

Antenatal diagnosis of microvillus inclusion disease

Abstract

Microvillus inclusion disease is a rare autosomal recessive disorder due to defective apical surface of the enterocytes presenting with severe watery diarrhea starting at birth. We describe a female infant who had antenatal diagnosis of microvillus inclusion disease. At 36th gestational week of a 32-year-old woman ultrasound examination revealed dilatation of fetal sigmoid colon. The amniotic fluid level was normal. An amniocentesis was performed to rule out congenital sodium and chloride diarrhea in the prenatal period. The patient didn't prefer to undergo genetic tests. In conclusion, prenatal ultrasonographic identification of dilated bowel loops without polyhydramnios suggests differential diagnosis of microvillus inclusion disease in addition to congenital chloride diarrhea, jejunoileal atresia, volvulus, meconium ileus, Hirschsprung disease, enteric duplications, anorectal atresia.

Keywords: congenital diarrhea, microvillus inclusion disease, prenatal diagnosis

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Introduction

Microvillus inclusion disease (MVID) is a congenital bowel disease characterized by severe diarrhea, malabsorption and growth retardation in infancy.¹ Severe watery diarrhea begins in the first days of life, with the loss of 30% of body mass in the first 24 hours. Metabolic acidosis and hypotonic dehydration develop in children with MVID.² Impaired kidney function, accompanied by nephrocalcinosis is a common complication.³ Children with MVID are dependent on parenteral nutrition throughout their lives, and most of these children are at risk of developing cholestasis and liver failure due to total parenteral nutrition (TPN).

The diagnosis of MVID is based on an intestinal biopsy. Light microscopy is characterized by accumulation of Periodic acid-Schiff (PAS) positive granules in immature enterocytes in upper crypts.⁴ There is no curative treatment for MVID. Trials of anti-inflammatory drugs, including steroids and anti-secretory agents, have not succeeded in significantly altering stool volumes over a long period.⁵ We describe a case of MVID in which antenatal ultrasound revealed structural deformities. A written informed consent was obtained from the patient before preparing for publication.

Case presentation

A 32-year-old G1 P0 woman was diagnosed to have dilatation of fetal sigmoid colon on prenatal ultrasound at 36th gestational weeks (Figure 1). The amniotic fluid index was 15cm. The parents were not consanguineous. First trimester screening and level 2 ultrasound results were normal. Anal atresia was ruled out based on the absence of U or V-shaped intestine in the pelvis, lack of enterolithiasis, condensation or meconium accumulation on prenatal ultrasounds at 24, 28, 32 and 34 weeks. Amniocentesis was performed to exclude congenital chloride diarrhea. The electrolytes were as follows: Na: 122, K: 3.8, Cl: 101, osmolality: 240mOsm/kg. The lack of fluid-debris levels, non-dilatation of the small intestine, and monitoring of bowel peristalsis in the coronal ultrasonography helped to rule out volvulus. The preliminary diagnoses were Hirschsprung's disease and microvillus inclusion disease.

The patient gave birth to a 3420g female vaginally at 40th gestational week. The APGAR scores at 1st and 5th minutes were 7 and 9,

respectively. On postpartum 3rd day, the neonate suffered from watery diarrhea and abdominal distension. Abdominal X-ray showed dilated intestinal loops and pneumoperitoneum (Figure 2). On postpartum 5th day, the infant was referred to the gastroenterology department due to 19% weight loss. An endoscopic biopsy revealed intra-cytoplasmic inclusions in the apical surface of the intestinal epithelial cells and villus loss, with a CD10 and PAS epithelial cytoplasmic staining pattern supporting the diagnosis of MVID.



Figure 1 Prenatal ultrasound at 36th gestational week showing fluid-filled large bowel.

The patient was placed on a central venous catheter due to the need for long-term total parenteral nutrition (TPN). Coagulase-negative staphylococci were produced in blood culture. Computed tomography revealed ascites, mucosal enhancement of the stomach and bowel loops, increased heterogeneous contrast in liver parenchyma, patched ground-glass areas in the lungs, inter-lobular septum thickening and bilateral pleural effusions potentially associated with hypoproteinemia and volume overload.

The infant died due to septic shock secondary to a catheter-related infection. The post-mortem genetic examination revealed compound

heterozygous mutation of *MYO5B* gene. Additionally, heterozygous presence of a variant of unknown significance (VOUS) in *MYO58* was also identified. It was determined c.1355_1363 dup heterozygosis mutation in *MYO5B* gene in paternal blood sample and 1463>Cand p.Ile 488 Thr heterozygosis mutation in gene *MYO5* in maternal blood sample.



Figure 2 Dilate intestinal loops and pneumoperitoneum in newborn.

Discussion

Microvillous inclusion disease is an autosomal recessive disease and usually caused by mutations in *MYO5B*. It presents with chronic, watery, life-threatening diarrhea which results in severe dehydration and metabolic acidosis.⁶ The prognosis of disease is very poor and usually fatal as a result of cholestatic liver disease or from sepsis. Today, a prenatal diagnosis of MVID is also available based on molecular genetics.

Differential diagnosis of MVID should be done for jejunoileal atresia, volvulus, meconium ileus, Hirschsprung's disease, enteric duplications, anorectal atresia, congenital salt loss diarrhea, Bartter syndrome and enteroendocrine cell dysgenesis. Anal atresia was ruled out based on absence of U or V-shaped intestine in the pelvis, lack of enterolithiasis, condensation or meconium accumulation and visualization of anus on prenatal ultrasound. The lack of fluid-debris levels, non-dilatation of the small intestine, and monitoring of bowel peristalsis in the coronal ultrasonography helped to rule out volvulus. Enteroendocrine cell dysgenesis can be differentiated from microvillous inclusion disease by the lack of enteroendocrine cells and the presence of normal microvilli. An antenatal differential diagnosis algorithm based on prenatal ultrasound findings for MVID has not been published yet. Figure 3 shows an algorithm created by the authors for the differential diagnosis of dilated intestinal loops at prenatal ultrasound.

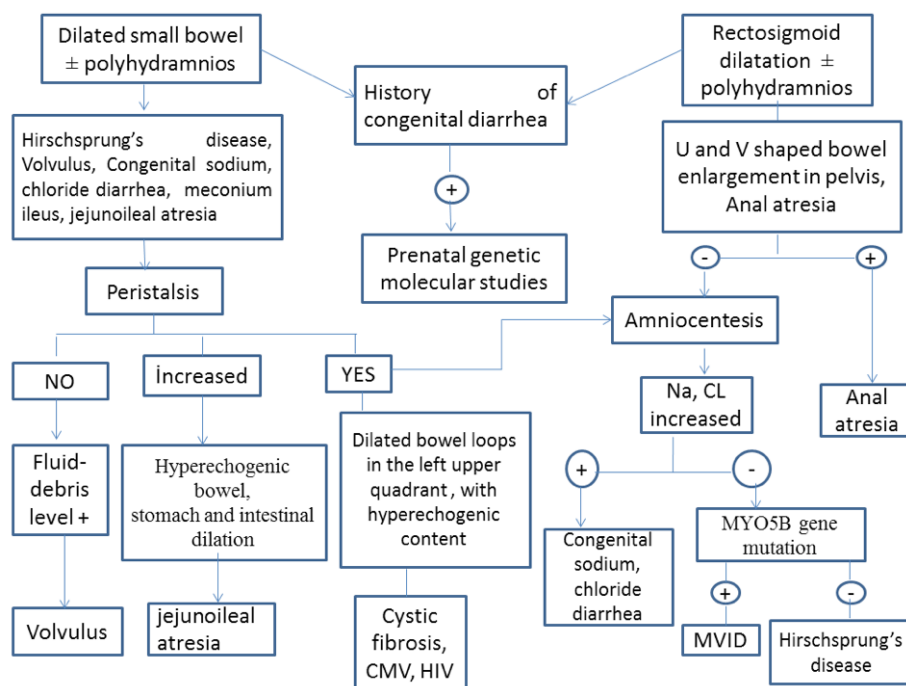


Figure 3 Differential diagnosis of dilated intestinal loops at prenatal ultrasound.

Several previous reports suggested excluding jejunoileal atresia, volvulus, meconium ileus, Hirschsprung disease, enteric duplications, anorectal atresia, congenital salt loss diarrhea, Bartter syndrome, and MVID from differential diagnoses when dilated intestines are detected on prenatal ultrasound.⁷⁻⁹ Fetuses with MVID may present with multiple dilated bowel loops and polyhydramnios mimicking intestinal obstruction in the early third trimester.⁷

Congenital chloride and sodium diarrheas may also present with polyhydramnios multiple dilated bowel loops, fluid filled intestinal obstruction on prenatal ultrasound and elevated amniotic fluid electrolyte concentrations.^{8,10}

Kennea et al.⁹ reported that polyhydramnios accompanied by dilated large and small bowel loops which resembled an intestinal

obstruction on antenatal ultrasound could lead to a postnatal diagnosis of MVID.⁹ The authors stated that bowel obstruction and congenital enteropathy should be considered if a prenatal ultrasound showed dilated bowel loops and polyhydramnios. In the present case, amniocentesis was helpful to rule out the diagnosis of congenital sodium and chloride diarrheas in the prenatal period.

Currently, there is no curative treatment for MVID. Although long-term TPN or bowel and liver transplantation are treatment options, MVID-related complications and reduced longevity are common. Novel genome editing technologies, such as CRISPR/Cas9, hold promise for MVID treatment. However, further studies are needed to shed light on.¹¹

Conclusion

When dilated bowel loops are detected regardless of the presence of polyhydramnios in prenatal ultrasound examination, MVID should be considered as a differential diagnosis. Prenatal genetic molecular studies should be performed to confirm the diagnosis of MVID.

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Conflicts of interest

No potential conflicts of interest are reported by the authors.

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