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A Antenatal Diagnostic of Lethal and a Rare Anomaly of Meckel Gruber Syndrome

A Case Report

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Abstract: Meckel-Gruber Syndrome (MKS) is a rare, lethal, congenital disorder, it's been linked to chromosome 17, characterized by a triad of occipital encephalocele, polycystic kidneys, and postaxial polydactyly, often accompanied by other anomalies such as a nervous system malformations and hepatic fibrosis. MKS can affect individuals of all races and ethnicities.

We present a case of a 25-week fetus diagnosed prenatally with features consistent with MKS on routine ultrasound. The diagnosis was confirmed postnatally with the presence of occipital encephalocele, bilateral enlarged echogenic kidneys, and postaxial polydactyly. Genetic counseling was provided to the parents, and the pregnancy outcome, as well as the clinical implications, are discussed. This case accentuates the importance of antenatal diagnosis, multidisciplinary management, and genetic counseling in cases of suspected Meckel-Gruber Syndrome.

Keywords: *Multicystic Dysplastic Kidneys, Encephalocele, Polydactyly, Prenatal Ultrasound Diagnosis, Autosomal Recessive Disorder, Meckel-Gruber Syndrome.*

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I. INTRODUCTION

Meckel-Gruber Syndrome (MKS) is a rare, lethal, congenital disorder , It's been linked to chromosome 17, characterized by a triad of , multicystic dysplastic kidneys, occipital encephalocele and postaxial polydactyly. First described by Johann Friedrich Meckel in 1822 (1) and further defined by Gruber in 1934 (2), The worldwide incidence is estimated from 1 in 13,250 to 1 in 140,000 live births (3.4).

MKS is autosomal recessive, restricted as a ciliopathy caused by mutations in several genes involved in primary cilia structure and function, inc ludingMKS1, TMEM67, and CEP290 (5,6). These mutations result in abnormal embryogenesis, leading to severe multisystemic malformations, most notably involving the central nervous system, renal system, and limbs.

Antenatal diagnosis is primarily based on ultrasound findings and can often be made in the first trimester. Typical sonographic features include occipital encephalocele, enlarged echogenic kidneys, and oligohydramnios or anhydramnios (7). The condition is uniformly fatal, with most affected fetuses dying in utero or shortly after birth (8).

This case report presents a prenatally diagnosed case of MKS in a non consanguineous couple, emphasizing the importance of early detection, appropriate counseling, and multidisciplinary management of such lethal congenital anomalies. In this article we report a case of Meckel-Gruber syndrome in a couple with no notion of consanguinity or previous genetic abnormalities, who benefited from a routine screening ultrasound at 25 weeks making us suspect this syndrome in front of the abnormalities, mainly encephalocele and polycystic kidneys, the pregnancy continued to full term at 38 weeks of amenorrhea.

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II. CASE REPORT

38-year-old with no significant medical history, gravida 3 para 3, with a history of 2 previous c-sections, who has been followed at our facility since the second trimester of her pregnancy, with no known consanguinity, with no significant family history of congenital disorders.

The ultrasound done at 25 weeks at our facility revealed in addition to a Large occipital encephalocele measuring 6 cm (Figure 1), Bilateral enlarged polycystic kidneys (Figure2) with loss of corticomedullary differentiation, Postaxial polydactyly noted on upper and lower limbs, and a non-visualized bladder, there was no history of medication or herbal product use during pregnancy, and the prenatal laboratory work-up was unremarkable. A medical termination of pregnancy was suggested but declined by the couple who chose to continue the pregnancy to full term, and the patient was scheduled for a c-section at 39 weeks. the patient was referred to our institution at 38 weeks of gestation, with ruptured membranes and Umbilical cord prolapse.

An emergency c-section was performed. She delivered a female neonate weighing 3200 grams, who died 1 hour after birth due to severe respiratory distress.

- *Postnatal External Examination Revealed Several Dysmorphic Features:*

Retrognathia and hypertelorism (Figure 3) and a posterior encephalocele on the cephalic pole (Figure 4); hepatosplenomegaly with ascites in the abdominal region; and limb anomalies including postaxial polydactyly involving all four extremities (Figure 5), bilateral clubfeet (Figure 6). Examination of the spine and external genitalia showed no abnormalities (Figure 7). The family declined autopsy.

Given the constellation of findings—central nervous system malformations, renal anomalies, hepatic involvement, and polydactyly, a diagnosis of Meckel-Gruber Syndrome was strongly considered.

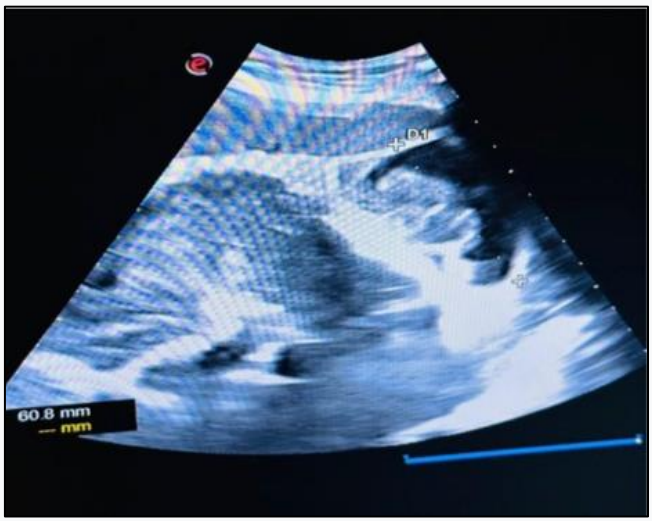


Fig 1 Ultrasound Examination of Posterior Encephalocele.

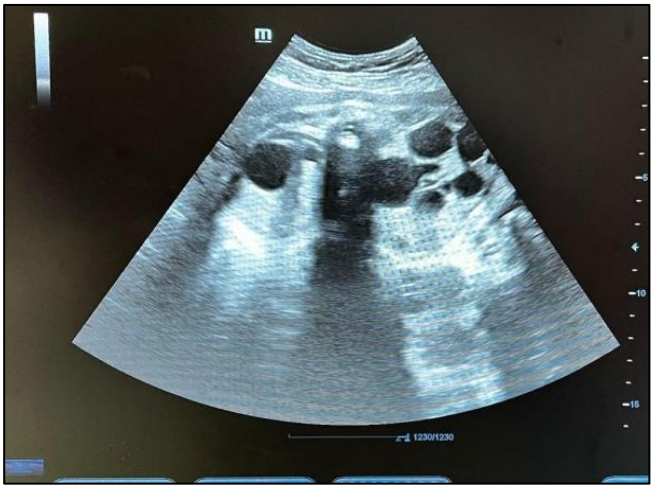


Fig 2 Ultrasound Showing Cystic Dysplasia of the Kidneys.

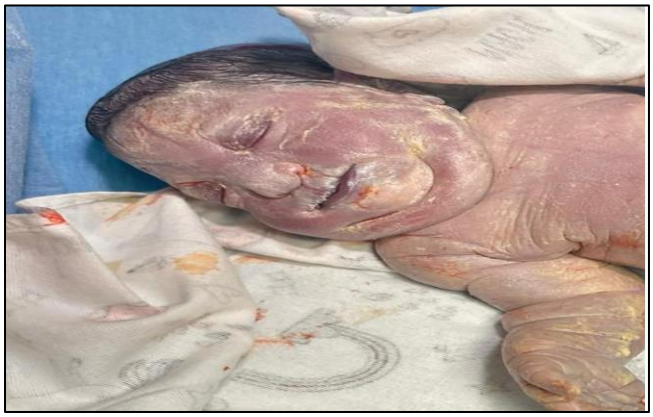
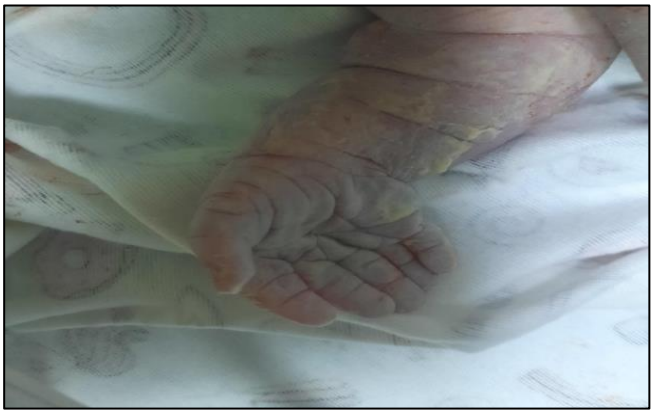


Fig 3 Neonatal Retrognatism and Hypertelorism Aspect


Fig 4 Posterior Encephalocele Aspect



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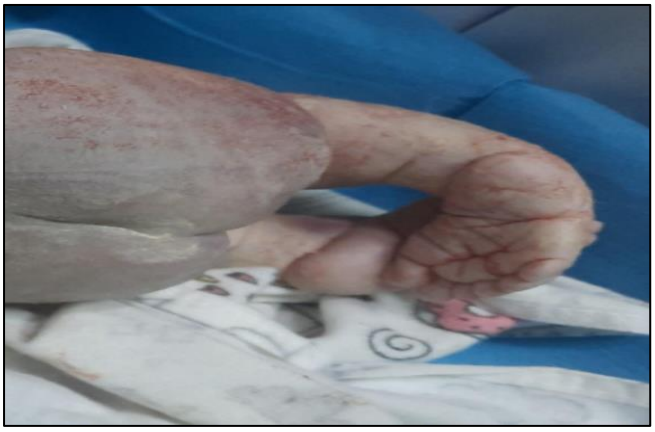

Fig 5 Polydactyly on Upper and Lower Limbs

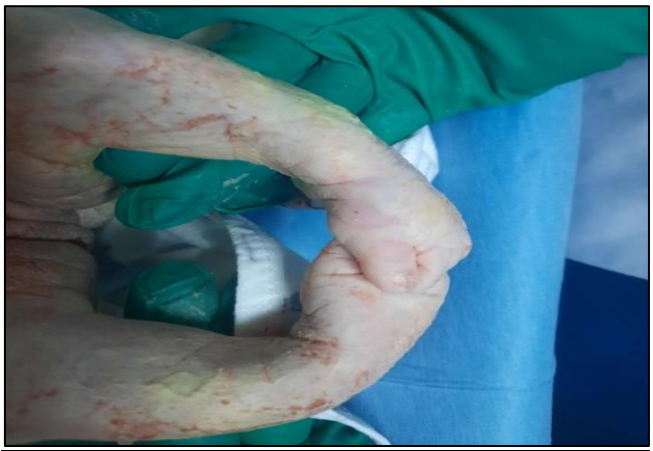

Fig 6 Clubfeet Aspect

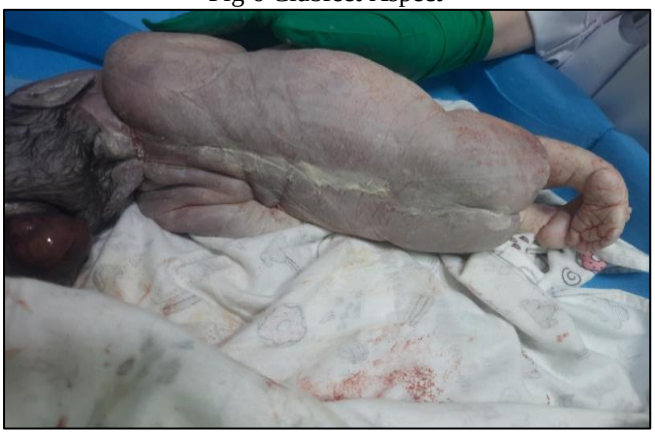

Fig 7 No Spinal Abnormalities

III. DISCUSSION

Meckel-Gruber Syndrome (MKS) is a rare, lethal, congenital disorder. and uniformly lethal ciliopathy characterized by a triad of occipital encephalocele, multicystic dysplastic kidneys and postaxial polydactyly (3). Our case illustrates a classic presentation of MKS, with additional malformations such as retrognathia, hypertelorism, clubfeet, and hepatosplenomegaly—findings frequently associated with the syndrome (4,7). Despite the absence of known consanguinity or family history, the clinical and imaging features in this fetus strongly supported the diagnosis.

MKS is caused by mutations in genes encoding proteins that localize to the primary cilium or basal body, such asMKS1, TMEM 67, CC2D2A, CEP290, RPGRIP1L, and others, have been implicated in MKS, confirming its genetic heterogeneity (9,10). These proteins play a vital role in cellular signaling during embryonic development (11, 12, 13), particularly in the development of the brain, kidneys, and liver (6,9). The phenotypic variability of MKS, even within the same family, reflects its genetic heterogeneity and variable expressivity.

Prenatal diagnosis of MKS is feasible through detailed ultrasonography, often in the late first or early second trimester. Key ultrasound findings include occipital encephalocele, large echogenic kidneys with loss of corticomedullary differentiation, oligohydramnios or anhydramnios, polydactyly, and in some cases, hepatic fibrosis (14). In this case, the diagnosis was suspected at 22 weeks and confirmed with follow-up imaging at 25 weeks, meeting all major diagnostic criteria. Despite early identification and counseling, the family chose to continue the pregnancy, a decision often influenced by personal, ethical, religious, or cultural considerations.

Neonatal outcomes in MKS are universally poor. Perinatal mortality approaches 100%, with most neonates dying in utero or shortly after birth due to complications such as pulmonary hypoplasia from prolonged oligohydramnios (15). In our case, the neonate died within an hour due to severe respiratory distress, consistent with reported outcomes.

In recent years, tools such as fetal MRI, fetoscopy, and maternal serum α-fetoprotein testing have enhanced diagnostic accuracy, particularly when ultrasound findings are ambiguous or when oligohydramnios limits visualization (16,17). Nevertheless, these techniques remain underutilized due to cost and limited accessibility.

Despite advances in prenatal diagnostics, therapeutic options for MKS remain limited, given its uniformly fatal outcome. Therefore, genetic counseling is a cornerstone in the management of affected families, especially those with a history of MKS. Couples should be informed about the recurrence risk (25%) and the potential for preimplantation genetic diagnosis (PGD) or early chorionic villus sampling in future pregnancies (18,19).

Anhydramnios and umbilical cord prolapse further complicated the delivery in this case, necessitating an emergency cesarean section. While delivery mode does not impact neonatal survival in MKS, careful planning and monitoring remain essential for maternal well-being, particularly in patients with prior cesarean deliveries.

Postnatal autopsy, though ideal for definitive diagnosis, may not always be feasible due to cultural or personal objections, as in our case. However, when performed, it can provide crucial diagnostic confirmation and contribute to familial risk assessment (20).

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The differential diagnosis of MKS includes a broad range of syndromes with overlapping features, such as Trisomy 13 (Patau syndrome), Bardet-Biedl syndrome, Smith-Lemli-Opitz syndrome, and Joubert syndrome (21,22). Differentiation from chromosomal disorders is possible via karyotyping, while distinguishing MKS from other ciliopathies often requires molecular genetic testing, which may not be readily available in low-resource settings (23,24).

Postnatal external examination revealed typical dysmorphic features. Although autopsy and genetic testing were declined—limiting definitive confirmation—clinical and radiological features were sufficient for a presumptive diagnosis. This highlights a common challenge in low-resource or culturally sensitive settings, where postmortem investigations are often declined.

The recurrence risk of MKS in future pregnancies is 25%, due to its autosomal recessive inheritance pattern. Genetic counseling is therefore crucial for affected families, even in the absence of a known genetic mutation, to discuss risks and options such as early prenatal screening or preimplantation genetic diagnosis (8).

This case reinforces the importance of early anomaly scanning, thorough counseling, and a multidisciplinary approach involving obstetrics, genetics, neonatology, and psychosocial support. Early diagnosis empowers families to make informed decisions regarding pregnancy management and future reproductive planning.

IV. CONCLUSION

This case highlights a classic presentation of Meckel-Gruber Syndrome with multiple characteristic anomalies detected antenatally and confirmed postnatally. Despite the absence of consanguinity or a family history of congenital disorders, the fetus exhibited the typical triad—occipital encephalocele, polycystic kidneys, and polydactyly—alongside other associated malformations. The case underscores the value of detailed prenatal ultrasound in diagnosing lethal congenital anomalies and the importance of early multidisciplinary counseling. While medical termination remains a sensitive issue, early detection offers families the opportunity to make informed decisions and plan for future pregnancies with appropriate genetic counseling.

- *Ethical Approval*

Ethics approval has been obtained to proceed with the current study.

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- *Author Contribution*

Hassnaa SARHANE, Kaoutar BAHIDA, Maha LHALOUI, Nada DOURAIDI: Manuscript editing, picture editing, data analysis and interpretation, paper writing.

Najia ZERAIDI, Amina LAKHDAR, Aziz BAIDADA: literature review, supervision.

- *Guarantor*

The corresponding author is theguarantor of submission.

- *Research Registration Number*

Not applicable.

- *Consent*

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

- *Availability Of Data and Materials*

Supporting material is available if further analysis is needed.

- *Declaration Of Competing Interest*

The authors declare that they have no competing interests.

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