J. Fetal Med. (December 2022) 9:75–78
https://doi.org/10.1007/s40556-022-00350-w

CASE REPORTS

Meckel-Gruber Syndrome in Twin Pregnancy: A Case Report

Kadir Atakir[1] · **Emine Aylin Atakir**[1]

Received: 7 December 2021 / Accepted: 13 July 2022 / Published online: 18 August 2022

Abstract Meckel-Gruber syndrome is a rare, OR-transitive and fatal disease. Prenatal diagnosis is important, especially in regions where consanguineous marriages are common. The classic triad of the disease is occipital meningoencephalocele, renal anomalies and postaxial polydactyly. The diagnosis is made by the presence of two of these three major features. Just over 200 cases have been reported in the world literature. The purpose of presenting our case is that all findings of the disease were detected in both fetuses in a twin pregnancy for the first time, which has not been reported in literature.

Keywords Meckel-Gruber syndrome · Twin pregnancy · Cystic kidneys · Encephalocele · Polydactyly

Introduction

Meckel-Gruber Syndrome (MKS) is a rare autosomal recessive fatal disease. It was first published by Meckel in 1822. In 1934, Gruber reported 16 patients with a similar structure and named it as 'Dysencephalia splanchnocystica'. The identity of the syndrome was not defined until 1969. Opitz and Howe suggested the name of the syndrome and defined the clinical-pathological features of the syndrome (1). The classic triade of MKS is meningoencephalocele, enlarged polycystic kidneys, and post-axial polydactyly. The diagnosis is made by the presence of 2 of 3 major abnormalities (2).

The worldwide incidence of MKS ranges from 1/140,000 (Great Britain) to 1/3500 (North Africa) live births. A higher incidence was noted in Gujarati Indians, Belgians and Bedouins (3). It occurs equally in both sexes. Oligohydramnios and secondary pulmonary hypoplasia develop due to renal dysfunction. The cause of mortality is often pulmonary hypoplasia (Figs. 1, 2, 3, 4, 5, 6).

Case Report

A monochorionic diamniotic twin pregnancy at 14 weeks of gestation was detected on transabdominal ultrasonography of a 26-year-old pregnant woman who presented to our clinic for fetal evaluation. There was no previous history of anomalous births. Both fetuses had a localized occipital encephalocele (Figs. 1, 2, 3 and 6) and large hypoechoic kidneys filling the entire fetal abdominal cavity (Figs. 5, 6). Polydactyly was detected in all extremities in both fetuses (Fig. 4). Based on these findings, a diagnosis of Meckel-Gruber was made. There was first-degree consanguinity in the family. The mother and father were healthy. The mother had previously delivered a term baby by cesarean section, and the baby lived and died for 15 min before any diagnosis could be made. This was the patient's second pregnancy.

The patient was informed about the described syndrome and explained about the 100% mortality. The patient opted for termination and the diagnosis was phenotypically confirmed. Genetic evaluation could not be performed because the patient refused.

✉ Kadir Atakir
kadir.atakir@istun.edu.tr

Emine Aylin Atakir
eaatakir@hotmail.com

[1] İstanbul Sağlık Ve Teknoloji Üniversitesi Istanbul, Istanbul, Turkey

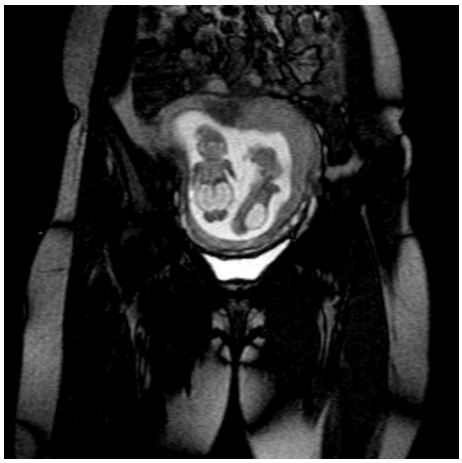

Fig. 1 Coronal T2W MR sections; Bilateral oversized kidneys, renal cystic lesions (red arrows), and occipital encephaloceles (blue arrows) in both fetuses

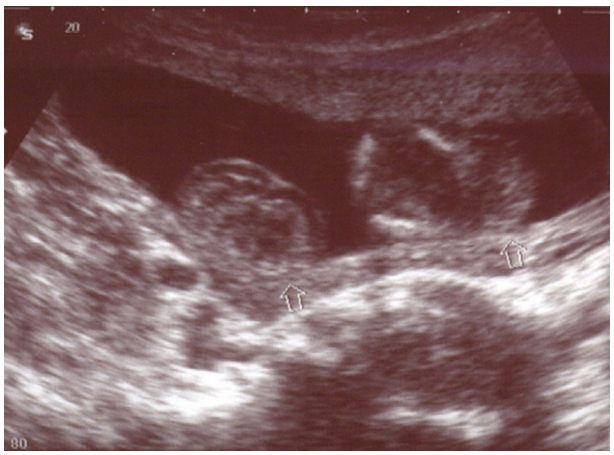

Fig. 2 Ultrasonography view of both fetuses' occipital encephalocele

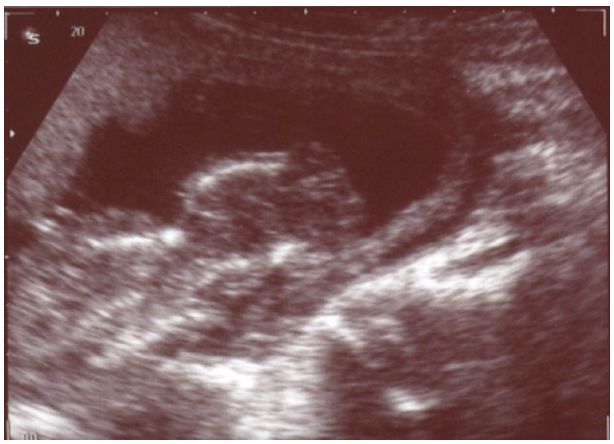

Fig. 3 Large posterior fontanel and encephalocele

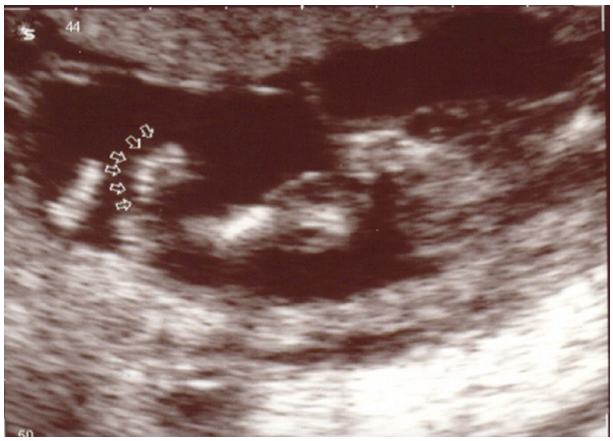

Fig. 4 Polydactyly of the foot of one of the fetuses

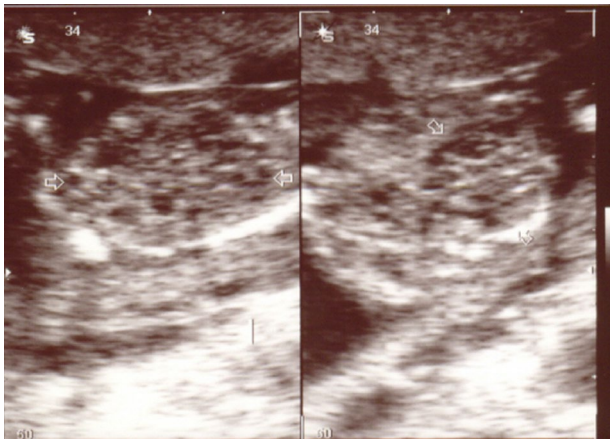

Fig. 5 Large kidneys filling the abdomen, accompanied by cystic hypoechogenicity in both fetuses

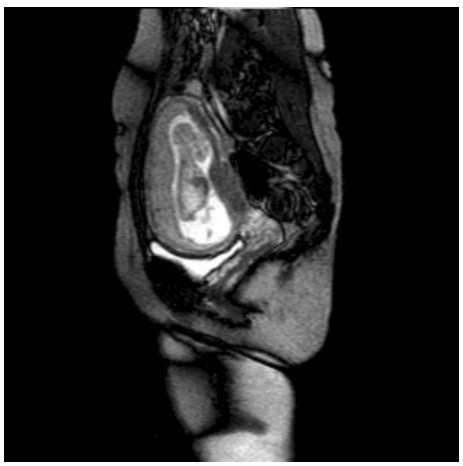

Fig. 6 Occipital encephalocele and a cystic kidney larger than normal in one of the fetuses in the sagittal T2W MR section

Discussion

The classic triad of Meckel-Gruber Syndrome is cystic renal dysplasia (100%), occipital encephalocele (90%) and postaxial polydactyly (83.3%.). Diagnosis is made by the presence of at least two of the three stigmata (2).

Occipital encephalocele is formed by extrusion or herniation of the rhombencephalon, cerebellar vermis, caudal portion of the 3rd ventricle and an enlarged 4th ventricle from the posterior fontanel which is larger than normal. AFP values may increase in maternal serum due to encephalocele (4).

Cystic dysplasia of the kidneys is the most characteristic and expected feature of MKS. Kidneys can be 10–20 times larger than their normal size. On ultrasonography, kidneys filling almost the entire fetal abdomen are observed. MRI examinations (especially coronal and sagittal T2W sections) may be helpful in doubtful cases. Oligohydramnios is usually present because of abnormal kidney functions. Oligohydramnios causes pulmonary hypoplasia. This is the most common cause of death (5).

Postaxial polydactyly can affect all four extremities. It is the most variable finding of the MKS triad. It may not be detected in some patients. An evaluation may be difficult in the first trimester, but it can be easily recognized in second-level ultrasonography examinations.

Apart from these findings, Dandy-Walker and Arnold Chiari malformations, central nervous system findings such as microcephaly, hydrocephalus, eye anomalies, cleft and palate lip, biliary duct malformation characterised by proliferation and fibrosis in the bile ducts in the portal areas of the liver, congenital heart anomalies, adrenal hypoplasia, pancreatic cysts and fibrosis, male genital organ hypoplasia, male pseudohermaphroditism, cryptorchidism, ureteral agenesis, hypoplasia or duplication, absence and hypoplasia of the bladder can be seen (6, 7).

The differential diagnosis of MKS includes Bardet-Biedl syndrome (BBS), Trisomy 13, and Smith Lemli Opitz syndrome. CNS abnormalities will not be seen in BBS, while karyotype analysis will be abnormal in Trisomy 13. The karyotype is normal in MKS cases. In Smith Lemli Opitz syndrome, liver dysfunction and cholestatic liver disease are seen because of 7 dehydrocholesterol gamma reductase mutations (8).

Owing to its autosomal recessive inheritance, the risk of recurrence of the disease is 25% in families with a history of giving birth to a baby with MKS. This situation makes prenatal research and diagnostic methods being applied more important, especially in the first trimester, in countries where consanguineous marriages are common.

Families with a previous history of childbearing with MKS should be informed that the risk of recurrence in their next pregnancy is 25%, and it should be explained that this disease cannot be diagnosed definitively with chromosome tests, but first trimester ultrasonography can help in the diagnosis. MRI may contribute to the diagnosis in pregnant women whose definitive diagnosis cannot be made by ultrasonography, especially in those with oligohydramnios.

Studies have revealed many different genetic mutations in the diagnosis of MKS, and 14 different genetic mutations have been identified so far. Despite this, it is known that genetic mutations explain only 60% of the cases (9). Therefore, a definitive prenatal genetic diagnosis for MKS is not yet known.

Cystic dysplasia of the kidneys should be investigated in cases with occipital encephalocele in routine first trimester ultrasonography scans. MRI examinations (especially sagittal and coronal T2W) may be useful in cases where ultrasonography is insufficient. Cases that are missed in the first trimester and those that present late to antenatal care can be diagnosed in the second trimester. During this period, oligohydramnios may be evident.

No cure has been found for this syndrome as yet. Termination is offered if the disease is diagnosed prenatally. For patients who do not accept termination, a conservative approach should be applied and the patient should be counseled.

Conclusion

MKS is a lethal disease. Fetal survival is impossible because of pulmonary hypoplasia. Parents should be informed about the prognosis and outcome of the fetus. Since the risk of recurrence in the next offspring of mothers with a history of infants with MKS is 25%, it is important to inform the families about the prenatal diagnosis.

Declarations

Conflict of ınterests We certify that there is no actual or potential conflict of interest in relation to this article. Kadir Atakır, M.D. Emine Aylin Atakır, M.D.

References

1. Opitz JM, Howe J. The Meckel syndrome (dysencephalia splanchnocystica, the Gruber syndrome). In: Bergsma D, editor. Malformation syndromes. New York: The National Foundation/Williams & Wilkins; 1969. p. 167–79.
2. Sergi C, Adam S, Kahl P, Otto HF. Study of the malformation of ductal plate of the liver in Meckel syndrome and review of other syndromes presenting with this anomaly. Pediatr Dev Pathol. 2000;3:568–83.
3. Jones KL. Meckel-Gruber syndrome. In: Jones KL, editor. Smith's recognizable patterns of human malformation. 6th ed. Philadelphia: Elsevier saunders; 2006. p. 198–9.

4. Gazioglu N, Vural M, Seckin MS, Tuysuz B, Akpir E, Kuday C, et al. Meckel-Gruber syndrome. Childs Nerv Syst. 1998;14:142–5. https://doi.org/10.1007/s003810050198.
5. Salonen R. The Meckel syndrome; clinicopathological findings in 67 patients. Am J Med Genet. 1984;18:671–89.
6. Gilbert-Barness EF, Opitz JM. Congenitalanomalies: malformation syndromes. In: Wigglesworth SS, Singer DB, editors. Textbook of fetal and perinatal pathology. 2nd ed. England: Blackwell Science; 1998. p. 323–57.
7. Sayhan S, Dicle N, Öner RS. Meckel-Gruber Sendromu. Perinatoloji Dergisi. 2004;12:99–101.
8. Chen CP. Meckel syndrome: genetics, perinatal findings and differential diagnosis. Taiwan J Obstet Gynecol. 2007;46:9–14.
9. Hartill V, Szymanska K, Sharif SM, Wheway G, Johnson CA. Meckel-Gruber syndrome: an update on diagnosis, clinical management, and research advances. Front Pediatr. 2017;5:244. https://doi.org/10.3389/fped.2017.00244.