Case report

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Prenatal diagnosis of congenital chloride diarrhea: A case report

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ABSTRACT

Congenital chloride diarrhea (CCD) is a rare but significant genetic disorder characterized by severe electrolyte imbalances resulting from impaired intestinal chloride absorption. Affected children experience persistent diarrhea, dehydration, and malnutrition, complicating medical and developmental care. The enhancement of prenatal detection is crucial for improved patient management, early interventions, and informed genetic counseling. However, despite advancements in medicine, the complex nature and rarity of CCD make prenatal detection challenging. In this study, we report a fetal case where prenatal magnetic resonance imaging (MRI) effectively identified the distinctive characteristics of CCD, providing insights into the complexities of diagnosis and suggesting avenues for enhanced early detection strategies.

Keywords: *congenital chloride diarrhea; fetal magnetic resonance imaging; polyhydramnios; prenatal diagnosis;* SLC26A3 *gene*.

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INTRODUCTION

Congenital chloride diarrhea (CCD) is a rare disorder originated from mutations in the *SLC26A3* gene with an autosomal recessive inheritance pattern.[1] Its prevalence is notably higher in Nordic nations like Finland and Sweden, attributed to distinct genetic mutations, with occurrences noted at 1 in 25,000 and 1 in 100,000 live births, respectively.[2] In contrast, higher occurrences in regions like Poland and the Middle East are linked to consanguineous marriages, while in China, CCD remains a rarity with limited documented cases.[3]

Symptoms of CCD often manifest during the neonatal phase, presenting a spectrum of severity and clinical features. Addressing complications such as dehydration, hypokalemia, and metabolic alkalosis –conditions intricately tied to the underlying chloride absorption impairment– require immediate diagnosis and treatment to safeguard the long-term health of affected individuals.[1]

Historically, ultrasound has been essentiall for prenatal diagnosis of CCD. However, the nuanced insights offered by the advent of fetal MRI have enriched our diagnostic approach, unveiling detailed anatomical and functional anomalies associated with CCD.[4]

In this report, we discuss the distinctive fetal MRI features observed in a specific CCD case, underscoring the technique's instrumental role in refining our comprehension and management of this rare condition. The emphasis is laid on the augmentation of prenatal diagnosis, pivotal for the early detection and optimized long-term health management of CCD patients.

CASE

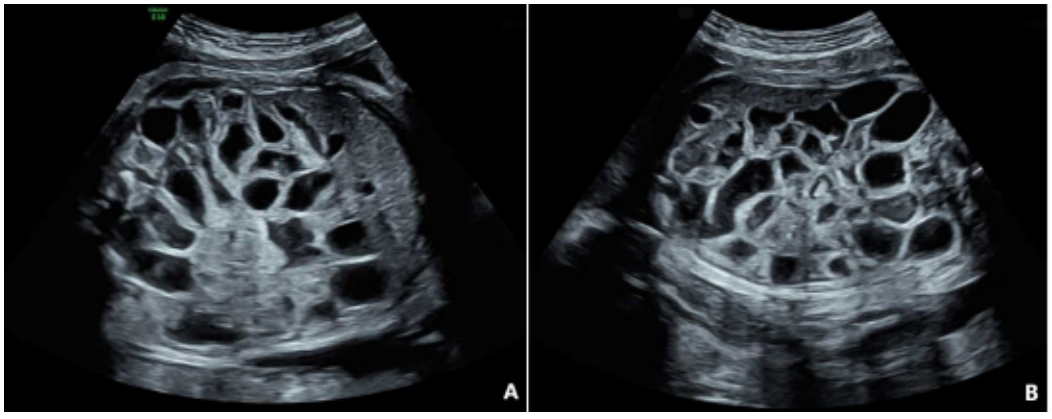
The patient was a 30-year-old woman (gravida 0, para 0), without family history of intestinal symptoms related to CCD. The pregnancy was screened for aneuploidy, yielding negative results. The first-trimester fetal ultrasound showed no abnormalities.

However, at 33 weeks of gestation, fetal bowel dilatations with refractory polyhydramnios were observed (*Figure 1*). The fetal intestine was diffusely dilated, displaying an inner diameter of approximately 10-14 mm. Real-time ultrasound revealed active intestinal peristalsis without significant ascites, and no morphological abnormalities were detected in the fetus and placenta.

Fetal MRI conducted at 34 weeks of gestation confirmed the presence of dilated bowel loops exhibiting heightened T2 signal intensity, indicative of fluid-filled intestines (*Figure 2a,b*). T1-weighted images showed hypointense fluid accumulation, primarily localized within the small intestine and extending into the colon (*Figure 2c*).

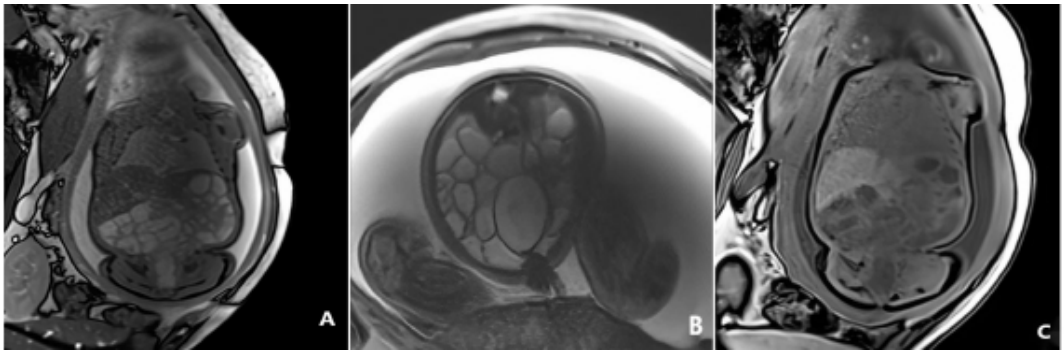
To elucidate the underlying cause, and following a review by the medical ethics committee and the acquisition of informed consent from the child's guardian, umbilical cord blood was collected for high-throughput sequencing. Genetic testing revealed a heterozygous variation in the *SLC26A3* gene, confirming the diagnosis of congenital chloride diarrhea type 1 (*Table 1*).

Figure 1. Ultrasound views at 33 weeks of gestation



Multiple extensive dilatations of the bowel loops with homogeneous hypoechoic content.

Figure 2. Fetal magnetic resonance imaging at 34 weeks of gestation



(A, B) T2-weighted image showing hypersignal of multiple bowel dilatation indicating fluid content. (C) T1-weighted image showing physiological hypersignal completely disappeared from the colon.

Table 1. Gene sequencing

Gene	Chromosomal coordinates (GRC7/hg19)	Nucleotide/amino acid change	Region	Zygosity	Variant classification	Disease/ phenotype	Inheritance mode	Variant origin
SLC26A3 (NM_000111.2)	Chr7:107434256	c.202C>T/ p.Arg68Trp	Exon 3	Heterozygous	VUS	Congenital chlorine diarrhea type 1	AR	Paternal
	Chr7:107418674	c.1460G>C/ p.Gly487Ala	Exon 13	Heterozygous	VUS			Maternal

VUS: variant of uncertain significance; AR: autosomal recessive.

DISCUSSION

The fundamental characteristic of congenital chloridorrhea is the Cl^-/HCO_3^- exchange impairment in the mucous membranes of the distal ileum and colon, leading to copious watery diarrhea, resulting in hypochloremia, hyponatremia, hypokalemia, metabolic alkalosis, and dehydration.[4] Without timely treatment, prolonged electrolyte imbalance and metabolic alkalosis can lead to a variety of complications, even endangering the life of the affected child. If this disease is diagnosed and treated promptly in the early stages after birth, most affected children will grow and develop normally.[5] Therefore, making an accurate diagnosis during the fetal period and treating it as soon as possible after birth helps to improve the prognosis.

Normal fetal gastrointestinal tract has certain characteristics on MRI, and different physiological signals can be observed at different gestational weeks.[6] In normal fetuses at 18 weeks of gestation, there is already a difference in physiological signal difference between amniotic fluid and intestinal meconium. At 20 weeks, high signals are detected on T1W and low signals on T2W, due to the early presence of meconium. Before 25 weeks of gestation, MRI signals in the small intestine are isosignal or low signal on the T1W sequence, as opposed to high signal in meconium in the colon; After 33 weeks, normal small intestine contents showed physiologically high signals on T2W and low signals on T1W, caused by intracellular fluid from the amniotic membrane. The contents of the distal small intestinal cavity generally show high signals on the T1W sequence, and the intensity is consistent with meconium.[7-9]

After ultrasound examination, this case showed polyhydramnios and intestinal dilation, making it difficult to make a definite diagnosis. A further MRI was performed using a Siemens Magnetom Skyra 3.0T MRI scanner using the sequence T2 weighted half-Fourier acquisition single-shot turbo-spin-echo (HASTE), T2 weighted true steady-state precession rapid imaging (TrueFISP), and T1 weighted multi-echo water and fat separation imaging (Dixon). The results showed that there was a fluid signal

in the dilated intestine, while the normal colonic meconium signal disappeared on T1W and the expected meconium was replaced by fluid in the colon, strongly indicating the presence of substantial watery diarrhea. The expansion of a high signal loop of the intestine to the end of the rectum, and the nature of the fluid accumulation in the intestine, made it reasonable to suspect CCD rather than lower intestinal obstruction or Hirschsprung's disease. Gene sequencing confirmed our hypothesis of CCD in this case. Therefore, MRI examination is very important for the early diagnosis of CCD. After 20 weeks of gestation, the disappearance of high signal on T1W in the fetal intestine is a relevant indicator.

In summary, congenital chloridorrhea is rare in clinical practice and easily misdiagnosed during the prenatal period. However, the fetal gastrointestinal tract has distinctive characteristics on MRI, and MRI examinations can aid in diagnosing fetal congenital chloridorrhea. ■

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