An antenatal appearance of megacystis-microcolon-intestinal hypoperistalsis syndrome

Yoichiro Oka[1,2], Koushi Asabe[1,2], Takayuki Shirakusa[1], Kazuki Nabeshima[3]

[1]Division of Pediatric Surgery, Department of Surgery, Fukuoka University School of Medicine, and [2]Maternity and Perinatal Care Center and [3]Department of Pathology, Fukuoka University Hospital, Fukuoka, Japan

SUMMARY: Oka Y, Asabe K, Shirakusa T, Nabeshima K. An antenatal appearance of megacystis-microcolon-intestinal hypoperistalsis syndrome. Turk J Pediatr 2008; 50: 269-274.

We herein present a megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS) case followed by ultrasound (US) examinations before birth.

During the prenatal US examination of a 34-year-old woman, an enlarged bladder with bilateral hydronephrosis and hydroureter of the fetus were detected. The amniotic fluid was normal in the second trimester but polyhydramnios was observed in the third trimester.

A female baby was born by cesarian section weighing 2632 g. Imaging studies detected an enlarged bladder with bilateral hydronephrosis, hydroureter and microcolon. Laparotomy on the 9th day confirmed a short small bowel with caliber change and the existence of ganglion cells and plexus of the nerve in the intestine. These findings correlated with the previously reported characteristics of MMIHS.

An enlarged bladder in the second trimester and polyhydramnios in the third trimester have been reported in many cases of MMIHS. These findings may thus help to accurately diagnose MMIHS before birth.

Key words: megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS), antenatal diagnosis.

Megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS) was reported for the first time in 1976 by Berdon et al.[1], and it is defined as a functional intestinal obstruction characterized by microcolon, non-obstructive bladder distension, and a decreased or absent peristalsis of bowel. It is a rare autosomal recessive disorder and differs from Hirschsprung disease with its mature ganglion cells and nerve plexuses in the intestinal wall. MMIHS is more likely to develop in female infants and to become complicated with microcolon and malrotation.

We herein present a case suspected as MMIHS before birth and also discuss the findings of MMIHS based on prenatal ultrasound examination.

Case Report

A 34-year-old woman, primigravida, was referred to our institution at 25 weeks of gestation for an evaluation of "large bladder", discovered by a routine ultrasound examination at 23 weeks of gestation at another hospital. The prenatal course was otherwise unremarkable.

The first ultrasound evaluation in our Obstetrics and Gynecology (OB-GYN) Department revealed a large bladder measuring 50×60×56 mm (estimated volume 90 cm^2), bilateral hydronephrosis with right renal pelvis measuring 12×13×15 mm and a left renal pelvis measuring 13×17×17 mm (Fig. 1). At 31 weeks of gestation, ultrasound-guided bladder puncture was performed and 175 ml of urine was aspirated. An analysis of the urine showed Na 45 mEq/L, Cl 41 mEq/L, and osmolarity 112 mOsm/L. After aspiration, the bladder was atonic without contraction (6 hours later the refilling of urine was confirmed by an ultrasound examination) and a distended stomach was also found (Fig. 2). Non-ionic contrast material was injected into the bladder but no ureters could be visualized bilaterally. As a result, urine

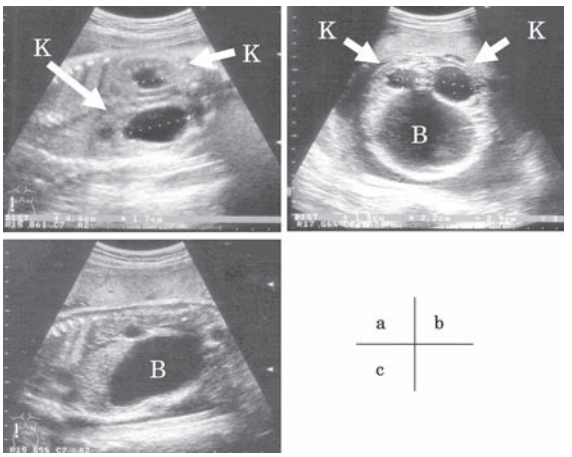

Fig. 1. Sections through the fetal abdomen. a: coronal section. b: transverse section. c: sagittal section. K: Kidney. B: Distended bladder.

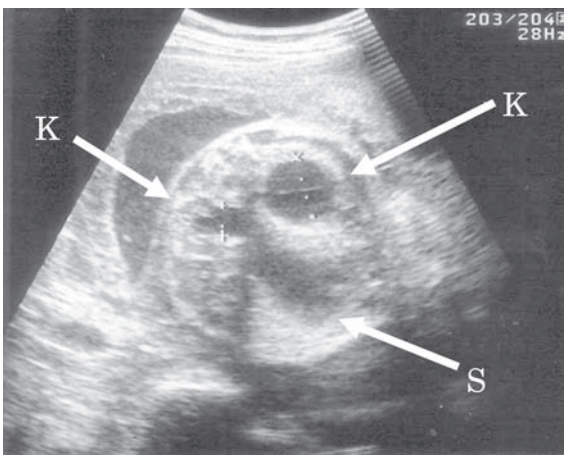

Fig. 2. Sonogram after bladder puncture. S: Distended stomach. K: Kidney.

production with no vesicoureteral reflux (VUR) was thus confirmed. In addition, the amount of amniotic fluid was normal.

At 37 weeks of gestation, she was admitted to the OB-GYN Department with a diagnosis of a premature rupture of the membrane. By ultrasound examination at admission, the estimated weight was 3630 g; the bladder measured 107×80×84 mm, right renal pelvis 31×26×36 mm, and left renal pelvis 38×40×56 mm. Because of hydramnios, 1300 ml of amniotic fluid was aspirated. At 37 weeks and 3 days of gestation, the patient underwent a primary cesarean section after induction failure because fetal distress was suspected. The infant was female, weighing 2632 g, with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. She was admitted to the Neonatal Intensive Care Unit (NICU) for an evaluation of large bladder and bilateral hydronephrosis.

The physical examination in the NICU showed a normally developed 37-week gestation infant (no visible findings of external malformation, no distended abdomen), except for the presence of a somewhat less audible intestinal sound.

After spontaneous micturition (89 ml) was seen, the first ultrasound examination was performed. The bladder was remarkably distended and bilateral hydronephrosis and hydroureters were also seen. The expansion of the right renal pelvis and ureter was severe. A gastric tube was inserted to treat gastric distension. The chest-abdominal X-ray the next day showed a distended stomach with little movement of intestinal tract gas. On the 7th day after birth, a view of "microcolon" was confirmed by a contrast enema while an upper gastrointestinal (GI) series demonstrated an atonic distended stomach and little passage of contrast media from the stomach to the duodenum (Fig. 3).

On the 9th day, a laparotomy was performed. Inspection of the total intestinal tract demonstrated absence of Treitz ligament with no Ladd band and ileocecal region located on right upper quadrant, which thus indicated non-rotation type malrotation. The small

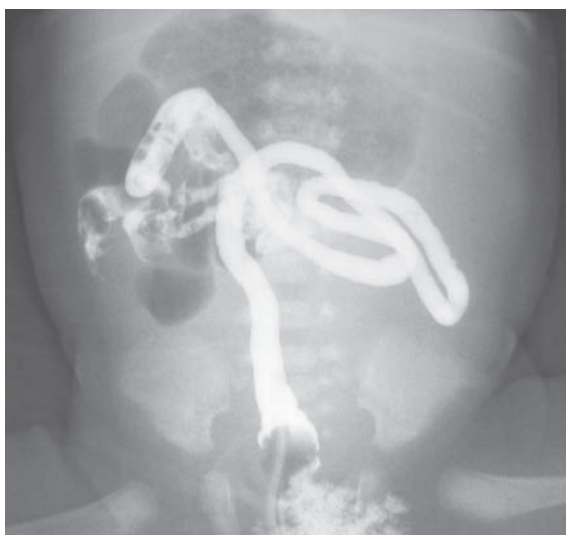

Fig. 3. A contrast enema demonstrated microcolon and an abnormal position of the cecum.

intestine was short, at 70 cm, and had caliber change at the point of 40 cm from the end of the duodenum. The presence of microcolon was also confirmed. An intraoperative frozen-paraffin inspection of full-thickness specimen at the point of caliber change of the small intestine was done to rule out Hirschsprung disease, and the existence of ganglion cells and the plexus of the nerve was confirmed (Fig. 4). A double lumen jejunostomy was thus performed at the point of caliber change and biopsy of ascending colon and appendectomy were also done.

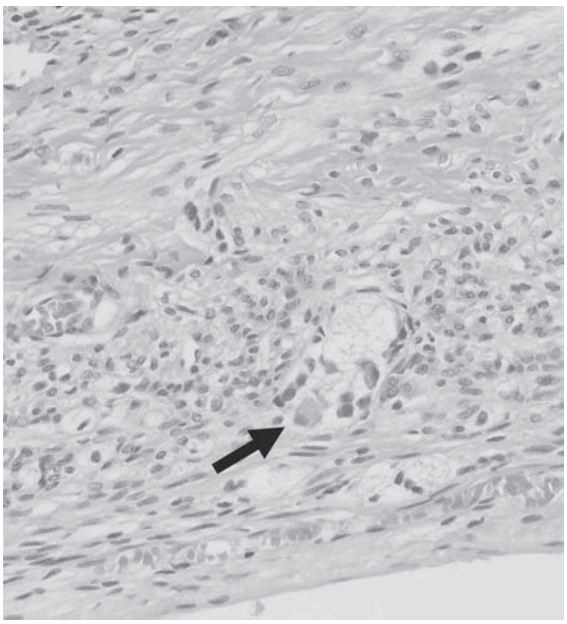

Fig. 4. A ganglion cell is detected (arrow) in histopathological examination of the muscle layers of the intestinal specimens.

Pathological inspection after the operation confirmed the Auerbach nerve plexus and ganglion cells were in the proper position of specimens of the vermiform appendix and ascending colon. Numerous S-100 protein-positive cells were recognized and were regarded as Schwann cells.

After operation, in addition to total parenteral nutrition (TPN), oral feeding was initiated. The increased oral intake, however, induced an increase in intestinal juice from the jejunostomy, thus causing dehydration and weight loss. As a result, an adjustment of the oral intake was often needed.

A balloon catheter was inserted after admittance to NICU. Intermittent urinary catheter insertion had been initiated at one week of age. The urinary volume and renal function had been kept normal without episode of urinary tract infection (UTI) for two months. However, the first episode of UTI appeared and antibiotic therapy was thus initiated. As left pyonephrosis had been detected by both ultrasound examination and a computerized tomography (CT) scan, left nephrostomy was made. Left ureteropelvic junction stenosis was suspected by pyeloureterography, and pyeloureteroplasty was performed at seven months of age. The passage of urine from each kidney to its ureter was confirmed by intravenous pyelography (IP) after the operation.

The long-term intravenous hyperalimentation (IVH) and frequent episodes of infectious diseases such as catheter sepsis and UTI caused a progression of liver dysfunction. The symptoms of multi-organ failure including pulmonary edema, liver failure, and portal hypertension had appeared after the episode of infection in the subdermal implant port for IVH at 1 year 6 months of age. The repeated episodes of upper and/or lower GI bleedings induced by portal hypertension could not be controlled by attempts of endoscopic sclerotherapy. As a result, the condition of the patient worsened. The patient was transferred to another institution at 1 year 10 months of age in order to prepare for a transplant of the liver and small intestine, but the scheduled transplant could not be performed due to the patient's poor condition and she died at two years of age.

Discussion

Megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS) is a rare disorder characterized by a remarkable decrease in peristalsis of the intestinal tract. The patient cannot take appropriate oral feeding and therefore is required to undergo long-term TPN. Most children with MMIHS tend to die of complications related to TPN, including catheter sepsis or liver failure, etc. Although a few long-term survivors of MMIHS have been reported[2,3] due to recent progress in the management of TPN, such patients still cannot tolerate full oral intake and therefore TPN cannot be discontinued. MMIHS is one of the diseases for which treatment is difficult and

prognosis remains poor at the present time. Establishing a prenatal diagnosis of MMIHS as early as possible using antenatal ultrasound examinations may help not only the physicians but also the parents in selecting and preparing the appropriate treatment.

Since Penman et al.[4] first described their findings of fetal ultrasound examinations of MMIHS in 1989, there have only been a few findings of fetal ultrasound examinations of MMIHS in the literature and thus standard of diagnosis is still unclear.

In our case, the findings of an enlarged bladder with bilateral hydronephrosis and hydroureter were determined on ultrasound examination in the second trimester of pregnancy and an absence of VUR was confirmed by transuteral cystoradiogram. The renal function and urine production of the fetus were normal based on an analysis of fetal urine. The volume of amniotic fluid was normal. In the third trimester, the findings of distended stomach and polyhydramnios were detected.

The diseases that show an enlarged bladder in the second trimester can be divided into two categories, consisting of obstructive and non-obstructive urethral diseases. Post urethral valve (PUV) in males and urethral atresia in females are considered to be obstructive urethral disease, whereas neurogenic bladder, severe VUR without urethral atresia as well as MMIHS are thought to be non-obstructive disease. The amount of amniotic fluid in patients with obstructive urethral disease tends to be normal in the second trimester of pregnancy but oligohydramnios is seen in the third trimester of pregnancy[22,23]. Other findings such as VUR, hydronephrosis, and hydroureter are also seen in obstructive urethral disease. The finding of increased renal echogenicity relative to the neighboring liver parenchyma in such obstructive urethral disease because of injury to the renal cortex by high pressure to the urinary tract has also been reported[22,24].

As for non-obstructive urethral disease, there is a male predominance regarding the incidence in severe VUR, whereas MMIHS has a female predominance. Although hydronephrosis and hydroureter are seen in both disorders, VUR is not seen in MMIHS[12].

We reviewed the pertinent literature to obtain related findings regarding ultrasound examination of MMIHS[4-22] and thus identified 22 cases (including our case) (11 boys and 11 girls). According to their gestation period, birth weight, and Apgar score (with the exception of cases whose details were unknown or cases terminated), almost all were full-term babies and asphyxia at birth was rare (Table I).

The prenatal findings of MMIHS are summarized in Table II. Although MMIHS is a disorder with morphological and functional anomalies both of the intestinal and urinary tract system, abnormal findings of the urinary tract system such as bladder distension, hydronephrosis and hydroureter were more frequent than those of the intestinal tract system such as a distended stomach or intestine. The former were detected in the second trimester whereas the latter were detected in the third trimester of pregnancy in many cases. Regarding the amount of amniotic fluid, many cases showed a normal volume in the second trimester of pregnancy but polyhydramnios in the last trimester of pregnancy.

Polyhydramnios is one of the most common findings in MMIHS cases. One previous study described polyhydramnios as present in more than 90% of all MMIHS cases[25]. In MMIHS cases, the findings of an enlargement of the stomach and intestine seen in the second and third trimesters of pregnancy are induced by a functional obstruction of the digestive tract. Therefore, many cases of MMIHS had polyhydramnios because of an ineffective absorption induced by a decreased functional

Table I. Characteristics of MMIHS Cases Diagnosed Prenatally

No. of cases	22 (21 cases from literatures and present case)
Sex	
Male	11
Female	11
Gestation*	36.9±2.0 weeks (32~40 weeks)
Birth weight*	3106.3±678.1 g (1770~4280 g)
Apgar score	
1 minute	7.2±1.9 (4~6)
5 minutes	8.4±1.3 (6~10)
Prognosis	
Termination	2
Alive	5
Death	13
Unknown	2

*unknown and terminated cases were excluded.

Table II. Prenatal Ultrasound Findings of MMIHS

	1st trimester (0~15W)	2nd trimester (16~27W)	3rd trimester (28W~)	Total
Urinary tract				
Enlarged bladder		13	7	20
Hydronephrosis or hydroureter		10	2	12
Amount of amniotic fluid				
Oligohydramnios		1		1
Normal		8		8
Polyhydramnios		1	6	7
Digestive tract				
Distended stomach		3	1	4
Distended intestine		1	2	3

peristalsis of the digestive tract between the second and third trimester of pregnancy, whether or not impaired urine production of the fetus actually existed[26].

Cases of sibs among MMIHS patients have been reported[6,10,27]. There were two cases in which selective termination was chosen, as seen in Table II. The mother of one case had a previous history of delivering a baby with a diagnosis of MMIHS. Some studies had reported MMIHS to be an autosomal recessive disease[4,27].

In conclusion, findings of an enlarged bladder with hydronephrosis in the second trimester of pregnancy and polyhydramnios in the third trimester of pregnancy were reported in many cases of MMIHS. The combination of these prenatal findings and a previous history of delivery of a baby with MMIHS therefore suggest a diagnosis of MMIHS before birth.

REFERENCES

1. Berdon WE, Baker DH, Blanc WA, Gay B, Santulli TV, Donovan C. Megacystis-microcolon-intestinal hypoperistalsis syndrome: a new cause of intestinal obstruction in the newborn. Report of radiologic findings in five newborn girls. AJR 1976; 126: 957-964.
2. Ohashi S, Nagashima K, Tsuchiya H, Ishimaru Y, Nemoto T. An experience in long-term management of a girl with megacystis microcolon intestinal hypoperistalsis syndrome (MMIHS). Jpn J Pediatr Surg 1999; 31: 212-217.
3. Yokoyama S, Fujimoto T, Tokuda Y, Mitimi T. A case of MMIHS who has been raised by TPN for 6 years. Jpn J Pediatr Surg 1988; 20: 751-756.
4. Penman DG, Lirford RJ. The megacystis-microcolon-intestinal hypoperistalsis syndrome: a fatal autosomal recessive condition. J Med Genet 1989; 26: 66-67.
5. Carlsson SA, Hökegård KH, Mattsson LA. Megacystis-microcolon-intestinal hypoperistalsis syndrome. Antenatal appearance in two cases. Acta Obstet Gynecol Scand 1992; 71: 645-648.
6. Köhler M, Pease PW, Upadhyay V. Megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS) in siblings: case report and review of the literature. Eur J Pediatr Surg 2004; 14: 362-367.
7. White SM, Chamberlain P, Hitchcock R, Sullivan PB, Boyd PA. Megacystis-microcolon-intestinal hypoperistalsis syndrome: the difficulties with antenatal diagnosis. Case report and review of the literature. Prenat Diagn 2000; 20: 697-700.
8. Hsu CD, Craig C, Pavlik J, Ninios A. Prenatal diagnosis of megacystis-microcolon-intestinal hypoperistalsis syndrome in one fetus of a twin pregnancy. Am J Perinatol 2003; 20: 215-218.
9. Chen CP, Wang TY, Chang CY. Sonographic findings in a fetus with megacystis-microcolon-intestinal hypoperistalsis syndrome. J Clin Ultrasound 1998; 26: 217-220.
10. Garber A, Shohat M, Sarti D. Megacystis-microcolon-intestinal hypoperistalsis syndrome in two male siblings. Prenat Diagn 1990; 10: 377-387.
11. Vintzileos AM, Eisenfeld LI, Herson VC, Ingardia CJ, Feinstein SJ, Loderiro JG. Megacystis-microcolon-intestinal hypoperistalsis syndrome. Prenatal sonographic findings and review of the literature. Am J Perinatol 1986; 3: 297-302.
12. Ciftci AO, Cook RC, Velzen D. Megacystis microcolon intestinal hypoperistalsis syndrome: evidence of a primary myocellular defect of contractile fiber synthesis. JPS 1996; 12: 1706-1711.
13. Levin TL, Soghier L, Blitman NM, Vega-Rich C, Nafday S. Megacystis-microcolon-intestinal hypoperistalsis and prune belly: overlapping syndrome. Pediatr Radiol 2004; 34: 995-998.
14. Peter M, Krook MD. Megacystis-microcolon-intestinal hypoperistalsis syndrome in a male infant. Radiology 1980; 136: 649-650.
15. Vezina WC, Morin FR, Winsberg F. Megacystis-microcolon-intestinal hypoperistalsis syndrome: antenatal ultrasound appearance. AJR 1979; 133: 749-750.
16. Young ID, McKeever PA, Brown LA, Lang GD. Prenatal diagnosis of the megacystis-microcolon-intestinal hypoperistalsis syndrome. J Med Genet 1989; 26: 403-406.

17. Nelson LH, Reiff RH. Megacystis-microcolon-hypoperistalsis syndrome and anechoic areas in the fetal abdomen. Am J Obstet Gynecol 1982; 144: 464-467.

18. Puri P, Lake BD, Gorman F, O'Donell B, Nixon HH. Megacystis-microcolon-intestinal hypoperistalsis syndrome: a visceral myopathy. J Pediatr Surg 1983; 19: 206-208.

19. Vinograd I, Mogle P, Lernau OZ, Nissan S. Megacystis-microcolon-intestinal hypoperistalsis syndrome. Arch Dis Child 1984; 59: 169-171.

20. Manco LG, Osterdahl P. The antenatal sonographic features of megacystis-microcolon-intestinal hypoperistalsis syndrome. J Clin Ultrasound 1984; 12: 595-598.

21. Willard DA, Gabriele OF. Megacystis-microcolon-intestinal hypoperistalsis syndrome in a male infant. J Clin Ultrasound 1986; 14: 481-485.

22. Pinette MG, Blackstone J, Wax JR, Cartin A. Enlarged fetal bladder: differential diagnosis and outcome. J Clin Ultrasound 2003; 31: 328-334.

23. Shimada K, Hosokawa K, Sakaue K, Kishima Y. Fetal genitourinary abnormalities associated with oligohydramnios. Jpn J Urol 1994; 6: 990-995.

24. Kaefer M, Peters CA, Retik AB, Benacerraf RB. Increased renal echogenicity: a sonographic sign for differentiating between obstructive and nonobstructive etiologies of in utero bladder distension. J Urol 1997; 158: 1026-1029.

25. Gomi A, Okamatsu T, Nishi T, et al. Clinical features of megacystis microcolon intestinal hypoperistalsis syndrome (MMIHS). Jpn J Pediatr Surg 1996; 28: 1080-1085.

26. Nishikubo T, Horikoshi Y, Toriyama Y, et al. Megacystis-microcolon-intestinal-hypoperistalsis syndrome which compromised biliary sands. Jpn J Urol 2001; 27: 513-518.

27. Annerén G, Meurling S, Olsen L. Megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS), an autosomal recessive disorder: clinical reports and review of the literature. Am J Med Genet 1991; 41: 251-254.