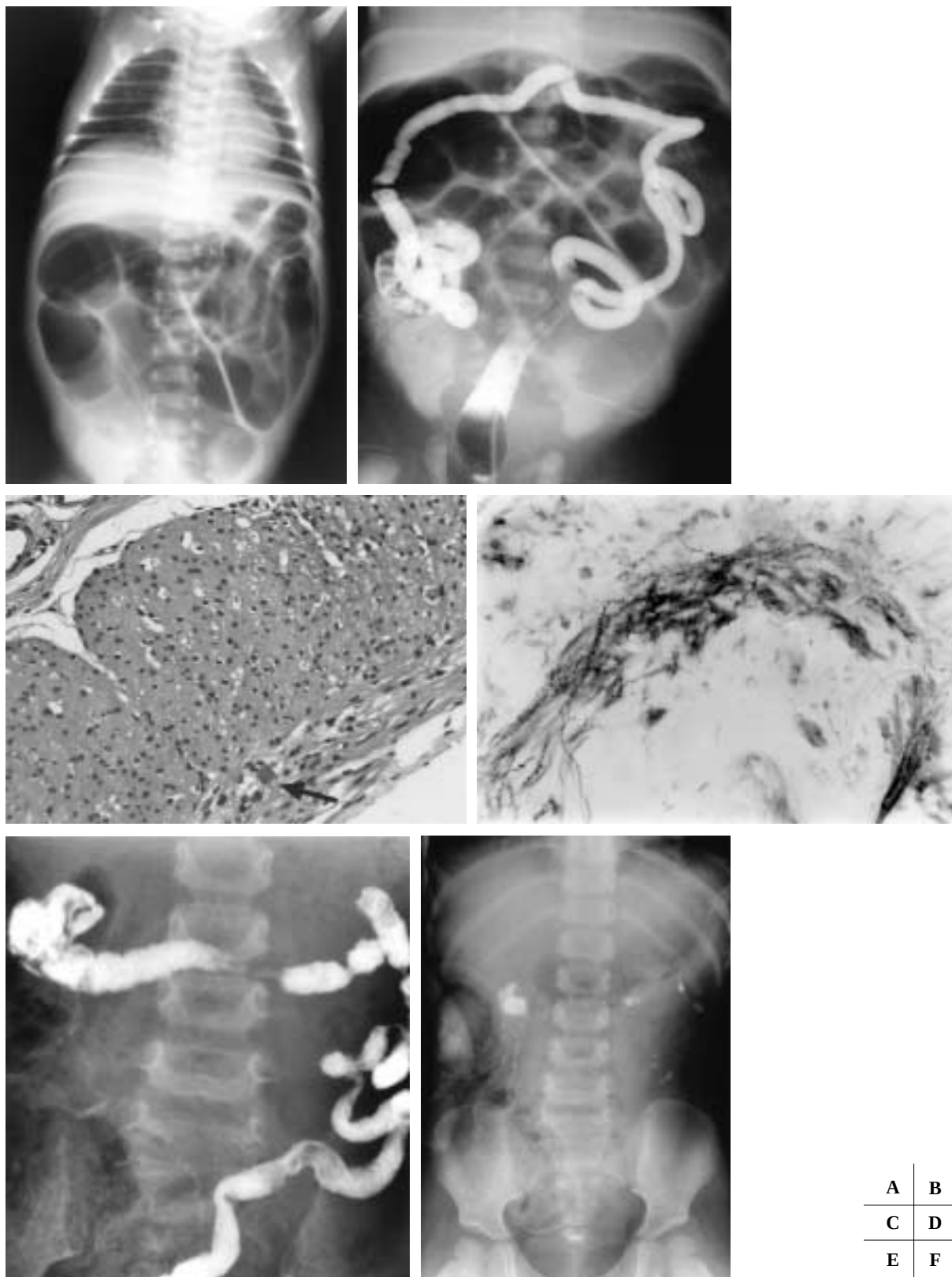


Fig. 3. Immature ganglionosis. (A) AP supine radiograph shows a markedly dilated bowel. (B) Barium enema study reveals microcolon, lack of contour irregularity at the colonic wall, and lack of colon shortening. (C) Hematoxylin-eosin stain of the specimen demonstrates normal numbers of ganglion cells, and immature ganglion cells (*arrow*), in which nuclear and nucleolar configurations are not clearly seen (original magnification, $\times 200$). (D) Immunohistochemical staining for acetylcholinesterase demonstrates no proliferation of neural fibers (original magnification, $\times 200$). (E) At the age of 3 years and 1 month, barium paste was injected via the anus. (F) By the following day, evacuation of the barium was complete, indicating efficient peristalsis.

Table 1. Classification of allied disorders of Hirschsprung's disease

Allied disorders with abnormal ganglion cells	
Hypoganglionosis (oligoganglionosis)	Decreased numbers of ganglia and normal ganglion cells
Immature ganglionosis (immaturity of ganglia)	Normal population of ganglion cells, immaturity of ganglion cells
Hypogenesis of ganglia	Decreased number and immaturity of ganglia
Intestinal neuronal dysplasia	Increased number of ganglia, giant ganglia, ectopic ganglia
Allied disorders with normal ganglion cells	
Chronic idiopathic intestinal pseudo-obstruction syndrome	
Megacystis-microcolon-intestinal hypoperistalsis syndrome	

Table 2. Comparison of barium enema findings in the neonatal period

	Aganglionosis	Hypoganglionosis	Immature ganglionosis
Microcolon	Negative	Negative	Positive
Transition zone	Negative	Negative	Negative
Irregular contraction	Positive	Positive	Negative
Rectosigmoid index	Normal	Normal	Normal
Shortening of colon	Positive	Positive	Negative
Lack of redundancy	Positive	Positive	Negative
Mucosal irregularity	Negative	Positive	Negative
Reflux of barium into ileum	Positive	Positive	Positive
Retention of contrast on delayed film	Positive	Positive	Positive

to as immature ganglionosis or immaturity of ganglia.⁷ In this disease, immunohistochemical staining for acetylcholinesterase also demonstrates no proliferation of neural fibers. When the number of ganglion cells is decreased and the ganglion cells are immature, the disease is referred to as hypogenesis of ganglia. Intestinal neuronal dysplasia is characterized by malformation of the parasympathetic submucosal plexus, including hyperganglionosis, giant ganglia, and ectopic ganglia.¹⁰

Immature ganglionosis is manifested at birth as neonatal bowel obstruction.¹² The male-to-female ratio in a small series of six patients was 4:2.¹² Laparotomy reveals caliber changes to the ileum 18-120 cm upwards from the terminal ileum. Follow-up studies reveal maturation of ganglion cells after 4-6 months of age.¹⁰ Timing of stoma closure is still controversial. Peristalsis started in our patient at the age of 2 years and 5 months, and final closure of the stoma was performed when the patient was 3 years old.

Hypoganglionosis also presents as neonatal bowel obstruction.¹² The male-to-female ratio in a small series of 12 patients was 5:7.¹¹ At laparotomy, caliber changes are found at the distal ileum. Follow-up histopathological studies reveal enlarged ganglion cells but no increase in their number.¹² Therefore, efficient development of bowel peristalsis cannot be expected, and treatment of this disorder is essentially the same as that for TCA and EA.

The radiological findings in TCA in the neonatal period have been described in the literature.¹³⁻¹⁷ De Campo *et al.* reviewed the radiological findings in 13 patients with TCA and concluded that there were no specific pathognomonic findings on barium enema studies.¹³ Seventy-seven percent of patients had a normal-caliber colon, 23% had microcolon, 23% had a shortened colon, 46% had colonic wall irregularity, and 33% had significant ileal reflux. Other nonspecific findings included shortening and lack of redundancy of the colon, with rounded hepatic and splenic flexures and retention of barium on delayed films.

There are a few reports on the radiological diagnosis of allied disorders of Hirschsprung's disease. The radiological findings in the neonatal period of our three cases are shown in Table 2. Barium enema findings including no transition zone, normal rectosigmoid index, reflux of barium into a dilated ileum, and retention of barium on delayed film were observed in all three patients. In aganglionosis and hypoganglionosis, a normal-sized colon, irregular contraction, shortening of the colon, and lack of redundancy were observed. In immature ganglionosis, microcolon was present but there was no shortening of the colon or lack of redundancy. Lack of shortening of the colon, lack of redundancy, and a normal-sized colon were not observed in immature ganglionosis, and might therefore be differential features between immature ganglionosis and the other two

diseases. In fact, barium enema examination revealed microcolon in four of five patients with immature ganglioneurosis.¹⁰ Conversely, a normal-sized colon was demonstrated in two patients with hypoganglioneurosis.¹²

After the neonatal period, radiological gastrointestinal examination showed no apparent peristalsis in the patients with aganglioneurosis and hypoganglioneurosis, resulting in resection of the colon. Conversely, in the patient with immature ganglioneurosis, development of peristalsis was observed on serial intestinal studies, resulting in conservation of the colon. Water-soluble iodine contrast medium was found to overestimate peristalsis, because it stimulated the bowel mucosa and induced motility of the bowel loops. Barium paste seemed more appropriate than barium sulfate, since the former had the consistency of feces and was suitable for estimation of peristalsis. The other material used for estimation of bowel motility is imitation stools prepared from *Konnyaku* paste mixed with radio-opaque materials.¹⁸ *Konnyaku* is a Japanese food containing the unabsorbable starch mannan. These imitation stools were used to confirm effective defecation via the anus and for daily rehabilitation of the unused anal ileocolonic segment.

In conclusion, the clinical features and radiological findings of Hirschsprung's disease and allied disorders appear to be similar in the neonatal period. However, follow-up radiological examination of the gastrointestinal tract is helpful to assess maturation of colonic motility.

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