

Meckel Grubers Syndrome- An Antenatal Diagnosis

Dr Dhruva R¹, Dr Bharat MP²

¹(Vishwa Guru Scanning and Diagnostic center ,Tumkur,India)

²(Department of Radiology ,Subbiah institute of medical sciences , Shivamogga /RGUHS, India)

Abstract:

Background: Meckel syndrome (MKS), also known as dysencephaliasplanchnocystica, Gruber syndrome, or Meckel-Gruber syndrome, is a lethal, autosomal recessive disorder characterized by occipital encephalocele, bilateral renal cystic dysplasia, hepatic ductal proliferation, fibrosis and cysts, and polydactyly. The worldwide incidence of the disease varies from 1/13,250 to 1/140,000 live births, but in Finland, there is a prevalence of 1/9,000 births [1]. It can be associated with many other conditions. Antenatal ultrasound examination can establish the correct diagnosis by identifying at least two of the major features described. Here we describe an antenatal presentation of MKS in our diagnostic center. Ultrasonography and necropsy correlation for better specificity of the case report findings .

Key Word: Ultrasonography ,Polydactyly , dysplastic kidneys

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I. History

In 1822, the German anatomist Johann Friedrich Meckel (1781–1833) first described two newborn siblings, a female and a male, that died of identical malformations of occipital meningoencephalocele, polycystic kidneys, polydactyly, and cleft palate [2]. In 1934, George B. Gruber reported several familial cases with encephalocele, polycystic kidneys, and polydactyly using a disease name “dysencephaliasplanchnocystica”, and suggested a genetic origin of the disease [3]. In 1969, Opitz and Howe [4] delineated the clinical features and proposed a disease name “Meckel syndrome”. In 1970, Journal of American Medical Association [5] and in 1984, American Journal of Medical Genetics [6] separately published biographical information on Meckel. In 2006, Opitz et al [7] gave a detailed review of the role of Meckel in developmental pathology.

II. Case Report

A 28-year-old woman with 29 weeks of amenorrhea was referred for an antenatal ultrasonogram to detect fetal anomalies to our center. Ultrasonography was performed with a volumetric probe and images were archived into the database.

Ultrasonography revealed severe oligohydramnios on the first look with amniotic fluid index measuring 4.4 cms (fig-1). On detailed evaluation there was a large cranial vault defect noted in the occipital region with herniation of meninges & cerebral parenchyma (fig-2). Bilateral lungs revealed relatively increased echogenicity with no other abnormalities. Abdominal circumference was increased and was more than 2 standard deviations. There was bilateral enlarged heteroechoic kidneys with multiple cysts of varying sizes. Fetal MRI also showed the enlarged cystic dysplastic kidneys (fig-3). Urinary bladder was not distended. No evidence of anterior abdominal wall defect / bladder extrophy was noticed. Survey of the extremities revealed bilateral lower limb post axial polydactyly (fig-5).

With presence of occipital encephalocele, bilateral renal cystic dysplasia, post-axial polydactyly and severe oligohydramnios diagnosis of Meckel- Gruber syndrome was given.



(Fig- 2a)

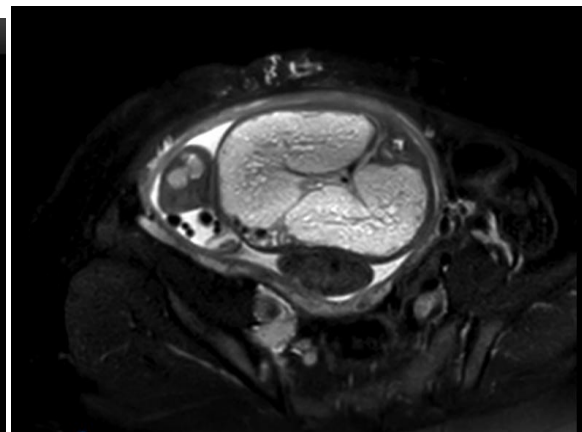


(Fig- 2b)

Ultrasound demonstration of occipital carnial vault defect (Fig-2a) and encephalocele (Fig- 2b).

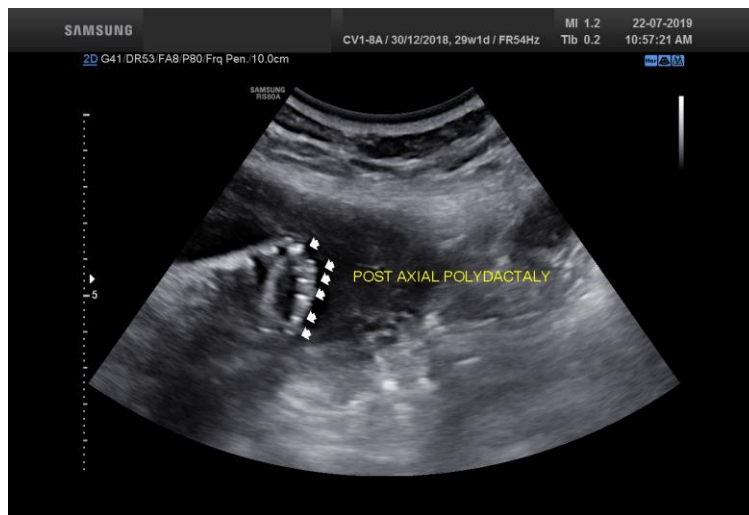


(Fig-3a)



(Fig-3b)

Abdominal survey showing bilateral enlarged kidney with multiple cysts of vaying sizes on USG (fig-3a) & T2 fat saturated axial fetal MRI (Fig-3b).



(fig-4)

Survey of the extremities reveals postaxial polydactaly.

Post abortus images confirmed the ultrasonography findings:



Polydactyl



Encephalocele



Small head & large Stomach

Diagnosis:

The first sonographic finding in most cases is oligohydramnios, due to renal dysfunction, and it develops early in the second trimester. The concurrence of oligohydramnios and bilateral severe renal anomalies should initiate a search for other anomalies indicative of the Meckel-Gruber syndrome. Some cases of Meckel syndrome have normal amniotic fluid and the presence of normal fluid does not exclude the diagnosis. Sometimes absence of the bladder can also be recognized. An early normal sonogram in a family at risk for recurrence, does not exclude Meckel syndrome. A follow-up scan at 20 weeks of gestation is recommended.

Cystic dysplastic kidneys are a constant anomaly in Meckel syndrome and therefore must be present in addition to at least two minor defects to make the diagnosis. The reported incidence of renal disorder in this syndrome varies from 95% to 100%. The kidneys have initially microscopic cysts that destroy the parenchyma and enlarge the organ up to 10 or 20 times.

Occipital cephalocele is present in 60% to 80% of fetuses. Maternal serum or amniotic fluid fetoprotein level may be normal, as a membrane may cover the cephalocele. Post-axial polydactyly is present in 55% to 75%. Other limb anomalies such as bowing and shortening may also be present.

Finding at least two of the three features of the classical triad, in the presence of normal karyotype makes the diagnosis[8].

Genetics:

It is an autosomal recessive disorder with a recurrence risk of twenty-five percent. The locus for Meckel syndrome is on chromosome 17, long arm, region 2, and bands 1-4. Phenotype variability and cases that did not have confirmed linkage to 17q suggests that there is some degree of locus heterogeneity[9].

Differential diagnosis:

Differential diagnosis for MKS includes autosomal recessive PKD, trisomy 13, Smith-Lemli-Opitz syndrome (SLOS), hydroletharus syndrome, SLSN, JBTS, BBS, and OFD1 [10,11,12].

Prognosis:

Meckel syndrome is a lethal disorder. Most infants are stillborn or die hours or days after birth. Occasionally infants survive a few months with poor quality of life.

Management:

A karyotype study should be obtained when Meckel syndrome is suspected, to exclude chromosomal disorders. If the diagnosis is made before viability, termination can be offered. When the family decides to continue the pregnancy, or if the diagnosis is made after viability, the standard obstetrical management is not altered. Recurrence of Meckel-Gruber syndrome may be evaluated as soon as 14 weeks, but it may not be reliably excluded until 20 weeks. Parents should be counseled of the likely recurrence of Meckel-Gruber syndrome[13].

III. Conclusion:

This article overviews prenatal diagnosis and differential diagnosis of MKS. The ciliopathy underlies the pathogenesis of MKS. Prenatal diagnosis of bilateral enlarged multicystic kidneys should alert MKS and prompt a thorough investigation of central nervous system malformations and polydactyly.

Table 1

Table 1: Associated Anomalies	
CNS	Occipital cephalocele, microcephaly, holoprosencephaly Cerebellar hypoplasia, hypoplasia of pituitary gland, Dandy – Walker malformation
Face	Cleft lip / palate, micrognathia, ear anomalies microphthalmia, epicanthal folds, nasal anomalies, hypotelorism or hypertelorism
Mouth	Lobulated tongue, cleft epiglottis, neonatal teeth
Skeletal	Polydactyly, short limbs, talipes, bell-shaped thorax, syndactyly, club foot, clinodactyly
Kidneys	Polycystic kidneys, renal agenesis, renal hypoplasia, horseshoe kidneys, double ureters
Liver	Hepatic fibrosis, ductal agenesis portal fibrosis
Genitalia	Hypoplasia, ambiguous genitalia, hermaphrodites, cryptorchidism
Heart	Ventricular or atrial defects, aortic hypoplasia or coarctation, aortic valve stenosis, rotational anomalies, pulmonary stenosis
Lungs	Hypoplasia of the lungs
Others	Growth restriction, short webbed neck, malrotation of the guts, accessory spleen, adrenal agenesis, omphalocele, hypoplasia or absent bladder, imperforate anus, enlarged placenta, single umbilical artery

Associated anomalies with Meckel-Gruber Syndrome.

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