

CASE REPORT:**Prenatal diagnostic and management of megacystis microcolon intestinal hypoperistalsis syndrome: A report on a rare case in Cipto Mangunkusumo Hospital, Jakarta, Indonesia****Fita Maulina,^{1*} Yuditiya Purwosunu²**¹Resident of Obstetrics and Gynecology Faculty of Medicine University of Indonesia, ²Consultant of Obstetrics and Gynecology Faculty of Medicine University of Indonesia, General Hospital Cipto Mangunkusumo, Jakarta**ABSTRACT**

Megacystis Microcolon Intestinal Hypoperistalsis Syndrome (MMIHS) is a rare and the most severe form of functional intestinal obstruction in the newborn. The characteristic features of this congenital and fatal disease are abdominal distension, absent or decreased bowel peristalsis. Abdominal distension is a consequence of the distended, unobstructed urinary bladder with or without hydro nephrosis. Some previous reports have revealed that the typical antenatal sonographic findings are as follows: a greatly distended bladder, bilateral hydro nephrosis, and a normal amount of amniotic fluid; however, the antenatal diagnosis of this syndrome is occasionally difficult.

Keywords: MMIHS; intestinal obstruction; newborn; prenatal diagnosis

ABSTRAK

Megacystis Microcolon Intestinal Hypoperistalsis Syndrome (MMIHS) adalah bentuk obstruksi usus fungsional yang jarang dan paling parah pada bayi baru lahir. Ciri khas penyakit bawaan dan fatal ini adalah perut kembung, tidak ada atau berkurangnya gerak peristaltik usus. Distensi abdomen adalah konsekuensi dari kandung kemih yang membesar dan tidak terhalang dengan atau tanpa hidro nefrosis. Beberapa laporan sebelumnya telah mengungkapkan bahwa temuan sonografi antenatal yang khas adalah sebagai berikut: kandung kemih yang sangat membesar, hidro nefrosis bilateral, dan jumlah normal cairan ketuban; namun, diagnosis antenatal dari sindrom ini terkadang sulit.

Kata kunci: MMIHS; obstruksi usus; neonatus; diagnosis prenatal

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INTRODUCTION

Megacystis Microcolon intestinal hypoperistalsis syndrome (MMIHS) is a rare and lethal disease. This syndrome firstly reported by Berdon and his colleagues in 1976.¹ After that time, limited cases have been reported, 200 cases have been reported in the medical literature. This syndrome characterizes with abdominal distension due to the large non obstructive urinary bladder that always as gold diagnostic in prenatal to MMIHS, Microcolon with no peristalsis or hypoperistalsis of the gastrointestinal system. It represents the most severe form of functional intestinal obstruction in the newborn and is generally associated with a fatal outcome.^{1,2,3}

Megacystis micro colon intestinal hypoperistalsis syndrome (MMIHS) is a congenital disorder characterized by loss of smooth muscle contraction in the bladder and intestine. Pathologic study shows vascular degenerative changes in the smooth muscle of bladder and bowel. Most patients die within one year after birth due to severe sepsis, renal failure, liver failure, malnutrition and complication of TPN. Treatment is supportive.⁴ The majority of patients died within one year after birth Only a few cases have been reported to stay alive until 11 years of age.⁵ Although most cases of MMIHS syndrome occurs sporadic, the risk of recurrence in next pregnancies and sibling is about 25%. This issue has declared the probability of autosomal recessive transmission of disease.^{5,6}

The presumable role of genetic, neurogenic, myogenic and hormonal mechanism have been suggested.⁴ The disease is common in a female infant. This ratio is 3-41. Gosemann et al., reported a clear preponderance for female to male (70.6 vs. 29.4%).⁴ The present case was female. Prenatal ultrasonography is a very good diagnostic tool for diagnosis of this syndrome.⁴ The performance of sonography in the 16th week of gestation can identify large bladder in 88% cases and fetal hydro nephrosis in 57% cases.

Three genes are known to be involved in MMIHS pathogenesis: ACTG2, MYH11, and LMOD1. However, for approximately 10% of affected individuals, the genetic cause of the disease is unknown, There's journal found that subjects from two consanguineous families with no variants in the known MMIHS-associated genes. By performing homozygosity mapping and whole-exome sequencing, they found homozygous variants in myosin light chain kinase (MYLK) in both families. Expression studies and splicing assays indicated that both variants affect normal MYLK expression. Because MYLK encodes an important kinase required for myosin activation and

subsequent interaction with actin filaments, it is likely that in its absence, contraction of smooth muscle cells is impaired. The existence of a conditional MYLK knockout mouse model with severe gut dysmotility and abnormal function of the bladder supports the involvement of this gene in MMIHS pathogenesis. The ACTG2 gene provides instructions for making α protein called gamma (γ)-2 actin. The γ -2 actin proteins organize into filaments that are important for the testing of muscle fibers (muscle contraction), specifically contraction of smooth muscles of the urinary and intestinal tracts. These contraction s empty urine from the bladder and move food through the intestines.^{7,8}

Amniotic fluid index in the second trimester, and polyhydramnios, intestinal and/or stomach dilatation in the third trimester. The presence of oligohydramnios or normal amniotic fluid, progressive bladder wall thickening, hydro nephrosis, echogenic kidneys and dilated posterior urethra are more suggestive of obstructive uropathy caused by a distal urethral obstruction such as PUV. For this reason, amniotic fluid analysis and fetal urinalysis are also helpful in the prenatal diagnosis of MMIHS, Fetal MRI may also improve the diagnosis, especially when upper gastrointestinal tract distension (esophagus, stomach or small bowel) and micro colon are observed.⁹

CASE REPORT

The case was on Mrs. A, 29 years old with G2A1, singleton live breech presentation, fetus with multiple congenital anomaly (megavesica, bilateral hydronephrosis, small gaster, single umbilical artery) mother with Gestational hypertension, history of vesicosintesis due to diagnostic chromosomal. This patient presented for prenatal care in the second trimester of pregnancy. She referred by Pangkal Pinang Hospital after found bladder abnormality and perform puncture 60cc to chromosomal diagnostic, the result was Karyotyping 46XX. Patient was examined by Fetomaternal and in our hospital when she was 19 wga. In Our examination we found fetus with anomaly congenital: mega vesical, unvisual gaster, umbilical cyst. Patient did routinely ANC and consult to Perinatology, Perinatology surgery. Patient was hospitalized at Cipto Mangunkusumo Hospital 3x, 1st was due to premature contraction and get lung maturation for fetus. 2nd was because premature contraction and high blood pressure, the 3rd was because high blood pressure

In this case, during prenatal care of 29 year old pregnant woman, there was a sonographic report that showed live female fetus with a large cystic mass in pelvis with

hydro nephrosis. The fetus with the volume of amniotic fluid, heart rate and movement of the fetus were normal so we continued to observed fetus with serial Ultrasound examination. Prenatal ultrasonography of subject 1 at 18 weeks of gestation revealed a distended bladder .

At 37 week gestational age this patient came with hypertension in gestational age with oligohydramnios, fetus was in breech presentation, we decided to perform Caesarean section due to Breech presentation on primi gravida. Born baby girl 2200 gram, 41 cm, Apgar score 3/5/7, After birth, the newborn presents with symptoms of intestinal obstruction and difficulties in bladder evacuation, mostly vomiting with no sound of gaster. plan to laparotomy for cystostomy.

After birth the perinatology performed Abdominal US examination for the baby, and the result was both renal size 34x20mm and 25x15mm, pelvicalises both renal enlarged with clubbing kaliks, dilatation both proximal

ureter until distal part, no sign of stone or focal infection. Enlarged Vesica urinaria with irregular thicken line with echointernal, hipoechoic mass with posterior enhanchment and internal echo in anteroinferior bladder size 32x31x37mm no sign of uterus, Conclusion: cystic lesion on right hemiabdomen sugestif gaster dd/malrotasi gaster with Hydreneffphrosis grade III and bilateral hydroureter, cystic lesion in anteroinferior vesica urinaria, sugestif genitalia interna with hydrometrocolpos.

Laboratory result for Kidney function slightly increased (Urea/ Creatinine 40mg/dl /1 mg/dl), and continued impairment of peristalsis (hypoperistalsis) often causes a digestive condition called intestinal pseudo obstruction. Baby mostly vomiting in the 1st day babyborn. The vomit usually contains a green or yellow digestive. From abdominal x- ray found that Colon dilatation with suspected pneumoperitoneum without atresia ani.



Figure 1. Prenatal ultrasonography of subject 2 at 22 weeks of gestation, Prenatal ultrasonography of subject 3 at 32 week.



Figure 2. The newborn with symptoms of intestinal obstruction and difficulties in bladder evacuation

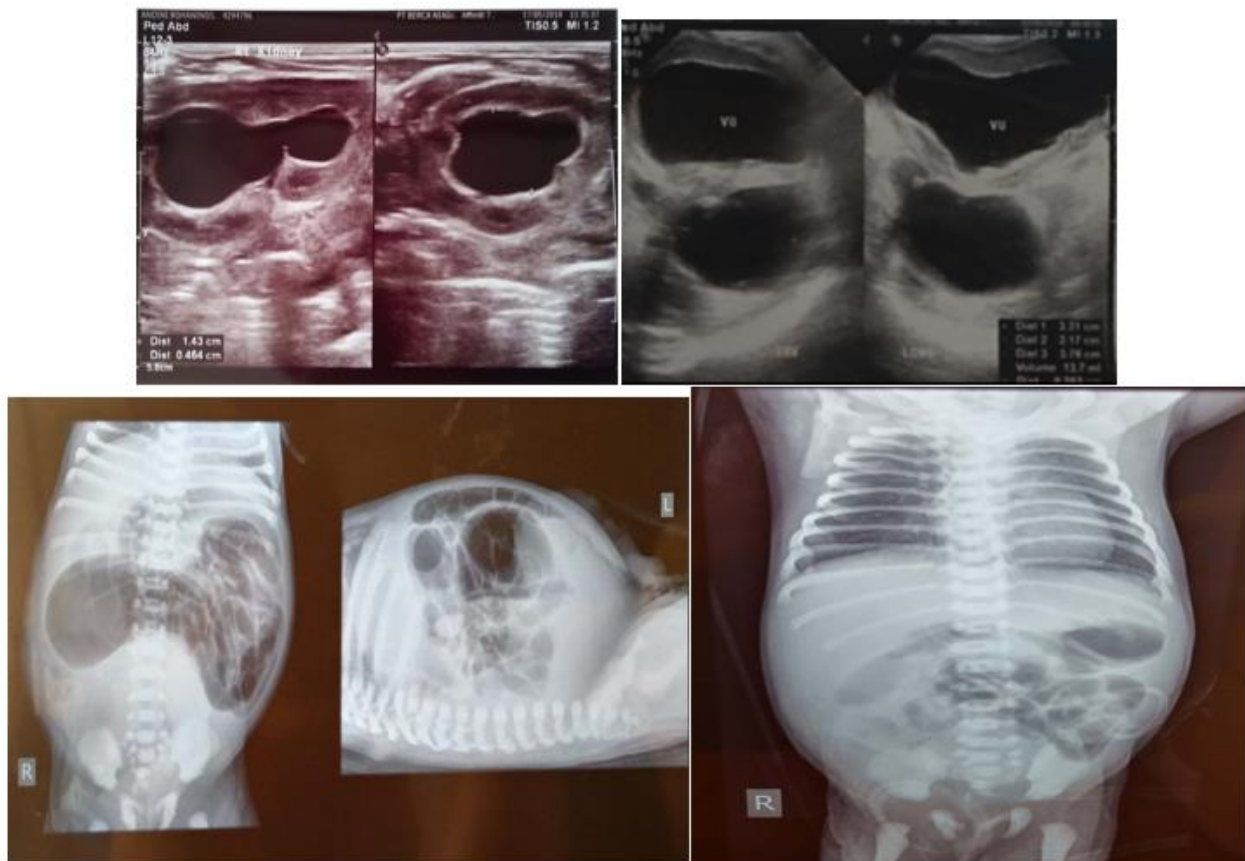


Figure 3. Abdominal US examination for the baby, and the result was hydronephrosis grade III bilateral renal, hydroureter right kidney, x- ray found that Colon dilatation with suspected pneumoperitoneum without atresia ani.

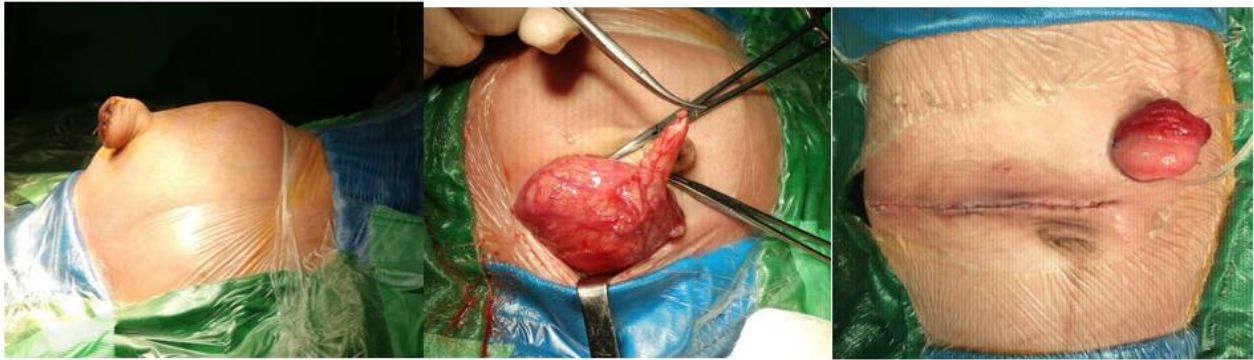


Figure 4. Picture of intraoperative of baby found urach diverticulum and no peristaltic of gaster.

Perinatology surgery scheduled her to have elective laparoscopy cystostomy and colostomy, and for other anomaly like ambiguous genitalia, from perinatology medicine want to perform analysis chromosomal and in intraoperatively they will ensure about the existence of the uterus.

Intraoperatively they found dilatation of the vesical urinary, seen Urach's diverticula that connecting with fibroid cord to the umbilicus and they perform the resection until the tip of the vesical urinary and perform cystostomy, On the exploration, seen uterus, both tube and both ovaries within normal limit, but the rectum found dilated with no peristaltic and they perform colostomy.

DISCUSSION

From this case we can see intraoperatively Urach diverticulum that made surgery medicine though that possibility of congenital diverticle of Uretra is main problem for this baby, but the complication by urachal anomalies were not happen in this patient, like persistent periumbilical urinary leakage, umbilical mass, abdominal pain, dysuria, recurrent UTI, urinary stasis, etc. In this baby we observed that there's no periodic either spontaneously miction after delivery or persistent periumbilical urinary leakage. there's no periodic of fever and abdominal pain, and not proved recurrent UTI happen by urinalysis.^{7,10,11,12}

An urachal anomaly develops from failure of the urachal communication between the bladder and umbilicus to properly obliterate during fetal development. A major theory is that fetal bladder outlet obstruction may cause urine to escape via umbilicus. A congenital bladder diverticulum is typically located in the lateral aspect of the bladder trigone and is thought to occur due to an inherent weakness in the destrussor

muscle.^{7,11,12} From this theory we can concluded that weakness in the destrussor muscle of bladder back to theory about three genes are known to be involved in MMIHS pathogenesis.

CONCLUSION

Megacystis micro colon intestinal hypoperistalsis syndrome (MMIHS) is a rare and lethal disease. Important to have prenatal findings so we can having numerous fetal interventions even though neonatal outcome may be favorable. Prenatal diagnosis of mega vesical in fetus not always because obstructive urinary bladder, in further exploration we still need to analyse combine strategy of homozygosity mapping and whole exome sequencing to identify the genetic cause.

REFERENCES

1. Berdon WE, Baker DH, Blanc WA, et al. Megacystis- microcolon-intestinal hypoperistalsis syndrome: a new cause of intestinal obstruction in the newborn: report of radiological findings in five newborn girls. *AJR Am J Roentgenol.* 1976;126(5):957-64.
2. Puri P, Shinkai M. Megacystis microcolon intestinal hypoperistalsis syndrome. *Semin Pediatr Surg.* 2005;14(1):58-63.
3. Gosemann JH, Puri P. Megacystis microcolon intestinal hypoperistalsis syndrome: a systematic review of outcome. *Pediatr Surg Int.* 2011;27(10):1041-6.
4. Tarlan S, Mahyar A, Chegini V, Chegini V. Megacystis microcolon intestinal hypoperistalsis syndrome: Report of a rare case in newborn. *Acta Med Iran.* 2015;53(8):518-522
5. Manop J, Chamnanvanakij S, Wattanasarn C. Megacystis microcolon intestinal hypoperistalsis

- syndrome (MMIHS): a case report in Thailand. *Journal of the Medical Association of Thailand Chotmaihet Thangphaet*. 87;11:1385-8.
- 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(5):362-7.
 - Bauer SB, Retik AB. Urachal anomalies and related umbilical disorder. *Urol Clin North Am*. 1978;5:195-211.
 - Wangler MF, Gonzaga-Jauregui C, Gambin T, et al. A heterozygous de novo and inherited mutations in the smooth muscle actin (ACTG2) gene underlie megacystis- Microcolon intestinal hypoperistalsis syndrome. *PLoS Genet*. 2014;10(3):e1004258.
 - Halim D, Brosens E, Muller F, et al. Loss of Function variants in MYLK cause recessive megacystis microcolon intestinal hypoperistalsis syndrome. *The American Journal of Human Genetics*. 2017;101:123-9.
 - Baradaran N, Stec AA, Gearhart JP. Urachal anomalies and congenital diverticulum. [Internet] Cancer therapy advisor, decision support in medicine. [cited 2019 Mar 3]. Available from : <https://www.cancertherapyadvisor.com/home/decision-support-in-medicine/pediatrics/urachal-anomalies-and-congenital-diverticulum/>
 - Powell CR, Kreder KJ. Treatment of bladder diverticula, impaired detrusor contractility, and low bladder compliance. *Urol Clin North Am*. 2009;36:vii-25.
 - Gearhart JP, Rink RC, Mouriouand PDE. *Pediatric urology*. Saunders Elsevier. 2010.