

ANTENATAL SONOGRAPHIC FEATURES OF INTESTINAL NEURONAL DYSPLASIA TYPE A ASSOCIATED WITH POLYDACTYLY AND MICROMELIA

Hyun Joo Son, MD¹, Yun Sung Jo, MD¹, Ji-Han Jung, MD², Dong Gyu Jang, MD¹, Guisera Lee, MD¹

Departments of ¹Obstetrics and Gynecology, ²Pathology, St. Vincent Hospital, The Catholic University of Korea School of Medicine, Seoul, Korea

Type A intestinal neuronal dysplasia is a congenital abnormality that is a very rare disease. Here, we report on a patient who had intestinal dilatation with serial changes and polydactyly, as shown on prenatal ultrasound. Bowel obstruction symptoms were shown at 16 days of life. An open abdominal surgery was performed. Malrotation of the bowel and narrowing of the area from 15 cm above the ileocecal valve were noted. Therefore, a right hemicolectomy, including lesions was performed. The patient was diagnosed with type A intestinal neuronal dysplasia by pathology.

Keywords: Intestinal neuronal dysplasia; Polydactyly; Micromelia; Ultrasonography

Intestinal neuronal dysplasia (IND) is a congenital abnormality in the intestinal innervation system – hyperganglionosis [1]. IND is classified histologically as types A or B. Type A of IND is a congenital hypogenesis or agenesis of the innervation of the intestinal adrenergic sympathetic nerve and IND type B has abnormal parasympathetic innervation [2]. Of the patients with intestinal neuronal dysplasia, 5%–15% are type A and 70%–95% are type B [2]. Type A is very rare, and thus the precise incidence is not known. The incidence of type B is 1 in 4,000–60,000 live births [3]. IND is a congenital disease, the symptoms of which manifest during the neonatal period. Nevertheless, the prenatal features and diagnosis of intestinal neuronal dysplasia have not been reported.

We report a patient who had intestinal dilatation with serial changes and polydactyly, which was shown on prenatal ultrasound. The patient was diagnosed with type A intestinal neuronal dysplasia.

Case Report

A 28-year-old primigravida was transferred to our hospital for evaluation of fetal polydactyly at 32-week gestation. At the time of ultrasonography, the fetus was in the breech presentation, and had polydactyly with 6 fingers on both hands and 6 toes on both

feet. Within the abdomen, several dilated loops of bowel (approximately 1.72 cm) were noted (Fig. 1A, 1B). The volume of amniotic fluid was normal. Micromelia was shown in all long bones (<3rd percentile). After 2 weeks (34 weeks gestation), follow-up ultrasonography was performed. The diameters of bowel loops were shown to be decreased, but the number was increased (Fig. 1C). After 2 weeks (36 weeks gestation), follow-up ultrasonography was performed again. Several bowel loops disappeared, with only 3 small bowel loops remaining (Fig. 1D). At 39 weeks and 5 days, a female infant weighing 3,490 g was delivered by Cesarean section because of the breech presentation. The Apgar scores were

Received: 2011.10.5. Revised: 2012.1.28. Accepted: 2012.3.4.

Corresponding author: Guisera Lee, MD

Department of Obstetrics and Gynecology, St. Vincent's Hospital, The Catholic University of Korea School of Medicine, 93 Jungbu-daero, Paldal-gu, Suwon 442-723, Korea

Tel: +82-31-249-7300 Fax: +82-31-249-7060

E-mail: leegsr@catholic.ac.kr

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Copyright © 2012. Korean Society of Obstetrics and Gynecology

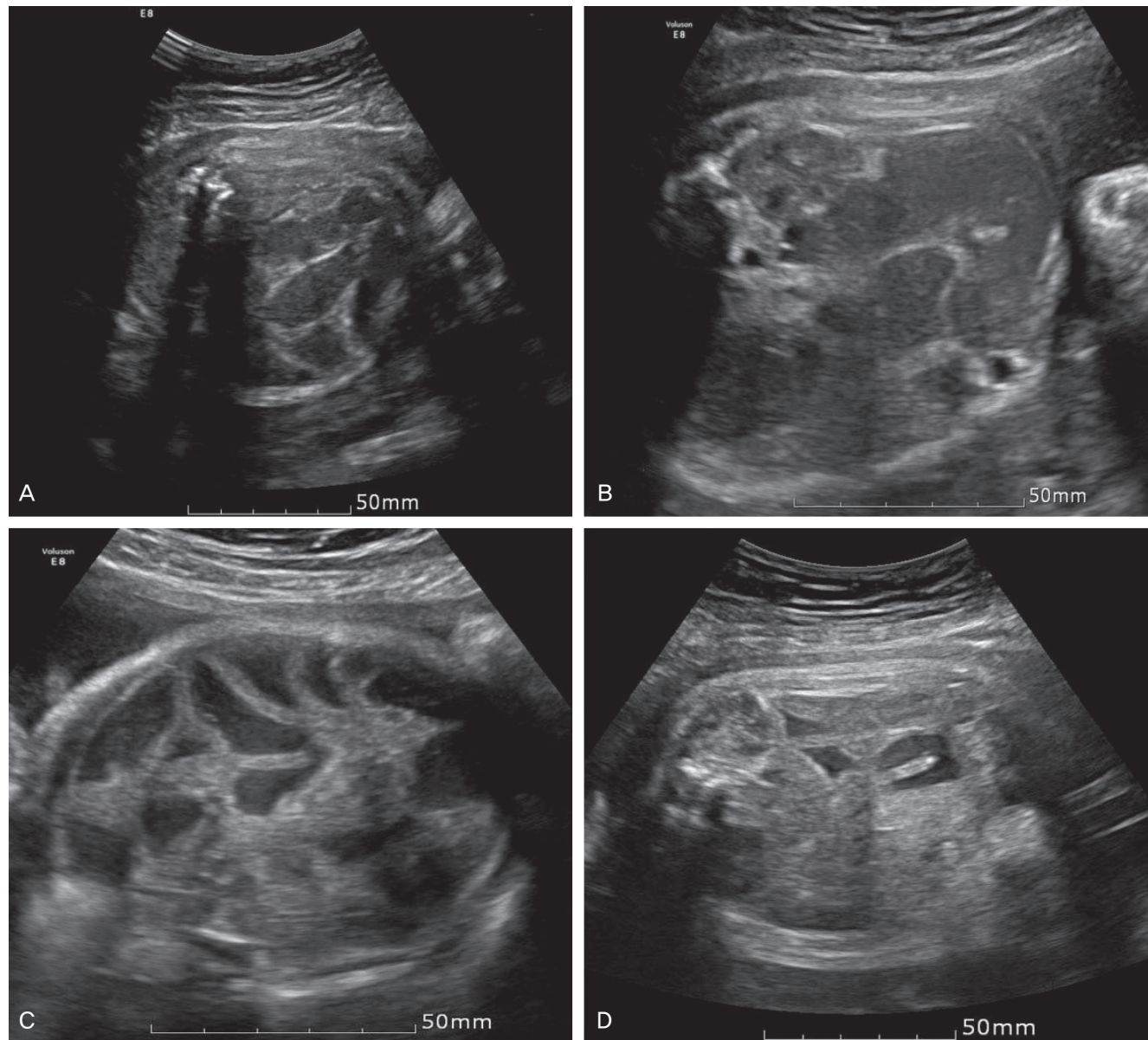


Fig. 1. (A, B) Dilated multiple bowel loops (approximately 1.72 cm) at 32 weeks gestation. (C) Shortened and multiple bowel loops detected at 34 weeks gestation. (D) Normal sized bowel lumen at 36 weeks gestation.

6 and 8 at 1 and 5 minutes, respectively; the condition of the neonate was good. Height was 50.5 cm, the head circumference was 38.5 cm, and the chest circumference was 31 cm. With the exception of polydactyly and micromelia, no additional external deformities were noted (Fig. 2). On abdominal X-ray obtained after birth, only mild dilatation of the intestine was observed. On abdominal ultrasound, the mild thickening of the intestinal wall was observed, but other abnormal features were not detected. From 4 days after birth, projectile vomiting symptoms were shown once a day, nonetheless, defecation patterns and breast feeding condi-

tions were good. Thus, the patient was discharged at 9 days of life. At 16 days of life, the infant's weight had decreased to 3.17 kg. An upper gastrointestinal (UGI) series was obtained to evaluate green bilious vomit; the bowel movements were severely reduced, the jejunum was dilated, the ileum and the ascending colon were not observed, and the sigmoid colon was detected 24 hours after the UGI series. Because malrotation of the ileum and partial obstruction of the distal jejunum were suspected, open abdominal surgery was performed. At surgery, malrotation of the bowel and narrowing of the area from 15 cm above the ileocecal valve were

noted, thus a right hemicolectomy, including the lesions, was performed with an end-to-end anastomosis of the ileum and colon. The length of the entire resected intestine was 24.0 cm; an area narrowed by approximately 6.0 cm was observed. Dilation of the bowel (13.0 cm in length) forming the transitional zone to the proximal area was observed. On microscopic examination, acute and chronic inflammatory findings were observed throughout the entire intestine, and findings consistent with enterocolitis and the destruction of crypts were observed (Fig. 3A). In addition, in the narrowed area as well as the dilated area, a hypertrophic and tortuous myenteric plexus with 2-5 cells per ganglia was observed (Fig. 3B), and it was proven clearly by immunohistochemical staining for the S-100 protein (Fig. 3C). Neither ectopic nor giant ganglia were detected. Because fresh tissues were not available, enzyme histochemistry for acetylcholinesterase was not performed. Based on the findings, the patient was diagnosed with type A in-

testinal neuronal dysplasia. Starting at day 4 after the operation, oral feeding was started, but projectile vomiting symptoms were shown. On abdominal X-ray obtained, significant dilatation of the intestine was observed. Total parenteral nutrition and oral feeding try was performed, but the patient condition had not improved. The patient died at post-operative 138 days due to multi-organ failure.

Discussion

Type A of intestinal neuronal dysplasia is congenital abnormality and is a very rare disease. The ratio of male children-to-female children is 5:3 and it has a tendency to develop more often in male children. The time-to-diagnosis in male and female children is 5 and 3 months after birth and is diagnosed earlier in female children [4]. The clinical symptoms of type B manifest at more than 6 months after birth, and include progressive severe constipation. Many cases of type B are clinically indistinguishable from Hirschsprung's disease (aganglionosis). Type B is commonly associated with Hirschsprung's disease [5]. Barium enema can help with the differential diagnosis [6]. Clinical symptoms of type A is a functional ileus with hematochezia, with symptoms that progress rapidly. Thus, prompt surgical treatment is needed [7]. Without timely surgical intervention, the condition may deteriorate rapidly and lead to death [8]. The clinicopathologic findings in IND types A & B are shown in the Table 1, as compared to our case. From the above comparison, it can be concluded that our case fits in with type A.

Associated anomalies have been reported in 30.5% of patients (29 of 95 patients) with type B intestinal neuronal dysplasia; the most common anomaly is the gastrointestinal system, accounting for



Fig. 2. Micromelia of long bone shortening.

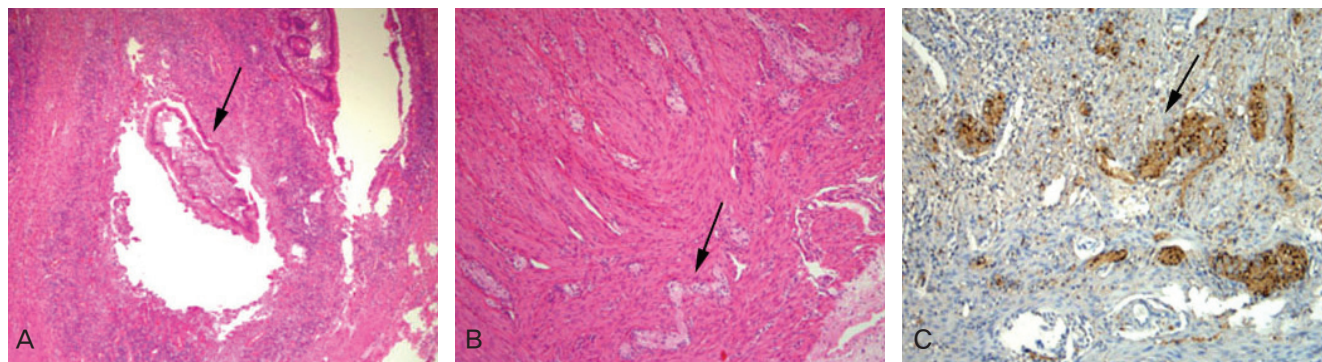


Fig. 3. (A) The mucosa showed a ruptured crypt with acute and chronic inflammation-arrow (H&E, ×40). (B) The colonic wall showed hypertrophic and tortuous myenteric plexus-arrow (H&E, ×100). (C) Immunohistochemistry for S-100 protein showed strong positivity for hypertrophic nerve bundles-arrow (×100).

Table 1. Clinicopathologic finding in our case in comparison with intestinal neuronal dysplasia (IND) type A and B

Feature	Present case	IND type A	IND type B
Age	Neonate	Neonate/early life	After 6 months of age
Clinical findings	Intestinal obstruction	Diarrhea, bloody stool, intestinal obstruction	Constipation, megacolon, mimic Hirschsprung's disease
Histologic features	1. Hyperplasia myenteric plexus 2. Mucosal inflammation 3. Ganglia abscent	1. Hyperplasia myenteric plexus 2. Mucosal inflammation 3. Ganglia abscent	1. Hyperplasia submucosal plexus 2. Inflammation abscent 3. Ectopic ganglia +/-

67.4% of all anomalies, short stature was reported in the skeletal system [9]. Combined anomalies of IND type A reported infrequently because of the rarity. Congenital anomalies with colonic obstruction have been reported in patients with IND type A [10]. Congenital anomalies with colonic obstruction have been reported in patients with IND type A [10]. It has been reported that type A intestinal neuronal dysplasia may be associated with colitis or necrotic colitis based on histologic evaluation [7,11,12]. In addition to intestinal malrotation, our patient had musculoskeletal anomalies (micromelia and polydactyly).

Because clinical features of intestinal neuronal dysplasia are non-specific and it is a very rare disease, the diagnosis may be delayed. All of the reported cases of intestinal neuronal dysplasia were diagnosed after birth on the basis of symptoms, even though intestinal neuronal dysplasia is a congenital disease. Prenatal features of intestinal neuronal dysplasia have not been reported. In our case, at 32 weeks gestation, long, dilated loops of bowel were demonstrated that changed with time. The finding of several dilated loops of bowel may exist in patients with small bowel obstruction, the most frequent cause of which is intestinal atresia [13]. The fetal sonographic findings of small bowel obstruction detected during pregnancy are very diverse, and are detected in the third trimester; moreover, the patterns are not consistent from patient-to-patient and can change with time. The ultrasonographic diagnosis of type A intestinal neuronal dysplasia may also show diverse features like other small bowel obstruction. If several bowel loops that change with time are shown during pregnancy, intestinal neuronal dysplasia must be considered in the differential diagnosis, and may be associated with deformities of the skeletal system. Thus, a comprehensive evaluation of the skeletal system is required.

References

1. Meier-Ruge W. Casuistic of colon disorder with symptoms of Hirschsprung's disease (author's transl). *Verh Dtsch Ges Pathol* 1971;55:506-10.
2. Fadda B, Maier WA, Meier-Ruge W, Schärli A, Daum R. Neuronal intestinal dysplasia. Critical 10-years' analysis of clinical and biopsy diagnosis. *Z Kinderchir* 1983;38:305-11.
3. Martucciello G, Caffarena PE, Lerone M, Mattioli G, Barabino A, Bisio G, et al. Neuronal intestinal dysplasia: clinical experience in Italian patients. *Eur J Pediatr Surg* 1994;4:287-92.
4. Meier-Ruge W. Epidemiology of congenital innervation defects of the distal colon. *Virchows Arch A Pathol Anat Histopathol* 1992;420:171-7.
5. Kobayashi H, Hirakawa H, Surana R, O'Briain DS, Puri P. Intestinal neuronal dysplasia is a possible cause of persistent bowel symptoms after pull-through operation for Hirschsprung's disease. *J Pediatr Surg* 1995;30:253-7.
6. Montedonico S, Acevedo S, Fadda B. Clinical aspects of intestinal neuronal dysplasia. *J Pediatr Surg* 2002;37:1772-4.
7. Schärli AF, Meier-Ruge W. Localized and disseminated forms of neuronal intestinal dysplasia mimicking Hirschsprung's disease. *J Pediatr Surg* 1981;16:164-70.
8. Rajalakshmi T, Makhija P, Babu MK, Kini U. Intestinal neuronal dysplasia type A. *Indian J Pediatr* 2003;70:839-41.
9. Corduk N, Koltuksuz U, Bir F, Karabul M, Herek O, Sarioglu-Buke A. Association of rare intestinal malformations: colonic atresia and intestinal neuronal dysplasia. *Adv Ther* 2007;24:1254-9.
10. Briner J, Oswald HW, Hirsig J, Lehner M. Neuronal intestinal dysplasia: clinical and histochemical findings and its association with Hirschsprung's disease. *Z Kinderchir* 1986;41:282-6.
11. Puri P. Variant Hirschsprung's disease. *J Pediatr Surg* 1997;32:149-57.
12. Schofield DE, Yunis EJ. What is intestinal neuronal dysplasia? *Pathol Annu* 1992;27:249-62.
13. Reyes HM, Meller JL, Loeff D. Neonatal intestinal obstruction. *Clin Perinatol* 1989;16:85-96.

다지증과 소지증을 동반한 장신경형성이상 A형의 산전초음파 양상가톨릭대학교 의과대학 ¹산부인과학교실, ²병리학교실손현주¹, 조윤성¹, 정지한², 장동규¹, 이귀세라¹

장신경형성이상(intestinal neuronal dysplasia)은 선천성 내장신경계 이상이며 직장, 대장 혹은 모든 장을 침범하는 드문 질환이다. 저자들은 산전초음파상 다지증(polydactyly)이 동반되고 장의 확장 소견 양상이 시간적 변화를 보였으며 출생 16일에 장폐쇄 증상이 나타나 개복하에 장절제술을 시행하여 장신경형성이상 A형으로 진단된 증례를 보고하고자 한다.

중심단어: 장신경형성이상, 다지증, 소지증, 초음파