CASE REPORT

# Meckel Gruber Syndrome (MKS): A rare and lethal congenital disorder

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**Abstract**

Meckel-Gruber Syndrome (MKS) is a rare autosomal recessive and lethal congenital disorder distinguished by a triad of dysplastic cystic kidneys, malformations of the Central Nervous System (CNS) and ductal plate malformation of the liver. This condition carries a 25% recurrence risk and a dismal prognosis with 100% fetal or neonatal mortality. A thorough autopsy examination is essential for accurate diagnosis. We report a case of MKS in a 30-year-old female, in which the fetus exhibited bilateral enlarged cystic kidneys, CNS malformation and liver fibrosis. Differentiating MKS from phenotypically overlapping conditions such as Bardet-Biedl syndrome and Trisomy 13, is crucial for proper management and genetic counselling. This case highlights the importance of awareness and early recognition of MKS, enabling healthcare providers to provide appropriate care and support to affected families.

**Keywords**: Meckel Syndrome, Autosomal Recessive Disorders, Kidney Diseases, Cystic, Encephalocele

## Introduction

Meckel Gruber Syndrome (MKS) also called as dysencephalia splanchnocystica was originally described by Johanna Freidrick Meckel in 1822 and later by George B Gruber in 1934 [1]. It is an autosomal recessive, lethal, multisystem disorder resulting from pathogenic genetic mutations affecting ciliogenesis [2]. Since the time it was first diagnosed, approximately 200 cases have been described to date with worldwide incidence of 1 in 3,500 to 1,40,000 [3, 4]. This case is presented to emphasize the characteristic clinicopathological features of MKS and to highlight the educational importance of meticulous autopsy examination in establishing an accurate diagnosis and guiding genetic counselling as emphasized in similar rare congenital anomaly case reports [5].

## Case Report

A 30-year-old female, gravida 3 para 2 living 2 (G3P2L2), presented with 18 weeks of amenorrhoea. A prenatal anomaly scan revealed a single live intrauterine pregnancy with multiple congenital abnormalities including hydrocephalus, encephalocele, shallow posterior cranial fossa, hypoplastic cerebellum, and bilateral enlarged cystic kidneys, prompting medical termination of pregnancy.Post-termination examination disclosed a male fetus with external malformations including cervical meningoencephalocele, hypertelorism, neonatal teeth, micrognathia, hypospadias, and polydactyly (Figures 1-4).

Its internal examination revealed bilateral cystic kidneys, a shallow posterior cranial fossa with hypoplastic cerebellum, and meningoencephalo-

cele (Figures 5-6). Microscopic examination of the liver showed fibrosis, while the kidney parenchyma revealed dysplastic mesenchyme with cysts (Figures 7-8). Thus, a definitive diagnosis of MKS was made.

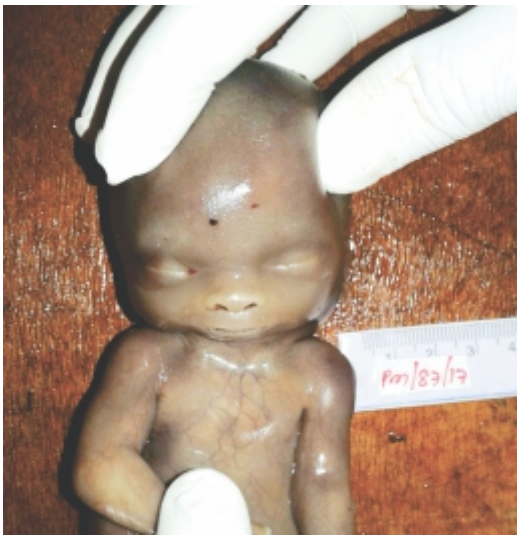

**Figure 1: Autopsy findings in the present case of MKS: Dysmorphic facial features including low-set ears, micrognathia, and hypertelorism were noted.**

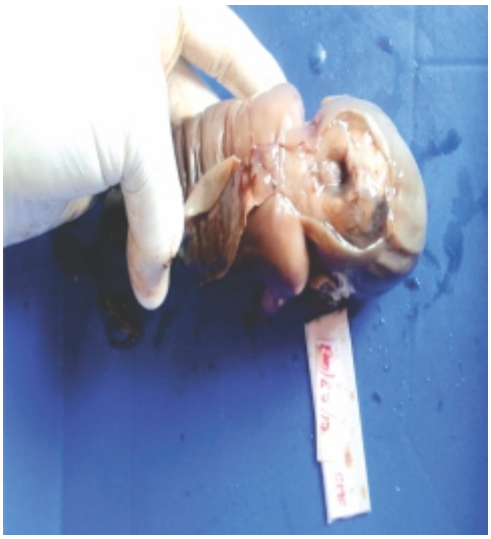

**Figure 2: Autopsy findings: Presence of a meningoencephalocele**

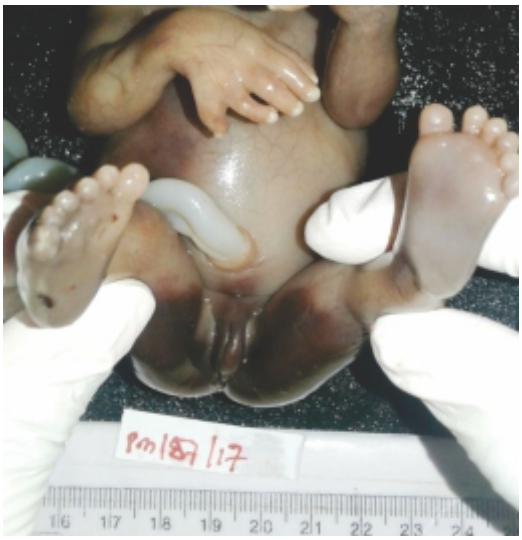

**Figure 3: Autopsy findings: hypospadias.**

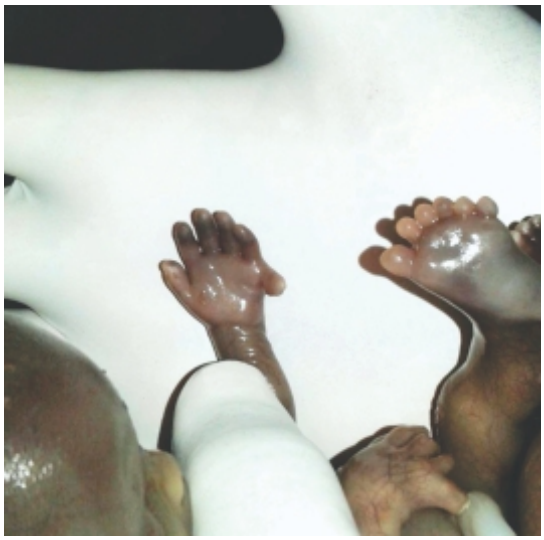

**Figure 4: Autopsy findings: postaxial polydactyly of the upper and lower limbs**

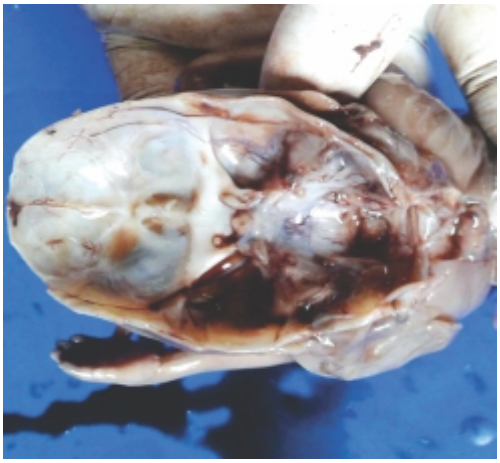

**Figure 5: Autopsy finding—hypoplastic cerebellum with a shallow posterior cranial fossa**

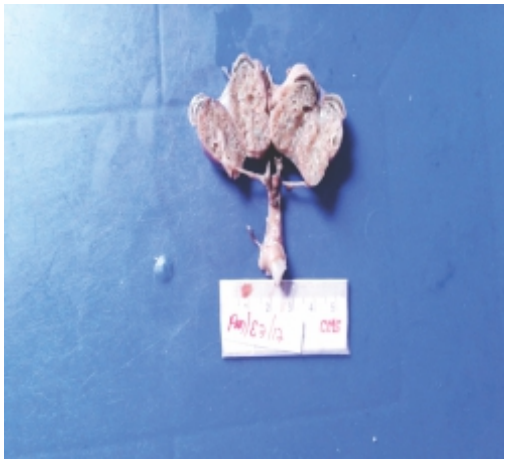

**Figure 6: Autopsy finding: Right and left kidneys measuring 2 × 1.8 × 1 cm, with grossly visible tiny cysts on the cut surface**

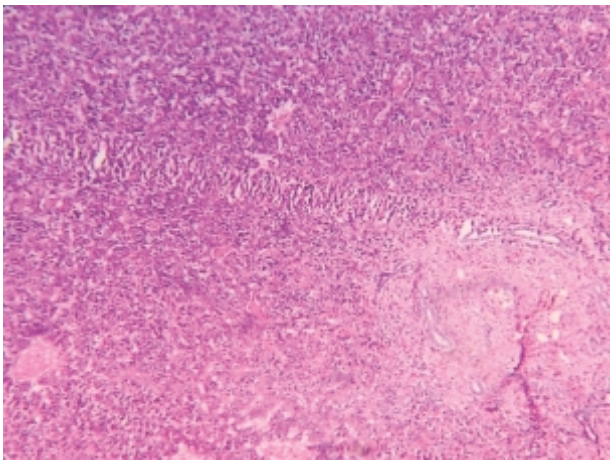

**Figure 7: Micrscopy of liver parenchyma showing periductal fibrosis (H&E, ×10)**

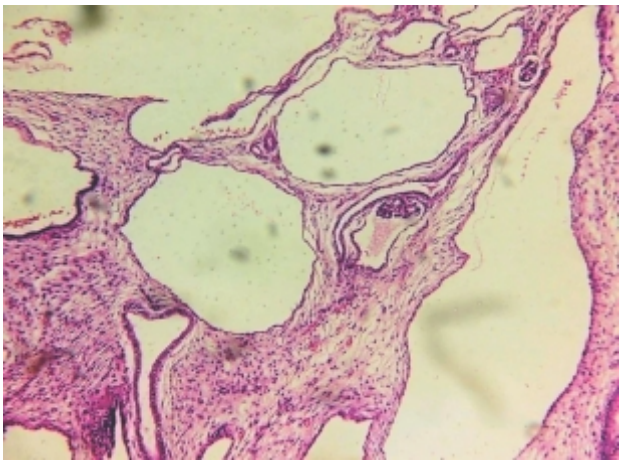

**Figure 8: Microscopy of kidney parenchyma displaying dilated cysts surrounded by immature mesenchyme (H&E, ×10)**

## Discussion

MKS is characterized by triad of renal cystic dysplasia, central nervous system malformation and ductal plate malformation of liver. In nearly 80% of cases, postaxial polydactyly is present. Two out of the three defining anomalies or two other anomalies in addition to the one classical finding are sufficient for a definitive diagnosis [4, 6, 7]. MKS results in 100% fetal or neonatal mortality and has a high risk (25%) of recurrence [4,8]. Hence MKS should be differentiated from its differential diagnosis like Bardet-Biedl Syndrome, Trisomy 13 and Smith-Lemli-Opitz syndrome [4, 9]. Given the autosomal recessive inheritance of MKS, genetic counselling is essential due to the 25% recurrence risk in future pregnancies[1,3,10].

The genetic heterogeneity of MKS highlights the role of molecular testing and early prenatal ultrasonography in enabling accurate risk assessment, timely diagnosis, and informed reproductive decision-making [2, 4, 7, 9]. Molecular testing in MKS focuses on the identification of biallelic pathogenic variants in ciliopathy-associated genes, reflecting the marked genetic heterogeneity of the disorder, and enables parental carrier detection and early prenatal diagnosis [2, 9]. Meticulous autopsy evaluation is crucial for confirming the diagnosis and guiding appropriate genetic counselling, a point highlighted across comparable reports of rare congenital anomalies [5]. Available evidence suggests that India may carry a substantial burden of birth defects, which contribute notably to neonatal mortality in the country. This highlights the urgent need for increased research investments to better understand the epidemiology and public health implications of birth defects in the Indian context. Additionally, there is a need to develop contextual educational and counseling materials, establish effective referral pathways for genetic counseling, and formulate appropriate ethical and regulatory guidelines [10].

## Conclusion

MKS is a severe and lethal congenital disorder with a high risk of recurrence. Pathologists may encounter clinically unsuspected or atypical cases, necessitating a meticulous autopsy to establish an accurate diagnosis. Identification of MKS is crucial for providing appropriate parental counselling regarding future pregnancies. This case underscores the importance of awareness and recognition of MKS, enabling healthcare providers to ensure timely diagnosis, appropriate care, and comprehensive support for affected families.

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