

## Case Report

# Meckel-Gruber syndrome: a case report with review of literature

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## ABSTRACT

Meckel Gruber syndrome is an autosomal recessive disorder, characterized by a combination of renal cysts or cystic renal dysplasia, developmental anomalies of the central nervous system, hepatic dysgenesis and polydactyly. It is a rare syndrome with highest incidence in Gujarati Indians and Finnish population. We report a case of Meckel Gruber syndrome in non Gujarati Indian which was diagnosed on fetal autopsy.

**Keywords:** Meckel-Gruber syndrome, Rare, Non Gujarati Indian

## INTRODUCTION

Meckel Gruber syndrome is a rare lethal autosomal recessive disorder with wide variety of systemic malformations mapped to 6 different loci in different chromosomes. Antenatal ultrasonography can identify major features, but neonatal autopsy is needed to document complete anomalies. We report a female baby with typical triad of Meckel Gruber syndrome.

## CASE REPORT

A 22 year old primigravida presented to the labor room with labor pains. On examination she was full term with breech presentation. The fetal heart sounds were very feeble. Emergency caesarean section was done and delivered a stillborn female fetus. With the consent of the parents the baby was sent for fetal autopsy. There was history of second degree consanguineous marriage. Past and family history was non-contributory. She was not on any teratogenic drugs. Routine antenatal scan was done during antenatal period at seventh month of pregnancy and showed anencephaly, congenital talipoequinovarus

and polydactyly. She was counselled for termination of pregnancy but refused as she came from rural area.

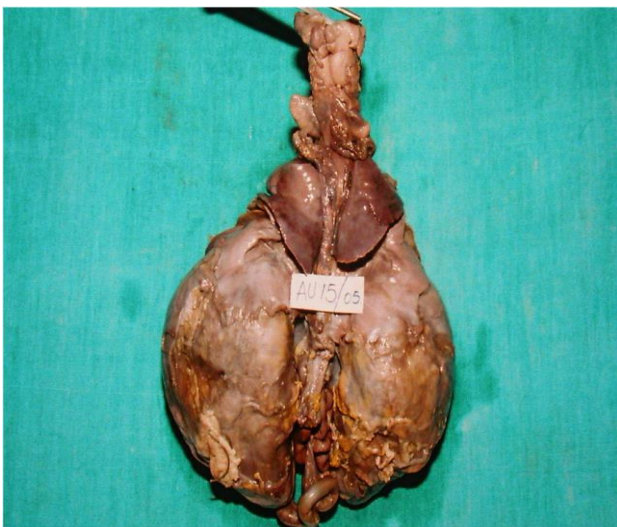
At autopsy the fetal weight was 2.650 gm, head circumference 26 cm, abdominal circumference 40 cm, chest circumference 33 cm, crown rump length 25cms and crown heel length of 32 cm. External examination showed anencephaly, bilateral club feet, post axial polydactyly of all four limbs, distended abdomen and encephalocele (Figure 1). On dissection only squamous portion of the occipital bone was present. Cerebral hemispheres were not identified. Spinal cord could be traced till the thoracic spine. Meningeal layer was continuous with the sac in the occipital region. Internal examination showed enlarged thymus gland, hypoplastic lung, normal liver, both kidneys enlarged with absence of adrenal glands. Other visceral organs were normal (Figure 2).

On gross examination of both the kidneys, each weighed 250gms, cut section showing indistinct corticomedullary differentiation with spongy appearance. Sections from the kidney showed dilated tubules with focal hamartomatous

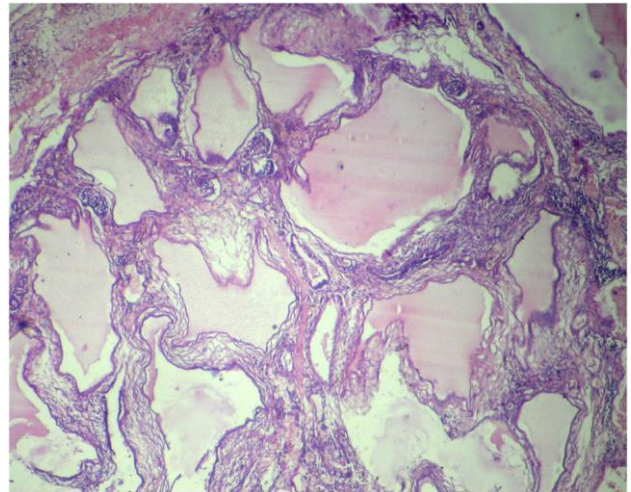
change and epithelial hyperplasia. Most of the glomeruli were normal with some showing glomerular cysts. Bundles of connective tissue, neural tissue and adipose tissue were seen around the dilated tubules. The interstitium showed focal areas of extramedullary hemopoiesis. Histological features were in favor of multicystic renal dysplasia (Figure 3). Sections from the liver showed bile duct hyperplasia, foci of extramedullary hematopoiesis and portal fibrosis suggesting the diagnosis of hepatic dysgenesis (Figure 4). Sections from the encephalocele showed choroid plexus and oligodendroglia favoring the diagnosis of encephalocele (Figure 5, Figure 5A). Based on the above features the diagnosis of Meckel Gruber syndrome was made. Both the parents did not give consent for genetic analysis.



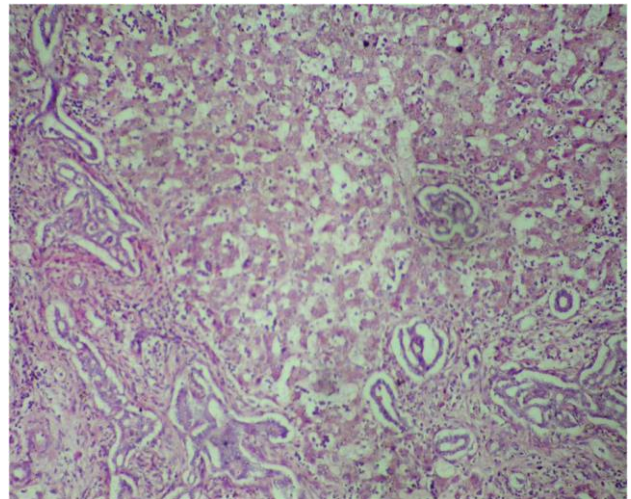
**Figure 1: External examination - Female baby with bilateral club feet and distended abdomen. Anencephaly with occipital encephalocele, polydactyly of one upper limb, polydactyly of other upper limb.**



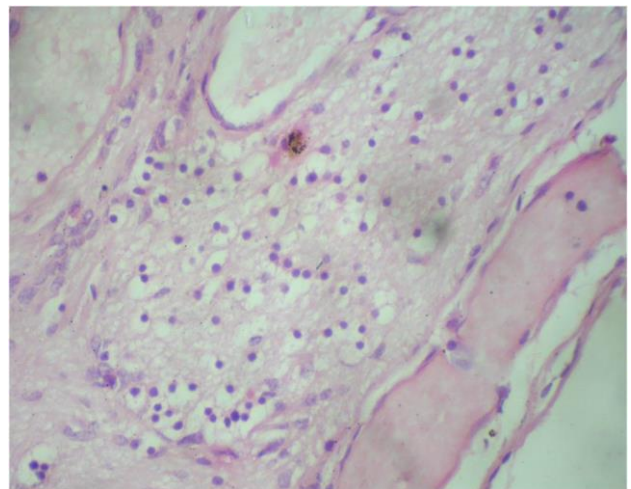
**Figure 2: Internal examination – Hypoplastic lungs, bilateral enlarged kidneys and absence of adrenal glands.**



**Figure 3: Cystic renal dysplasia - microscopy showing dilated tubules.**

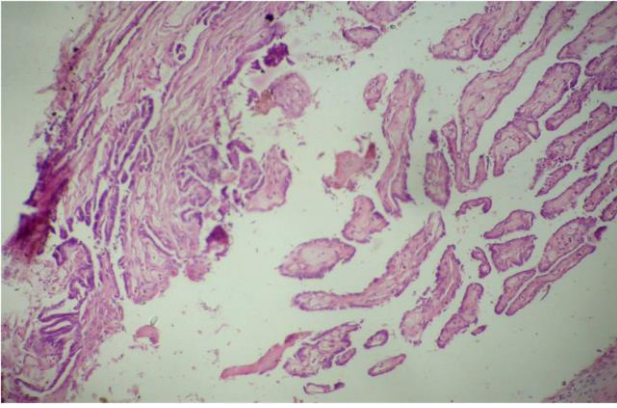


**Figure 4: Hepatic dysgenesis - microscopy showing bile duct hyperplasia with portal fibrosis.**



**Figure 5: Encephalocele - microscopy showing oligodendroglia.**





**Figure 5A: Encephalocele - microscopy showing choroid plexus.**

## DISCUSSION

Meckel Gruber Syndrome (MKS) was first described by Johann Friedrich Meckel in 1822 in two siblings who died of identical malformations of occipital encephalocele, polycystic kidney and polydactyly. George B. Gruber in 1934 reported many familial cases with similar features and coined the term “dysencephalia splanchnocystica”.<sup>1</sup> Opitz et al. gave the detailed review of developmental pathology of meckel syndrome.<sup>2</sup>

The incidence of this rare syndrome is 1 per 1300 live births in Gujarati Indian families, 1 per 3000 in Belgium and 1 in 9000 in Finland. The disease affects all races with males and females being equally affected. Chances of Meckel Gruber syndrome in subsequent pregnancies are 1 in 4 (25%).<sup>3</sup>

Meckel Gruber syndrome is highly heterogenous syndrome; six different loci have been identified. MKS 1 was mapped to chromosome 17q21-q24, in Finnish population. The tissue expression of this gene was reported mainly in the brain, liver, kidney and cartilage of the developing digits. MKS2 is mapped to chromosome 11q13. This locus is commonly observed in North Africa and Middle East. MKS3 is mapped to 8q24 which is having expression in adrenal gland, brain, kidney, lung and spinal cord explaining the rarity of polydactyly in MKS3.<sup>4</sup>

The diagnostic criteria for Meckel Gruber Syndrome (MKS) is presence of at least two of the classic features like cystic renal dysplasia, occipital encephalocele and polydactyly, which is 100%, 90% and 83.3% respectively.<sup>5,6</sup> Meckel Gruber syndrome is a condition characterized by ciliopathies caused by dysfunction of cilia. The anomalies observed in Meckel Gruber syndrome are as follows; in central nervous system: occipital encephalocele, hydrocephalus, microcephaly, anencephaly, absence of olfactory lobes and tract, holoprosencephaly, cerebellar hypoplasia, Dandy Walker malformation, Arnold Chiari malformation, schizencephaly and agenesis of corpus callosum, Face:

cleft lip and cleft palate, microphthalmia, micrognathia, epicanthal folds, hypo/hypertelorism nasal anomalies, Mouth: Lobulated tongue, cleft epiglottis, neonatal teeth, Skeletal: polydactyly, short limbs, talipes, bell shaped thorax, syndactyly, club foot, clinodactyly, Cardiovascular system: Atrial septal defect, coarctation of aorta, pulmonary stenosis, Respiratory system: hypoplasia of lungs, Renal system: polycystic kidneys, cystic dysplasia, renal hypoplasia, horse shoe kidney, double ureter, Liver: hepatic fibrosis, ductal agenesis, portal fibrosis, Genital system: hypoplasia, ambiguous genitalia, hermaphroditism, cryptorchidism, Others: malrotation of the gut, accessory spleen, omphalocele, imperforate anus, adrenal agenesis, enlarged placenta and single umbilical artery.<sup>7</sup>

In Meckel Gruber syndrome most infants are still born or die within few hours or days after birth. Review of literature reveals only ten neonates surviving beyond birth.<sup>8</sup> According to Ramadani, there is one report of a long survivor who died at the age of 28 months.

## CONCLUSION

Meckel Gruber syndrome is a rare autosomal recessive condition and is lethal. Counseling forms an integral part of management especially about the recurrence risk of subsequent pregnancies. Our aim of this review is to enhance the knowledge and spread awareness about this rare and lethal anomaly.

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