Yumed Text
OPEN ACCESS JOURNALS

Clinical Case Reports: Open Access

Case Report | Vol 8 Iss 4
ISSN: 2582-5038
https://dx.doi.org/10.46527/2582-5038.353

A Case Report on Meckel Gruber Syndrome: Clinical Management and Genetic Counseling

Hemamalini*, Bhat D, Vinutha SP, Manjunatha HN, Pushpalatha K and Vidya CS

Department of Anatomy, JSS Medical College, Mysuru

***Corresponding author:** Hemamalini, Associate Professor, Department of Anatomy, JSS Medical College, Mysuru, India; E-mail: shettyhemamalini@gmail.com

Received: September 10, 2025; **Accepted:** December 21, 2025; **Published:** December 31, 2025

Abstract

Introduction: Because of the pulmonary hypoplasia, Meckel-Gruber syndrome is an uncommon autosomal recessive condition with a 100% fatality rate. It results from mutations in genes that code for proteins that are essential to the primary cilium's structure and function. Global incidence varies between 1 in 1,300 to 1 in 140,000 live births.

Case report: At 22 weeks of pregnancy, a 26-year-old woman with a history of third-degree consanguineous marriage chose to end the pregnancy in accordance with the PCPNDT (Pre-Conception and Pre-Natal Diagnostic Techniques) Act after ultrasound revealed a single fetus with occipital encephalocele, bilateral enlarged kidneys with cysts, and decreased amniotic fluid. The fetus was delivered, the pregnancy was ended, and it was sent for autopsy. Examining the female fetus revealed postaxial polydactyly in all four limbs—hexapolydactyly—bilateral enlarged kidneys with cysts filling the entire abdomen, and occipital encephalocele. Potter's facies, clubfoot, dextrocardia with pulmonary hypoplasia, long bone bowing, and a short, webbed neck were also present in the fetus.

Conclusion: Polydactyly, hepatic fibrosis, renal cystic dysplasia, CNS malformations, cysts and duct proliferation, and pulmonary hypoplasia from oligohydramnios are all features of Meckel-Gruber syndrome, a rare autosomal recessive lethal ciliopathic genetic anomaly. To rule out trisomy 13, which mimics Meckel-Gruber syndrome, chromosome analysis is necessary. Meckel-Gruber syndrome has a 25% recurrence rate, while trisomy 13 has a 1% risk. Information about the prognosis of the fetus after diagnosis, carrier testing, future reproductive outcomes, and the occurrence/recurrence risk and the outcome through genetic counselling is very essential.

1. Abbreviations

MGS: Meckel-Gruber Syndrome; PCPNDT: Pre-Conception and Pre-Natal Diagnostic Techniques; ASD: Atrial Septal Defect; TIFFA: Targeted Imaging for Fetal Anomalies; CTEV: Congenital Talipes Equinovarus; Hh: Hedgehog; NCC: Neural Crest Cell; AFP: Alpha-fetoprotein;

2. Introduction

Bilateral dysplastic cystic kidneys, occipital encephalocele, and postaxial polydactyly [1] are the hallmarks of Meckel-Gruber syndrome (MGS), an uncommon autosomal recessive condition.

According to Hsia et al. and Mecke S et al., [2, 3], there should be at least two of the traditional triad of occipital encephalocele, polydactyly and cystic kidneys. However, Fraser et al. [4], study of 65 cases of MGS suggests that the diagnosis of MGS may not be reliable if there is no kidney cystic dysplasia. According to Salonen et al., occipital encephalocele or other CNS malformations, hepatic portal fibrosis, and cystic renal dysplasia should be the minimal diagnostic criteria to differentiate MGS [5]. Thus, extremes of the spectrum of abnormalities cause issues with prenatal diagnosis and genetic counseling [6].

Johann Friedrich Meckel was the first to report MGS in 1822. GB Gruber later reported several cases of MGS and renamed it as dysencephalia splanchnocystica [7].

MGS, which is mainly due to cilium dysfunction, primarily affects the kidneys, limbs, and nervous system. The presence of a meningoencephalocele, typically in the occipital region, is the classical malformation of the central nervous system. Along with this usually bilateral polycystic kidneys, a renal anomaly is also seen. Both the upper and lower extremities may be affected by postaxial polydactyly. Other abnormalities such as gonadal dysgenesis, liver fibrosis, oral clefts, and CNS malformations can also be present in people with MGS. cardiovascular abnormalities like pulmonary stenosis, coarctation of the aorta, and atrial septal defect (ASD) [1,5].

MGS causes intrauterine fetal death because its symptoms are severe and frequently incompatible with life. Meckel-Gruber syndrome affects 1 in 13,250 to 140,000 live births worldwide. Gujarati Indians are said to have the highest incidence, with one affected birth per 1,300 (carrier rate: 1 in 18) [6].

Furthermore, the clinical picture of MGS is more variable due to the presence of multiple congenital defects that mimic or overlap. These include anencephaly, holoprosencephaly, hydrocephalus, and cerebellar hypoplasia. Skeletal dysplasia, ambiguous genitalia, congenital heart disease, coloboma, and micro- or anophthalmia. Numerous Joubert syndrome [8] genotypic traits are present in MGS.

3. Case Report

A 26-year-old lady with a history of third-degree consanguineous marriage, at 22 weeks of gestation, during a TIFFA (Targeted Imaging for Fetal Anomalies) scan, revealed multiple anomalies. The pregnancy was terminated, and the fetus was subjected to a fetal autopsy. On examination, the female fetus showed occipital encephalocele, bilateral enlarged kidneys with cysts filling the entire abdomen, and postaxial polydactyly in all 4 limbs—hexapolydactyly. Along with this, the fetus also had Potter's facies, clubfoot, dextrocardia with pulmonary hypoplasia, bowing of long bones, and a short and webbed neck.

Multiple anomalies were discovered during a TIFFA (Targeted Imaging for Fetal Anomalies) scan at 22 weeks of gestation in a 26-year-old woman with a history of third-degree consanguineous marriage. A fetal autopsy was performed on the fetus after

the pregnancy was ended. Examining the female fetus revealed postaxial polydactyly in all four limbs—hexapolydactyly—bilateral enlarged kidneys with cysts filling the entire abdomen, and occipital encephalocele. Potter's facies, clubfoot, dextrocardia with pulmonary hypoplasia, long bone bowing, and a short, webbed neck were also present in the fetus.

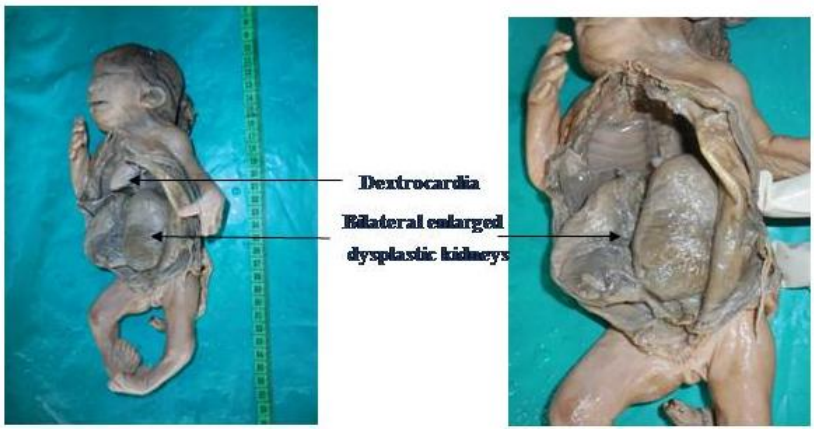

FIG. 1. **Foetus with Meckel-Gruber Syndrome Associated with Dextrocardia.**

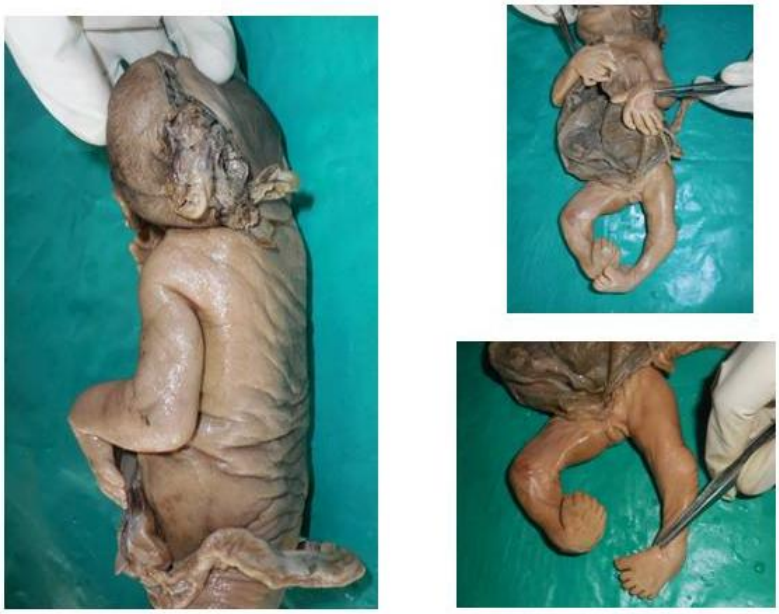

FIG. 2. **Occipital Encephalocele and Postaxial Polydactly.**

3.1 External examination

A female fetus with a short and narrow rib cage and distended abdomen was noticed. The fetus was first fixed in 10% formalin, which was also injected into the thoracic, abdominal, and cranial cavities for fixation of the internal organs. An autopsy was performed by the standard protocol [9]. Following are the findings of the autopsy:

Head: A brain herniation located at the occipital region with a size of 1 cm was found. The hernial sac contained meninges and brain tissue. The findings were described as occipital encephalocele.

Face: The fetus had a distinctive Potter's facies—slanting forehead, flattened nose, and low-set ears—which is secondary to oligohydramnios during intrauterine life.
Limbs: Postaxial polydactyly in both hands and feet with bilateral CTEV, bowing, and shortening of long bones.

It was observed that the female fetus had a distended abdomen and a short, narrow rib cage. In order to fix the internal organs, the fetus was first fixed in 10% formalin, which was also injected into the cranial, abdominal, and thoracic cavities. The standard protocol [9] was used to perform an autopsy. The results of the autopsy are as follows:
Head: A 1 cm brain herniation was discovered in the occipital area. Brain tissue and meninges were found in the hernial sac. The results were characterized as occipital encephalocele.
Face: The fetus's characteristic Potter's facies, which includes a low-set ear, flattened nose, and slanting forehead, is secondary to oligohydramnios during intrauterine life**.**
Limbs: bilateral CTEV, bowing, and shortening of long bones in both hands and feet due to postaxial polydactyly.

3.2 Internal examination of the cavities and organs

Upon opening the thoracic cavity, an unusual positioning of viscera was discovered. The heart was located on the right side of the thoracic cavity, and the cardiac apex was directed to the right and forward—dextrocardia. There also was irregular lobulation of the lungs. The right lung had one oblique fissure (two lobes), and the left lung had two fissures—one horizontal and one oblique (three lobes). The above findings suggest complete thoracic situs inversus. The diaphragm domes appeared normal.

The observation of the abdominal cavity showed the stomach in the supracolic compartment, in the right hypochondriac region. The spleen was located under the right dome of the diaphragm. The retroperitoneal organs showed abnormally large kidneys, giving a balloon-like configuration of the abdomen. The ureters were very thin and threadlike, coming out of each kidney. Karyotype was normal. Whole exome sequencing was suggested to the couple. However, due to financial constraints, they declined the genetic evaluation.

An odd visceral arrangement was found when the thoracic cavity was opened. The cardiac apex, or dextrocardia, was oriented forward and to the right, and the heart was situated on the right side of the thoracic cavity. Additionally, the lungs' lobulation was irregular. The left lung had two fissures, one horizontal and one oblique (three lobes), while the right lung had one oblique fissure (two lobes). Complete thoracic situs inversus is suggested by the aforementioned findings. The diaphragm domes looked typical.

When the abdominal cavity was observed, the stomach was located in the right hypochondriac region, in the supracolic compartment. The spleen was situated beneath the diaphragm's right dome. The kidneys in the retroperitoneal organs were abnormally large, giving the abdomen a balloon-like shape.

The ureters, which emerged from each kidney, were extremely thin and threadlike. Karyotype was typical. The couple was advised to undergo whole exome sequencing. However, they refused the genetic evaluation because of financial limitations.

4. Discussion

One of the most severe ciliopathies, Meckel-Gruber syndrome, is due to mutations in 14 genes (MKS1–MKS13 and TXNDC15) [10]. In addition to demonstrating allelism with other ciliopathies such as Joubert syndrome, Bardet-Biedl syndrome, and polycystic kidney disease [8,11], this mapping indicates extreme genetic heterogeneity.

A class of human diseases known as ciliopathies is characterized by cilium dysfunction. Skeletal abnormalities and congenital central nervous system defects are common clinical features of ciliopathies, which also involve renal, retinal, and hepatic involvement [12]. Heterotaxy, congenital heart disease, asplenia, infertility, and situs inversus are additional symptoms of the disease that affect 50% of patients [13]. MGS is fatal, and pulmonary hypoplasia or renal failure cause death either in utero or right after birth [8].

Three B9 domain-containing proteins involved in ciliogenesis—MKS1, B9D1, and B9D2—are present in almost all ciliated cells. Phenotypes similar to MGS are caused by mutations in either the B9d2 or MKS1 genes. The absence of B9d1 was linked to changes in ciliogenesis, ciliary protein localization, and Hedgehog (Hh) signal transduction, as well as polydactyly, kidney cysts, ductal plate malformations, and aberrant neural tube patterning. Meckel syndrome arises when B9d1 is disrupted because it is necessary for normal Hh signaling, ciliogenesis, and ciliary protein localization. Additionally, B9d1 and B9d2 are crucial parts of a B9 protein complex [14].

Abnormal proliferation and differentiation of the epithelial cells lining the renal tubules are hallmarks of cystic kidney disease. Autosomal dominant polycystic kidney disease is primarily caused by mutations in the genes encoding polycystin-1 and polycystin-2. In addition to being involved in cell proliferation and differentiation, polycystin 1 mediates the mechano-sensation of fluid flow by the primary cilium in the renal epithelium when fluid passes through the renal tubule. Autosomal recessive polycystic kidney disease is caused by mutations in the fibrocystin gene [15].

Cell-to-cell adhesions and a number of signaling pathways implicated in cystogenesis are mediated by both polycystin-1 and polycystin-2. Cystic kidney disease is largely caused by Wnt signaling. It plays a role in determining cell fate, polarity, and growth [16].

The normal state of Wnt signaling is disrupted by mutations in many ciliopathy genes. It is meticulously regulated throughout kidney development, and its downregulation results in the formation of cysts [17].

In vertebrates, cilia are also essential for the Hh signaling pathway. It is responsible for a number of skeletal abnormalities that are common in ciliopathies, including short limbs and craniofacial malformation, because it is necessary for healthy bone development and skeletal patterning [18,19].

Neural tube patterning and neural crest cell migration depend on Wnt and Hh signaling. In ciliopathy, distinctive craniofacial abnormalities are observed when NCC migration fails [20,21]. Three loci on 17q23 (MKS1), 11q13 (MKS2), and 8q24 (MKS3) have been mapped for MKS, which is genetically diverse and exhibits allelism with other ciliopathies [22]. Atypical neuronal migration and a disturbed Hh signaling pathway are linked to ciliopathies [23].

5. Clinical Management

Molecular diagnostic strategies include mutation screening of individual genes or multiple gene panels by sequence analysis and deletion/duplication analysis or whole-exome sequencing or whole-genome sequencing, which should be investigated for obligate carriers who are clinically unaffected but carry a gene mutation based on the family history.

Alpha-fetoprotein (AFP) level from either maternal blood or amniotic fluid may help to detect an encephalocele.

When MGS is suspected, a karyotype study should be obtained to exclude trisomy 13. Transvaginal ultrasound around the twelfth week of gestation is crucial for antenatal screening and the possible diagnosis of the Meckel-Gruber syndrome.

Molecular diagnostic techniques include whole-exome sequencing, whole-genome sequencing, deletion/duplication analysis, and mutation screening of individual genes or multiple gene panels. Based on family history, obligate carriers who are clinically unaffected but carry a gene mutation should be looked into.

Finding an encephalocele may be aided by measuring the amount of alpha-fetoprotein (AFP) in the mother's blood or amniotic fluid.

To rule out trisomy 13, a karyotype analysis should be acquired when MGS is suspected. For prenatal screening and the potential diagnosis of Meckel-Gruber syndrome, transvaginal ultrasonography is essential around the twelfth week of pregnancy.

The classic triad was solely seen in cases diagnosed before the 14th week of gestation. Later in the pregnancy, severe oligohydramnios makes it more difficult to establish the diagnosis by ultrasound alone. In these cases, a meticulous autopsy is necessary to establish the diagnosis of MGS. It is important that tissue for molecular genetic analysis be stored from all such families as a resource for more reliable diagnostic tests.

Deviation of the heart from the medial axis as well as abnormality in the position of the liver and spleen are simple ultrasound features to look for in the early diagnosis of an abnormality such as isomerism.

Only cases diagnosed prior to the fourteenth week of pregnancy exhibited the classic triad. Severe oligohydramnios later in pregnancy makes ultrasound diagnosis more challenging.

To confirm the diagnosis of MGS in these situations, a thorough autopsy is required. All of these families should have tissue saved for molecular genetic analysis as a resource for more accurate diagnostic procedures.

Simple ultrasound features to look for in the early diagnosis of an abnormality like isomerism include deviation of the heart from the medial axis and abnormalities in the position of the liver and spleen.

6. Genetic Counseling

Since MGS has an AR inheritance pattern, couples with a history of third-degree consanguinity and with a previously affected child should have the opportunity for genetic counseling in order to discuss the nature, inheritance, and implications of an MKS diagnosis. If the condition has occurred in previous pregnancies, then the recurrence risk is 25%. Parents can make an informed decision with an accurate perception of their genetic risk, a clear understanding of the impact of the genetic disorder, and their previous experience of having an affected child. It is therefore appropriate to discuss these issues at an early stage to ensure that families can make informed medical and personal decisions.

In order to discuss the nature, inheritance, and implications of an MKS diagnosis, couples with a history of third-degree consanguinity and a child who has already been affected should have the opportunity to receive genetic counseling because MGS has an AR inheritance pattern. The chance of recurrence is 25% if the condition has happened during prior pregnancies. With a clear understanding of the effects of the genetic disorder, a realistic assessment of their own genetic risk, and prior experience with an affected child, parents can make an informed choice. Therefore, it makes sense to have these conversations early on so that families can make well-informed personal and medical decisions.

Genetic evaluation of the fetus is an essential step to offer antenatal testing in future pregnancies. Due to genetic heterogeneity, it would be ideal to provide reproductive options in future pregnancies, and carrier couples must be educated regarding this. Offering antenatal testing in subsequent pregnancies requires a genetic assessment of the fetus. It would be ideal to offer reproductive options in subsequent pregnancies due to genetic heterogeneity, and carrier couples need to be informed about this.

REFERENCES

1. Wright C, Healicon R, English C, et al. Meckel syndrome: what are the minimum diagnostic criteria? J Med Genet. 1994;31(6):482-5.
2. Hsia YE, Bratu M, Herbordt A. Genetics of the Meckel syndrome (dysencephalia splanchnocystica). Pediatrics. 1971;48(2):237-47.
3. Mecke S, Passarge E. Encephalocele, Polycystic kidneys and polydactyly as an autosomal recessive trait simulating certain other disorders: the Meckel syndrome. Ann Genet (Paris). 1971;14(2):97-103.
4. Fraser FC, Lytwyn A. Spectrum of anamalies in the Meckel syndrome or “May be there is a malformation syndrome with at least one constant anomaly”. Am J Med Genet. 1981;9:67-73.
5. Salonen R, Norio R, Reynolds James F. The Meckel syndrome: clinicopathological findings in 67 patients. Am J Med Genet. 1984;18(4):671-89.
6. Salonen R, Norio R. The Meckel syndrome in Finland: epidemiologic and genetic aspects. Am J Med Genet. 1984;18(4):691-8.
7. Parelkar SV, Kapadnis SP, Sanghvi BV, et al. Meckel-Gruber syndrome: A rare and lethal anomaly with review of literature. J Pediatr Neurosci. 2013;8(2):154-7.
8. Kheir AE, Imam A, Omer IM, et al. Meckel-Gruber syndrome: A rare and lethal anomaly. Sudan J Paediatr. 2012;12(1):93-6.

9. Kale PP, Kanetkar SR, Shukla DB, et al. Study of congenital malformations in fetal and early neonatal autopsies. Ann Pathol Laborat Med. 2017;4(4):433-41.
10. Hartill V, Szymanska K, Sharif SM, et al. Meckel-Gruber Syndrome: An Update on Diagnosis, Clinical Management, and Research Advances. Front Pediatr. 2017;5:244.
11. Paavola P, Salonen R, Baumer A, et al. Clinical and genetic heterogeneity in Meckel syndrome. Hum Genet. 1997;101(1):88-92.
12. Braun DA, Hildebrandt F. Ciliopathies. Cold Spring Harb Perspect Biol. 2017;9(3):a028191.
13. Leigh MW, Pittman JE, Carson JL, et al. Clinical and genetic aspects of primary ciliary dyskinesis/Kartagener syndrome. Genet Med. 2009;11(7)473-87.
14. Dowdle WE, Robinson JF, Kneist A, et al. Disruption of a ciliary B9 protein complex causes Meckel syndrome. Am J Hum Genet. 2011;89(1):94-110.
15. Binu MP, Gregory B, Heuvel V. Kidney: Polycystic kidney disease. WIREs Dev Biol. 2014;3(6):465-87.
16. Komiya Y, Habas R. Wnt signal transduction pathways. Organogenesis. 2008;4(2):68-75.
17. Kawakami T, Ren S, Duffield JS. Wnt signalling in kidney diseases:dual roles in renal injury and repair. J Pathol. 2013;229(2):221-31.
18. Abraham SP, Nita A, Kreici P, et al. Cilia Kinases in skeletal development and homeostasis. Dev Dyn. 2022 Apr;251(4):577-608.
19. Onodera S, Azuma T. Hedgehog- related mutation causes bone malformation with or without hereditary gene mutations. Int J Mol Sci. 2023;24(16):12903.
20. Jeong J, Mao J, Tenzen T, et al. Hedgehog signalling in the neural crest cells regulates the patterning and growth of facial primordia. Genes Dev. 2004;18(8):937-51.
21. Maj P, Kunneke L, Loresch E, et al. Controlled levels of canonical Wnt signalling are required for neural crest migration. Develop Biol. 2016;417(1):77-90.
22. Smith UM, Consugar M, Tee LJ, et al. The transmembrane protein meckelin (MKS3) is mutated in Meckel-Gruber syndrome and the wpk rat. Nat Genet. 2006;38(2):191-6.
23. Andreu-Cervera A, Catala M, Schneider-Maunoury S. Cilia, ciliopathies and hedgehog-related forebrain developmental disorders. Neurobiol Dis. 2021;150:105236.