Meckel Gruber syndrome – a case report

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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, muticystic 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 postaxial 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
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 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
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
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 in-
fants 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, in-
cluding polycystic kidneys (from 9 weeks gestation), oc-
cipital encephalocele (from 13 weeks), and polydactyly
(from 11 weeks), in both high-risk and low-risk pregnan-
cies (Mittermayer et al. 2004). Prenatal diagnosis is also
possible by using a combination of these imaging tech-
niques, 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

Acknowledgements
The authors profusely thank the management of Apollo health & lifestyle limited & the leadership team of Apollo Diagnostics for allowing us to publish this study. Sincere thanks to Patho Consult, Mylapore, Chennai for aiding with the tissue processing.

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. Prema Agarwal researched on the disease & shared expertise on interpretation of the genetic findings. Mr. Suresh Lakki Reddy & Mr. SethuramalingaramV 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.

Funding
No funding was received & the study was done out of academic interest.

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 SAEP portal.

Competing interests
The authors declare that they have no competing interests.

Received: 27 September 2019 Accepted: 2 March 2020
Published online: 15 April 2020

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