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Meckel-Gruber Syndrome: A Case Report and Literature Review

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Abstract
Gruber syndrome is a rare Meckel polymalformative syndrome, autosomal recessive, defined by occipital encephalocele, polydactyly, and renal cystic dysplasia. Ultrasound is currently the best means of antenatal screening for this lethal polymalformation, and confirmation is by karyotype study.
We report the case of a second 31-year-old woman with a scarred uterus and no history of consanguinity, who had a full-term pregnancy in which the diagnosis of Meckel-Gruber syndrome was made at 19 weeks' gestation and confirmed at birth.
Keywords: *Meckel syndrome, renal dysplasia, prenatal diagnosis.*

Introduction

Meckel-Gruber syndrome, described by Meckel in 1822 and Gruber in 1934, is characterized by the association of encephalocele, cystic dysplasia of the kidneys, and polydactyly. The variability of the clinical presentations reported in the literature demonstrates that the polymorphism of this syndrome is a fundamental characteristic. Ultrasound is currently the best means of antenatal screening for this lethal polymalformation.[1] We report a case of Meckel-Gruber syndrome discovered by ultrasound at 19 weeks of gestation.

Case Report

A 31-year-old patient, second pare,, with no history of consanguinity, consulted for the first time for pregnancy monitoring at 19 weeks of gestation. A fetal morphological ultrasound was performed, revealing a progressive single-fetus pregnancy with fetal malformations, including major hydrocephalus (Figure 1) and encephalocele. Medical termination of pregnancy was proposed but not accepted by the couple, and the pregnancy was carried to term with cesarean delivery of a male fetus weighing 2800g. Macroscopic examination revealed retrognathism and posterior encephalocele in the cephalic pole (Figure 2), polydactyly, and club feet. Examination of the spine and external genitalia was normal. The family refused an autopsy examination. Given this polymalformative syndrome, the diagnosis of Meckel-Gruber syndrome was considered.

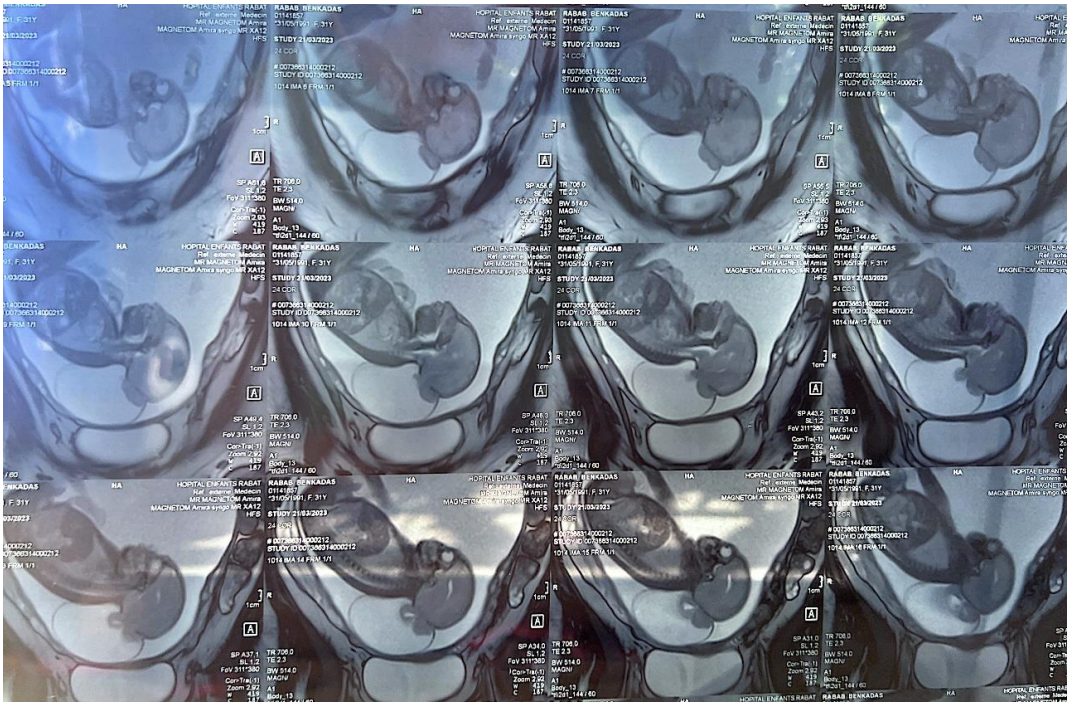

Figure 1

Figure 2

Discussion

Meckel-Gruber syndrome is a rare, severe genetic disorder characterized by a triad of features[2]:

- Cystic dysplasia of the kidneys
- Developmental defects of the central nervous system, such as encephalocele (protrusion of the brain through an opening in the skull)
- Polydactyly (extra fingers or toes)

Other common features include:

- Occipital encephalocele (protrusion of the brain through the back of the skull)
- Cleft lip and/or palate
- Hepatic fibrosis
- Cardiac defects
- Genital abnormalities

Meckel-Gruber syndrome is an autosomal recessive disorder, meaning an individual must inherit two defective copies of the responsible gene(s) to develop the condition. It is caused by mutations in several different genes, most commonly MKS1, MKS3/TMEM67, and MKS5/CEP290.[3]

Meckel syndrome affects 1 in 13,250 to 1,140,000 people worldwide. It is more common in Finland, where its birth prevalence is 1 in 9,000 and the mutation frequency is 1%.[4]

The pathogenesis of MGS is linked to the dysfunction of primary cilia, structures essential for signaling during embryonic development. Primary cilia play a crucial role in regulating signaling pathways such as the Hedgehog pathway, which is essential for organ development. Disruptions in these pathways due to dysfunctional cilia lead to a cascade of structural malformations, particularly in the kidneys, brain, and limbs.[5]

Prenatal diagnosis is crucial for Meckel-Gruber syndrome, given the severity of the disease. The following techniques are commonly used[6]:

- Prenatal ultrasound: Detection of structural anomalies such as encephalocele, multicystic kidneys, and polydactyly.
- Fetal MRI: Provides additional details on brain and other structural anomalies.
- Genetic diagnosis: Genetic testing to identify mutations in the genes associated with MGS. Next-generation sequencing (NGS) is often used for this analysis.

Given the lethal nature of Meckel-Gruber syndrome, management focuses primarily on appropriate genetic counseling and family support. Parents of an affected child have a 25% recurrence risk in each subsequent pregnancy. Prenatal diagnosis allows parents to make informed decisions regarding pregnancy management.

Trisomy 13 and 18 are ruled out in the presence of a normal karyotype.[7] Other polymalformative syndromes may present more significant diagnostic difficulties. Carpenter-Hunter syndrome combines encephalocele, renal cystic dysplasia, polydactyly, and generalized bone lesions

Conclusion

Meckel-Gruber syndrome is a rare but devastating genetic disorder characterized by a classic triad of encephalocele, multicystic renal dysplasia, and polydactyly. Advances in understanding the genetic bases and pathophysiological mechanisms have improved our ability to diagnose and counsel affected families. Continued research is essential to develop potential therapeutic approaches and improve the quality of life for families affected by this disease.

Declarations

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Informed consent: Written consent obtained from the patient.

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