

CASE REPORT

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Meckel Gruber syndrome – a case report



Marquess Raj*, Sujata Dhanuka, Purna Agarwal, Suresh Lakki Reddy and Sethuramalingam Vivekananthan

Abstract

Background: Meckel Gruber Syndrome (MKS) is a rare autosomal recessive malformation syndrome characterized by multiple congenital anomalies ultimately leading to the death of fetus in utero or shortly after birth. It is characterized by classical triad of occipital encephalocele, infantile polycystic kidneys and postaxial polydactyly. Diagnosis of MKS is made on the basis of ultrasonography, gross morphology & histopathological findings. Here, we describe a case of MKS presenting with the classical triad.

Case presentation: A 25 year old lady presented with missed abortion at 17 weeks of gestation on her first conception. There was no history of previous fetal demise or any congenital anomaly. History of consanguineous marriage was not present. Ultra sonogram revealed death of the fetus in utero. Planned termination of pregnancy was performed & the products of conception were sent for study to the laboratory for autopsy, histopathological examination & genetic studies.

Conclusion: Rare genetic anomalies can present with missed abortion & an understanding of the same is important considering the clinical as well as psychological strain it can have on the pregnant mother. The case moreover should be reported for it being a genetic anomaly which results in death at a young age & also for its historical value.

Keywords: Meckel Gruber Syndrome, MKS, multicystic kidneys, encephalocele, polydactyly

Background

Meckel Gruber Syndrome (MKS) is a rare autosomal recessive malformation syndrome with a neural tube defect leading to death of the fetus in utero or shortly after birth. First reports of MKS were published in 1822 by Johann Friedrich Meckel (Meckel 1822). G.B. Gruber also published reports of patients with MKS in 1934 and gave it the name dysencephalia splanchnocystica (Gruber 1934). MKS is characterized by triad of large polycystic kidneys (100%), occipital encephalocele (90%), and post-axial polydactyly (83.3%) (Sergi et al. 2000). Associated abnormalities include oral clefting, genital anomalies, CNS malformations and liver fibrosis. Mortality rate is 100% with most fetuses surviving only few days to weeks. Pulmonary hypoplasia is the leading cause of death. Worldwide incidence is 1/13,250–140,000 live births. There is a predilection for Belgian 1/3000) and

Finish (1/9000) populations (Salonen and Norio 1984). In India, highest incidence is in Gujarati Indians (1 affected birth per 1300) (Young et al. 1985). The aim of this study was to examine the products of conception & confirm the diagnosis of MKS.

Case presentation

A 25 year old lady presented with missed abortion at 17 weeks of gestation on her first conception. There was no history of previous fetal demise or any congenital anomaly. History of consanguineous marriage was not present. Planned termination of pregnancy was performed & the products of conception were sent for study to the laboratory for autopsy, histopathological examination & genetic studies. Informed consent was taken from the physician as well as the patient for genetic testing.

Discussion

Ultrasonography had revealed no fetal heart activity indicating fetal death in utero. Other positive findings were

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occipital encephalocele measuring - 12 X 3 Cm. Both kidneys were enlarged hyper echoic & multicystic. Right kidney measured 5.5 × 2.5 Cm. Left kidney measured 5.3 × 2.3 Cm. Rest of the organs did not reveal any gross abnormality. No further tests like karyotyping or AFP (alpha fetoprotein) were performed. The ultrasonogram image was not retrievable from the patient & further study was performed on the products of conception which was received in saline.

Fetal skin taken from the cubital fossa was sent for Karyotyping. A partial fetal autopsy was also performed in accordance with the statutory compliances of India & the state where the autopsy was performed (Paavola et al. 1997). Partial fetal autopsy was done with the intention of preserving the rare specimen for future academic study. Partial autopsy did not involve opening of the cranium considering the fragile nature of the encephalocele.

The ultrasonogram findings correlated with the gross findings of the conceptus. The stage of fetal development correlated with 17 weeks of gestation. There was an encephalocele measuring 12 × 3 cm in the occipital region of the abortus (Fig. 1). There were six digits both the lower limb extremities & right upper limb confirming polydactyly (Fig. 2) & male genitalia was noted (Fig. 3). All the abdominal, thoracic & pelvic organs corresponded to 17 weeks of gestation. Eg. Both the kidneys were fused in the midline. The only gross abnormality



Fig. 1 Showing occipital encephalocele



Fig. 2 Polydactyly in the right upper & lower limb

noted was that the kidneys showed multiple cysts (Fig. 4) ranging from 0.1 to 0.3 mm in diameter, confirming the ultrasonogram findings. No other gross abnormalities were found in the other abdominal & thoracic organs either on gross or on cut section.

Histopathological examination was done on sections taken from both the kidneys & liver. Sections studied



Fig. 3 Showing male genitalia



Fig. 4 Tiny cysts on cut section of kidney

from both the kidneys showed fetal glomeruli & cystic dilation of the tubules corresponding with the micro cysts on gross morphology (Fig. 5). The sections studied from the liver showed evidence of fetal hematopoiesis (Fig. 6).

Cytogenetic evaluation on the products of conception specimen revealed contamination at source in both short term & long term tissue cultures. However fluorescence is-situ hybridization on cells from direct culture reveals normal genetic constitution for the chromosomes 13,18, 21 & sex chromosomes in 50 interphase cells analyzed. Demonstration of genetic etiology of MKS requires

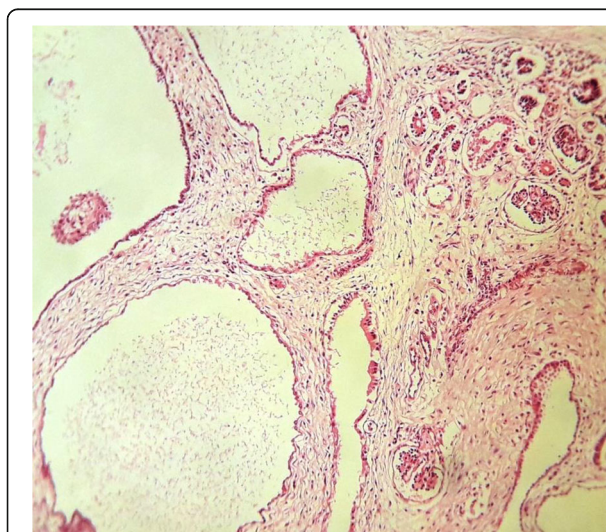


Fig. 5 Photomicrograph from section taken from the right kidney shows fetal glomeruli & multiple cystically dilated tubules (4 X). Sections studied from the left kidney also showed similar features

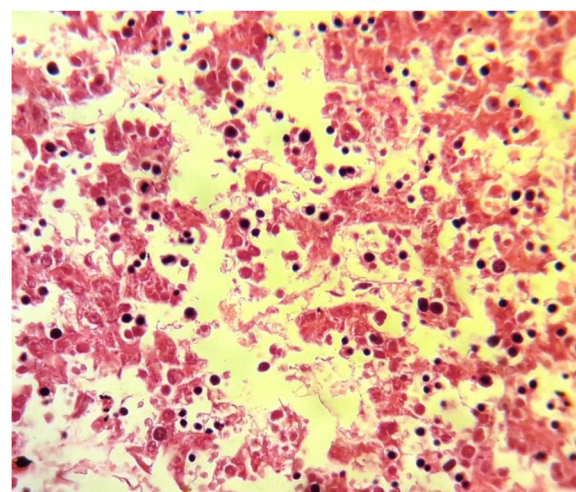


Fig. 6 Photomicrograph from section taken from the liver shows evidence of fetal hematopoiesis (4X)

advanced techniques than conventional karyotyping & FISH.

MKS is a rare genetic disorder characterized by early fetal demise. The diagnostic criteria for MKS is presence of at least two of the three classic features like cystic renal dysplasia, occipital encephalocele, and polydactyly, which are observed in 100, 90, and 83.3%, respectively. Meckel-Gruber syndrome is a lethal disorder. Most infants are stillborn or die in hours or days after birth. A few patients sometimes survive a few months with poor quality of life. In 1995, Paavola reported another atypical case of a long survivor who died at 18 months of life (Paavola et al. 1997). Chromosome analysis is essential to exclude trisomy 13, which mimics Meckel-Gruber syndrome. Trisomy 13 carries a 1% recurrence risk, as opposed to the 25% recurrence rate for Meckel-Gruber syndrome. The mortality is 100% and most babies die in utero or shortly after birth. Pulmonary hypoplasia is the leading cause of death. Other causes include liver and renal failure.

Transabdominal ultrasonography, performed at 10–14 weeks gestation, has been shown to successfully detect several of the fetal anomalies associated with MKS, including polycystic kidneys (from 9 weeks gestation), occipital encephalocele (from 13 weeks), and polydactyly (from 11 weeks), in both high-risk and low-risk pregnancies (Mittermayer et al. 2004). Prenatal diagnosis is also possible by using a combination of these imaging techniques, α -fetoprotein testing of amniotic fluid, and DNA testing of fetus and parents. For example, elevated levels of maternal α -fetoprotein during antenatal screening may be associated with MKS.

The case we encountered has all the features of MKS & is being reported for its rarity.

Abbreviations

AFP: Alpha fetoprotein; Cm: Centimeters; MKS: Meckel Gruber syndrome

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Declarations

Kindly note that ethics committee approval has been taken & the same has been forwarded to the editors email.

Authors' contributions

Dr. Marquess Raj is the primary author who led the study, did the autopsy & histopathological examination. Dr. Sujata Dhanuka & D. Perna Agarwal researched on the disease & shared expertise on interpretation of the genetic findings. Mr. Suresh Lakki Reddy & Mr. Sethuramalingam.V helped with organising the study & study material. The author(s) read and approved the final manuscript.

Authors' information

The corresponding author is a pathologist with 7 years & 7 months experience in pathology & lab medicine practice.

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Availability of data and materials

Karyotyping report & pathology images ve been provided.being a single instance analytical data has not been provided.

Consent for publication

Has been uploaded in SAEF portal.

Competing interests

The authors declare that they have no competing interests.

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