CASE REPORT

MECKEL-GRUBER SYNDROME - A RARE CASE REPORT

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ABSTRACT: We present an interesting case of a fetus which was delivered in our hospital after antenatal detection on ultrasonography. Clinical examination, ultrasonography findings, infantogram, autopsy and histopathology proved it to be a case of Meckel Gruber syndrome.

INTRODUCTION: Meckel Gruber syndrome is a rare, lethal syndrome characterized by occipital cephalocele, post axial polydactyly and dysplastic cystic kidneys. We report a case of Meckel Gruber syndrome diagnosed antenatally at 37 weeks of gestation and confirmed postnatally by postnatal radiographs, fetal autopsy and histopathology.

CASE REPORT: A 23 year old primigravida with no history of consanguineous marriage was referred for routine third trimester obstetric ultrasound. US evaluation revealed a single, live fetus of 37 weeks maturity with severe oligohydramnios. US of the fetal abdomen revealed bilateral enlarged echogenic kidneys with few cystic spaces [Fig- 1]. Fetal head showed a large occipital cephalocele. [Figure - 2] Fetal thorax and liver were compressed by the enlarged kidneys. However fetal liver did not show cysts. Fetal urinary bladder was visualized. The limbs were examined for polydactyly but could not be ascertained as the liquor was scanty. The lungs were hypoplastic. The umbilical cord had a normal trivascular appearance.

As the fetus showed lethal anomalies, she was admitted and delivery was induced. The baby was delivered stillborn.

On clinical examination, the face showed characteristic potter facies - micrognathia, hypertelorism, epicanthic folds, snubbed nose, and low set ears. The fetus had grossly distended abdomen, a bell shaped thorax and an occipital encephalocele, lobulated tongue, polydactyly, talipes and club feet [Figures 3, 4, 5].

Autopsy was done. The findings included large multicystic kidneys bilaterally. The lungs were hypoplastic. The bladder and ureters were seen and normal, uterus with ovaries was seen. [Figure 6]

Histopathologic examination revealed-Multicystic dysplastic kidneys, hypoplastic lungs, and hepatic fibrosis.

The finding of polydactyly in the autopsy specimen confirmed the diagnosis of Meckel Gruber syndrome.

DISCUSSION: Meckel Gruber syndrome is a rare, lethal syndrome characterized by occipital cephalocele, post axial polydactyly and dysplastic cystic kidneys. It is also known by the synonyms Dysencephalia Splanchnocystica, Gruber Syndrome used in European literature – (1) and Meckel Gruber Syndrome in some texts (2). The first reports of Meckel-Gruber syndrome were published in 1822 by Johann Friedrich Meckel. G.B. Gruber also published reports of patients with Meckel-Gruber

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syndrome in 1934 and gave it the name dysencephalia splanchnocystica. Meckel-Gruber syndrome is also known as Meckel syndrome and Gruber syndrome. (5)

Meckel-Gruber syndrome (OMIM 24900) is a lethal, rare, autosomal recessive condition mapped to 6 different loci in chromosomes 17q21-24

(MKS1), 11q13 (MKS2), 8q21.3-q22.1 (MKS3), 12q21.31-q21.33 (MKS4), 16q12.2 (MKS5), and 4p15.3 (MKS6). This mapping suggests genetic heterogeneity in Meckel-Gruber syndrome (5). Failure of mesodermal induction has been suggested to cause Meckel-Gruber syndrome. The induction cascades of early morphogenesis involve numerous growth factors, homeobox genes, and paired domain genes. (5) The incidence of Meckel-Gruber syndrome is 1 per 13,250-140,000 live births. Individuals of Finnish descent have a higher incidence (1 per 9000 live births, one person in 50 is a carrier). The male-to-female ratio is nearly equal, which is consistent with autosomal recessive inheritance. (5) Fetal ultrasonography can be used to detect an occipital encephalocele and dysplastic kidneys in fetuses with Meckel-Gruber syndrome (MGS)

Newborns die shortly after birth from pulmonary hypoplasia. The most striking feature is an occipital encephalocele. Also, polydactyly is easily seen. Postmortem examination of the kidneys reveals marked cystic dysplasia. Pregnancy history should be reviewed for stillbirths or early neonatal deaths with findings of polycystic kidneys, occipital encephalocele, and polydactyly, dandy walker malformation and congenital cardiac defects. Associated anomalies include cleft lip / palate, micrognathia, ear anomalies, micro-ophthalmia, lobulated tongue, and neonatal teeth (1) Most of these anomalies represent the Potter sequence which is thought to be due to severe oligohydramnios. (4)

CRITERIA FOR DIAGNOSIS: To make the diagnosis of MS cystic dysplastic kidneys is an essential component of the triad in addition to two other minor defects. (2) Second component of the triad is an occipital cephalocele. Cephaloceles are seen in 60 - 80% of the cases.(1),(2),(3),(4) This component may be responsible for the minimal amount of liquor in these patients which would otherwise have been absent in patients of bilateral cystic dysplastic kidneys. Maternal serum or amniotic fluid - Alpha fetoprotein levels may be normal as the cephalocele may be covered by a membrane. Other CNS anomalies which may be found are microcephaly, holoprosencephaly, cerebral and cerebellar hypoplasia, hypoplasia of the pituitary gland and Dandy Walker malformation. (1)

The third component of the triad is post axial polydactyly which is present in 55 - 77% of the cases. (1), (2), (3), (4)

Finding atleast two of the three features of the triad in the presence of normal karyotype makes the diagnosis. (1), (2), (3)

Differential diagnosis will depend on the type of associated anomalies. As the spectrum of anomalies overlaps with those of Trisomy13, karyotyping is essential. A normal karyotype points towards MS .(1) Asphyxiating thoracic dystrophy (Jeune Syndrome) Lawrence - Moon - Bardet - Biedl Syndrome, Short rib polydactyly syndromes and Cerebro - Hepato - Renal Syndrome (Zellweger Syndrome) figure in the differentials, as all these are autosomal recessive disorders associated with renal cysts .(2) Autosomal dominant polycystic kidney disease is another possible differential.(1)

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PROGNOSIS: Prognosis in MS is bad. Most infants are still born or die hours or days after birth. (1)The mortality rate is 100%. Most die before or right after delivery, but those who survive longer might have less severe abnormalities.

Autopsy provides valuable information that aids in diagnosis and genetic counseling for future pregnancies. (5)

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USG FINDINGS

Figure 1- Enlarged echogenic kidney in the abdomen

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Figure 2- Antenatal USG at 37 weeks –occipital encephalocele with small amount of brain tissue

GROSS EXAMINATION

Figure 3- Female fetus with encephalocele, grossly enlarged abdomen, characteristic potter facies, polydactyly and club feet

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Figure 4- Both feet showing six digits

Figure 5- Potter facies- hypertelorism, flattened nasal bridge, low set ears, micrognathia

AUTOPSY

Figure 6- Internal organs showing enlarged cystic kidneys, hypoplastic lungs, lobulated tongue and heart

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