Megacystis-Microcolon-Intestinal Hypoperistalsis Syndrome: A Rare Case Report

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Megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS) is an extremely rare congenital genetic disorder characterized by an enlarged bladder without renal obstruction, decreased intestinal motility, and microcolon. This genetic disease is challenging to diagnose prenatally because of its nonspecific ultrasonographic findings and low incidence. In a case study, a 36-year-old nullipara who was at 24 weeks of gestation and referred to Asan Medical Center with a chief complaint of fetal enlarged bladder. Fetal ultrasonography showed megacystis without definite renal obstruction, normal female genitalia, and a normal amniotic fluid index. Follow-up ultrasonography at 30 weeks of gestation revealed worsening bladder distention accompanied by hydronephrosis. At 34 weeks of gestation, ultrasonography showed dilatation of the stomach and small bowel and polyhydramnios. The final prenatal diagnosis was megacystis associated with hydronephrosis and additional small bowel obstruction. Thus, MMIHS was prenatally suspected. The patient underwent an elective cesarean section at 37 weeks of gestation. A female newborn was delivered, with a birth weight of 2,300 g, and was admitted to the neonatal intensive care unit. No urethral obstruction was confirmed by Foley catheter insertion; however, on neonatal abdominal ultrasonography, a long segment of the microcolon was observed. The newborn failed to defecate and urinate, and genetic testing was performed, which was ultimately diagnosed with MMIHS with an ACTG2 (actin gamma 2, smooth muscle) gene mutation. While MMIHS was once a fatal disease, treatments such as intestinal rehabilitation and transplantation have improved the survival rate. Therefore, prenatal diagnosis is crucial for counseling, early postnatal diagnosis, and treatment.

Key Words: Megacystis microcolon intestinal hypoperistalsis syndrome, Ultrasonography, Prenatal

Introduction

Megacystis-microcolon-intestinal hypoperistalsis syndrome (MMIHS) is an extremely rare congenital genetic disorder characterized by an enlarged bladder without renal obstruction, decreased intestinal motility, and microcolon. Affected infants experienced gastrointestinal and urologic manifestations. Patients diagnosed with MMIHS present intestinal dysmotility and could not pass meconium, which leads to dependence on total parenteral nutrition. Urologic comorbidities include a contractile bladder, vesicoureteral reflux, frequent urinary tract infection, and renal failure. The exact etiology and incidence are unknown, and this rare disorder is associated with significant morbidity and mortality. Although disease worsening might start at the fetal period in utero, it is challenging to diagnose prenatally because of its nonspecific ultrasonographic findings and low incidence. Quite a few cases were previously reported; however, this is a rare case in Korea in which MMIHS was suspected based on prenatal ultrasound findings.
Case

A 36-year-old nullipara at 24 weeks of gestation was referred to Asan Medical Center with a chief complaint of enlarged fetal bladder. Following preimplantation genetic testing (PGT) for aneuploidy, she conceived through in vitro fertilization and underwent amniocentesis during the second trimester, which confirmed a normal karyotype and microarray. Fetal ultrasonography showed megacystis (Fig. 1A) without hydronephrosis (Fig. 1B), normal female genitalia, and normal amniotic fluid index (AFI). Bladder aspiration was performed, and the sample was sent for biochemical analysis. The results showed levels of calcium at 9.8 mg/dL, sodium at 52 mmol/L, chloride at 43 mmol/L, osmolarity at 122 mOsm/kg, and ß2 microglobulin at 5.7 µg/mL in the urine. Follow-up ultrasonography at 30 weeks of gestation revealed worsening bladder distention and hydronephrosis (Fig. 2). Thus, to decompress the urinary tract, a vesico-amniotic (V-A) shunt was performed. Hydronephrosis was resolved after the V-A shunt was placed; however, the V-A shunt dislodged into the intra-abdominal cavity at 32 weeks of gestational age, so abdominal-amniotic shunt was applied. At 35 weeks of gestation, ultrasonography showed dilatation of the stomach and small bowel and polyhydramnios (Fig. 3), and the final prenatal diagnosis was megacystis associated with hydronephrosis. However, neurologic bladder or partial urethral obstruction could not be ruled out, and additional small bowel obstruction was present. Thus, these findings supported the prenatal diagnosis of MMIHS. The patient underwent an elective cesarean section at 37 weeks of gestation owing to a history of myomectomy and symptomatic polyhydramnios (AFI 28). The overview of the clinical course of the patient is shown in Table 1.

A female newborn was delivered with a birth weight of 2,300 g and was admitted to the neonatal intensive care unit. No urethral obstruction was confirmed by Foley catheter insertion; however, she failed to urinate. In addition, as she showed defecation difficulty, gastrografin radiography and abdominal ultrasonography revealed peristaltic dysfunction.

Fig. 1. Prenatal ultrasonographic findings of the patient at the initial visit (24 weeks of gestation). (A) 5×5×7 cm enlarged bladder (axial view). (B) Normal kidney, bilateral (sagittal view).

Fig. 2. Follow-up prenatal ultrasonography at 30 weeks and 3 days of gestational age. (A) 9×5×8 cm enlarged bladder at the axial view. (B) Markedly dilated calices of the right kidney (hydronephrosis grade II to III) at the sagittal view.
She underwent exploration laparotomy, and dilated small intestine and micro-intestine without malrotation were found from the terminal ileum to the colon (Fig. 4). Small bowel and colon biopsy was performed, and the loop ileostomy was created. After normal ganglion cell was observed in bowel biopsy, MMIHS was strongly suspected. ACTG2 heterozygous mutation was confirmed by genetic testing, and the newborn was finally diagnosed with MMIHS5. She was discharged on day 120 after birth with G-tube and Foley catheter.

**Discussion**

MMIHS is typically characterized by clinical symptoms such as megacystis, microcolon, and intestinal dysmotility. Although the exact cause of MMIHS remains unclear, several gene mu-

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**Table 1. Clinical Manifestations of the Patient**

<table>
<thead>
<tr>
<th>Prenatal ultrasonographic finding</th>
<th>Gestational age</th>
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<tbody>
<tr>
<td>Amniotic fluid index</td>
<td>Normal</td>
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<tr>
<td>Genitourinary</td>
<td>Normal</td>
</tr>
<tr>
<td>Bladder</td>
<td>Distended</td>
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<td>Kidney</td>
<td>Normal</td>
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<td>Gastrointestinal</td>
<td>Normal</td>
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<td>Small bowel</td>
<td>Normal</td>
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<td>Stomach</td>
<td>Normal</td>
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<tr>
<td>Hospital courses</td>
<td>Referred</td>
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<tr>
<td>Event</td>
<td>V-A shunt</td>
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<tr>
<td>V-A shunt dislodged, A-A shunt inserted</td>
<td>delivery</td>
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V-A, vesico-amniotic; A-A, abdominal-amniotic.
tations have been identified as contributing factors, including those in ACTG2, LMOD1, MYH11, MYL0, and MYLK.10 While MMIHS usually follows a recessive inheritance pattern, the mutation of ACTG2, which was thought to play a significant role in the pathogenesis of the disease, demonstrates an autosomal dominant inheritance pattern. ACTG2 produces gamma-2 actin and is found in smooth muscle cells of the intestinal and urinary tracts.11,12 Consequently, ACTG2 mutations can lead to megacystis, microcolon, and intestinal hypoperistalsis.13,14 Since it is inherited in an autosomal dominant manner, pathogenic variants may be present in the parents or affected siblings.

MMIHS, an extremely rare disease, is challenging to diagnose prenatally, particularly when there is no family history.15 In most cases, the initial presentation involves megacystis with or without hydronephrosis detected on prenatal ultrasonography, while stomach or bowel dilation is a less common manifestation.7 If a patient with a family history exhibits only one of these two symptoms, MMIHS could still be strongly suspected. Even in instances where diagnosis is difficult owing to the absence of family history, as in the presented case, MMIHS can be reasonably suspected if both symptoms (megacystis and dilated bowel) are observed on fetal ultrasonography. Prenatal diagnosis of MMIHS is crucial, as it allows for early detection through genetic testing and timely initiation of appropriate treatments. In the presented case, the female fetus showed abrupt onset of bladder distention without any obstructive lesion with normal AFI in the second trimester. Our first diagnostic impression was an isolated neurogenic bladder, but partial urethral obstruction could not be excluded. According to the advanced gestational age, ultrasonographic findings showed a distended stomach with prominent small bowel. These clinical findings strongly suggested the diagnosis of MMIHS. However, MMIHS could have been considered in a female fetus with megacystis and normal AFI since lower urinary tract obstruction is uncommon in female fetuses and is almost always accompanied by oligohydramnios.16

Intriguingly, the patient was conceived through advanced techniques of in vitro fertilization and embryo transfer. Before transfer, to ensure genetic stability, the embryo was subjected to PGT for aneuploidies (PGT-A). Subsequently, amniocentesis was conducted, confirming a normal karyotype and unremarkable chromosomal microarray analysis results. Despite these genetic tests, no single gene mutation was identified. Consequently, to address potential genetic concerns, meticulous prenatal counseling was recommended.

Historically, MMIHS has been considered a fatal disease and is characterized by a poor survival rate because of malnutrition, multiorgan failure, sepsis, and ultimately death.17 Several previous studies have used prenatal V-A shunts to prevent hydronephrosis and preserve kidney function, however, their use remains controversial.18 Recent advancements in treatments, such as personalized parenteral nutrition, intestinal rehabilitation and transplantation, have led to improvements in reducing malnutrition, preservation of renal function and therefore enhanced survival rates.5,19 Consequently, accurate prenatal diagnosis, counseling, and prompt postpartum management have become crucial in improving outcomes.

Through this case report, which documents the rare case of MMIHS in Korea, we aimed to increase awareness of this rare condition and contribute to the advancement of early prenatal diagnosis and counseling. Highlighting the importance of prenatal diagnosis and management will hopefully improve the outlook for future cases of MMIHS.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Authors’ Contributions

Conceptualization: HSW, SYK; Data curation: SC; Investig-
References


