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Meckel Gruber Syndrome –A Case Report

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Abstract: *Meckel Gruber Syndrome (MKS) is a rare and lethal autosomal recessive disorder .It is characterized by occipital encephalocele , bilateral dysplastic cystic kidneys, post axial polydactyly . We report a case of MKS which was diagnosed by antenatal ultrasound examination and confirmed later when aborted at 19 weeks of gestation by neonatal biopsy.*
Keywords: *Meckel Gruber syndrome, occipital encephalocele , dysplastic cystic kidneys, polydactyly .*

I. Introduction:

The first reports of Meckel gruber syndrome (MKS) were published in 1822 by Johann Friedrich Meckel[1]. G.B. Gruber also published reports of patients with MGS in 1934 and gave it the name dysencephalia splanchnocystica[2] .The triad of occipito-encephalocele , dysplastic kidneys and postaxial polydactyly characterizes Meckel Gruber Syndrome[3].MKS is characterized by wide variety of systemic malformations . The worldwide incidence of MKS varies from 1 in 13,250 to 1,40,00 live births[4].MKS is lethal rare, autosomal recessive condition mapped to 6 different loci in chromosomes 17q21-24(MSK1)[5], 11q13(MKS2) ,8q21.3-q22.1(MKS3) ,12q21.31-q21.33(MKS4), 16q12.2(MKS5) and 4p15.3(MKS6),this mapping suggest genetic heterogeneity in MKS.

II. Case History And Imaging Findings

A 19 years old primigravida presented with 20 weeks of gestation for routine antenatal examination with history of third degree consanguinity. Routine antenatal scan done showed features of occipital encephalocele , hyperechoic enlarged kidneys , post axial polydactyly with presence of sixth digit was noted in upper limb. The ventricles were dilated , the cerebellum was hypoplastic. Oligohydramnios was present .With the consent of the parents , termination of the pregnancy was undertaken. The pregnancy was terminated and post abortus radiograph was taken. The abortus was sent to histopathological examinations. At autopsy , it was a female fetus weighing 400 grams .On external examination , there was a defect in the occipital bone with encephalocele , and all the four limbs showed presence of post axial polydactyly. On dissection , liver showed biliary ductal plate malformation, kidneys showed multiple minute cysts of different size. Based on the above features diagnosis of MKS was made.

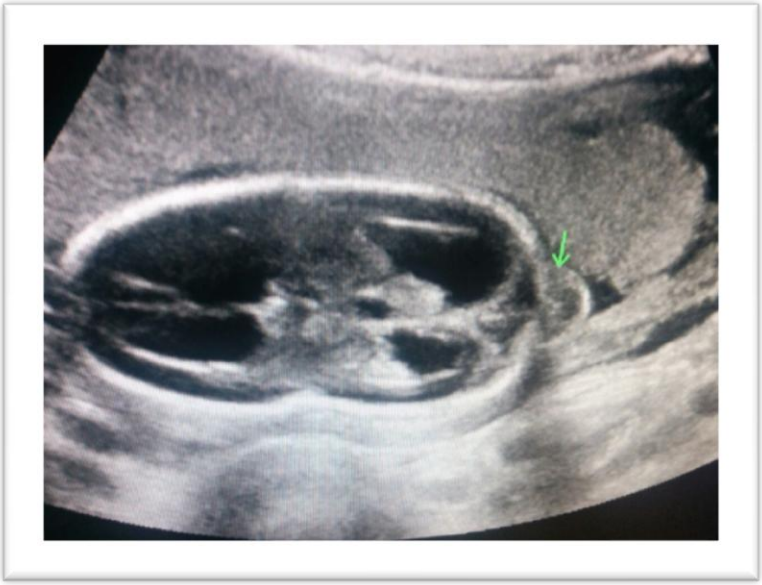


Fig: 1 -20 weeks gestation - occipital encephalocele .

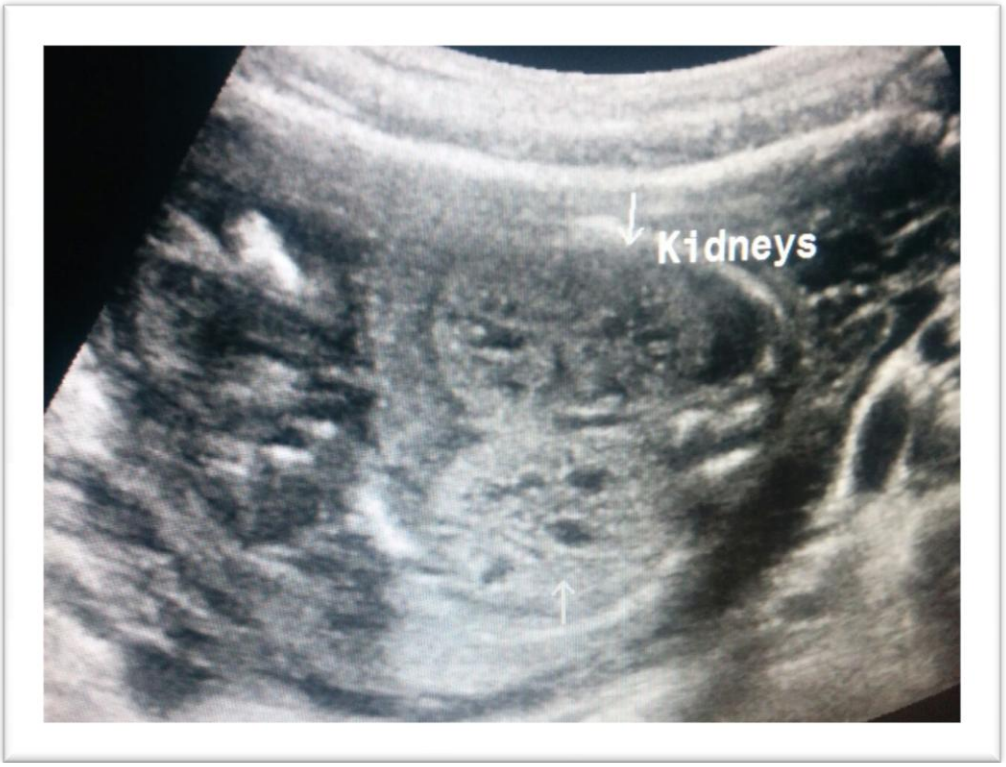


Fig 2–20 weeks gestation- bilateral dysplastic cystic kidneys

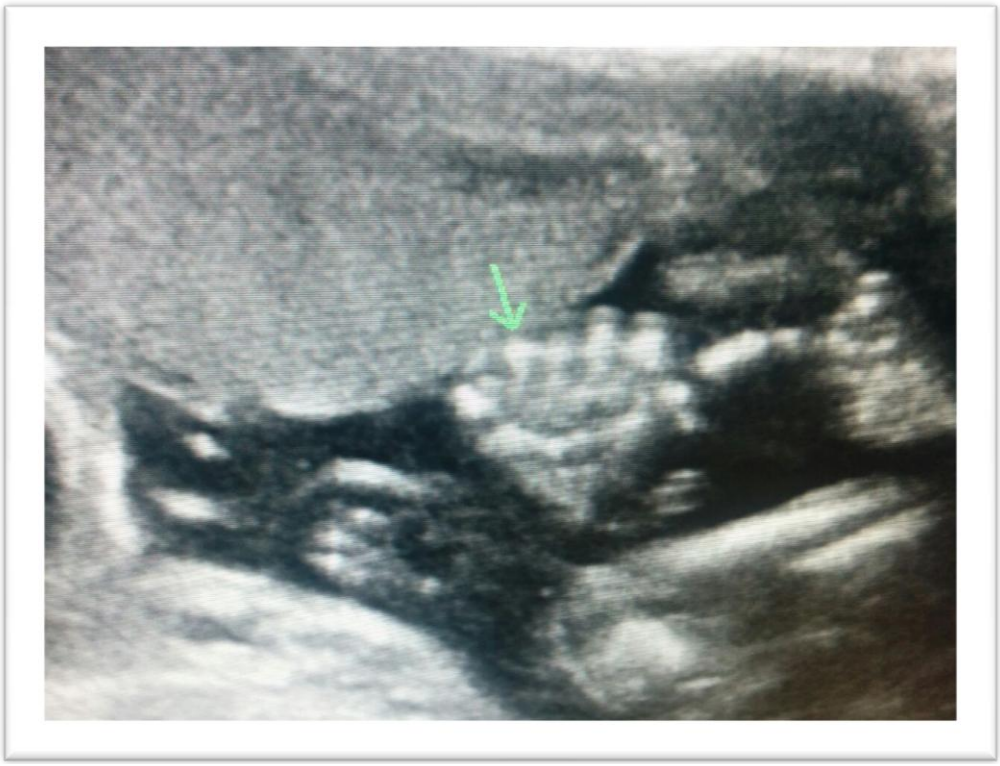


Fig 3- 20weeks gestation- Polydactyly.

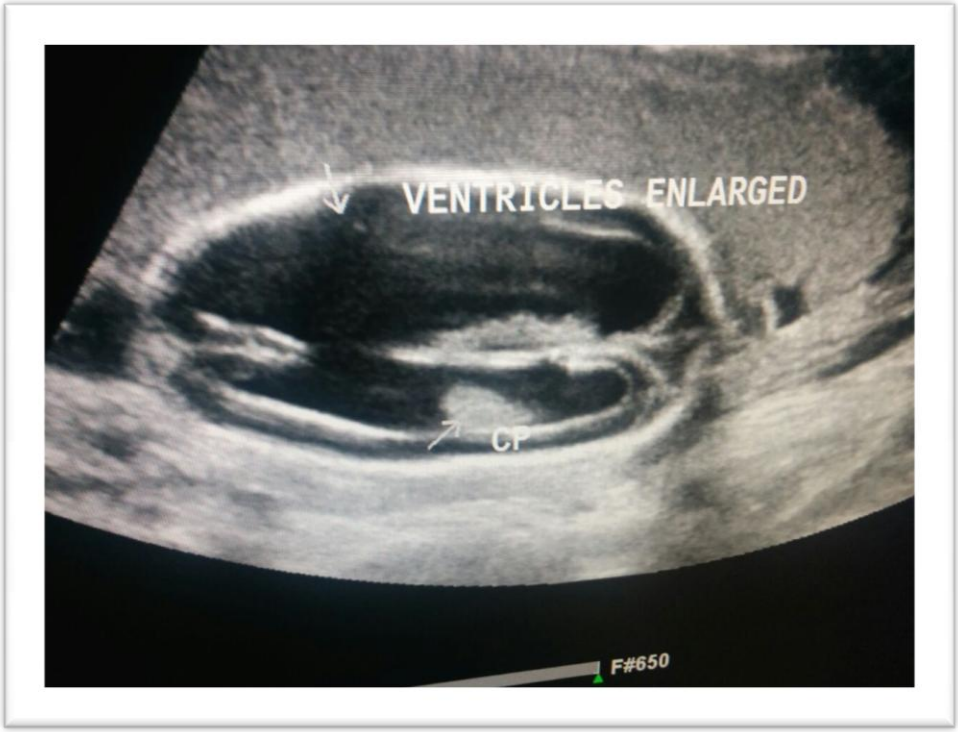


Fig:4 - 20 weeks gestation- dilated ventricles.

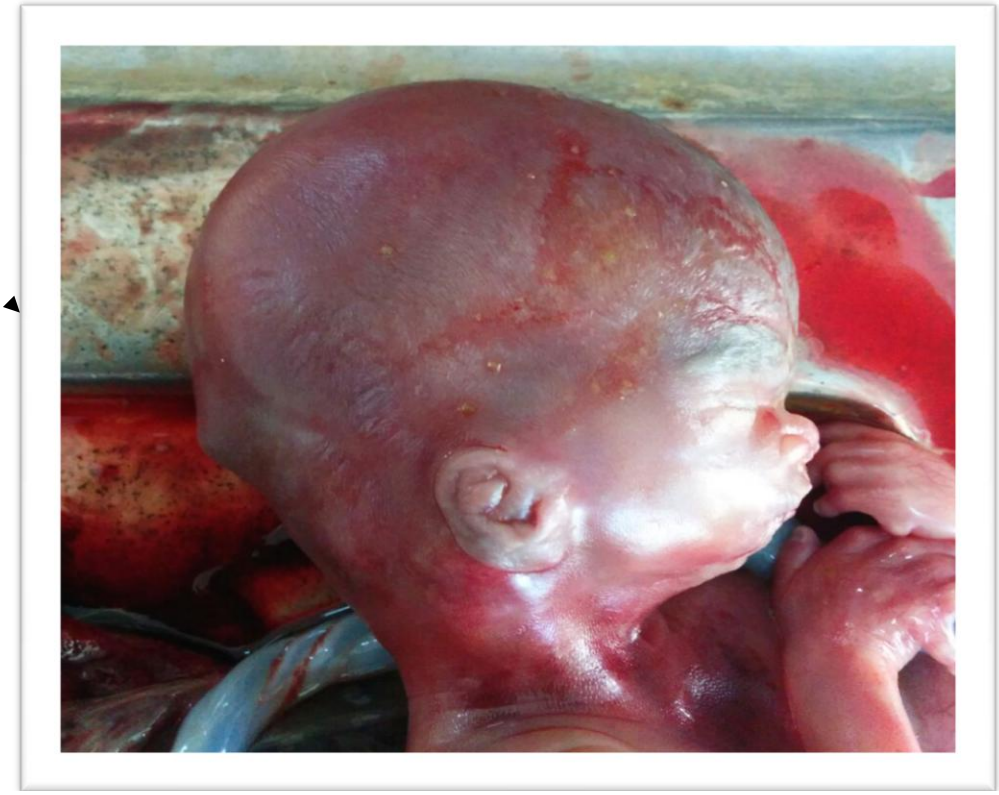


Fig:5 – 20 weeks gestation-occipital encephalocele and polydactyly

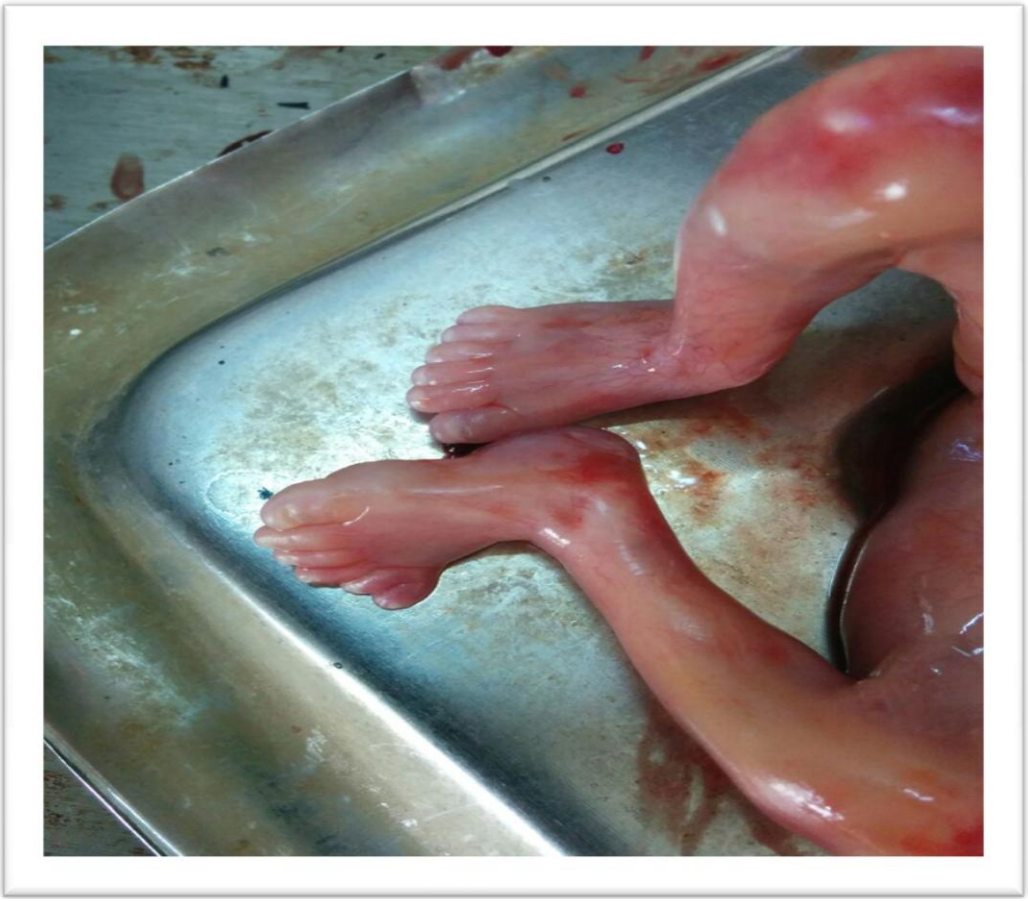


Fig:6–20 weeks gestation - polydactyly.

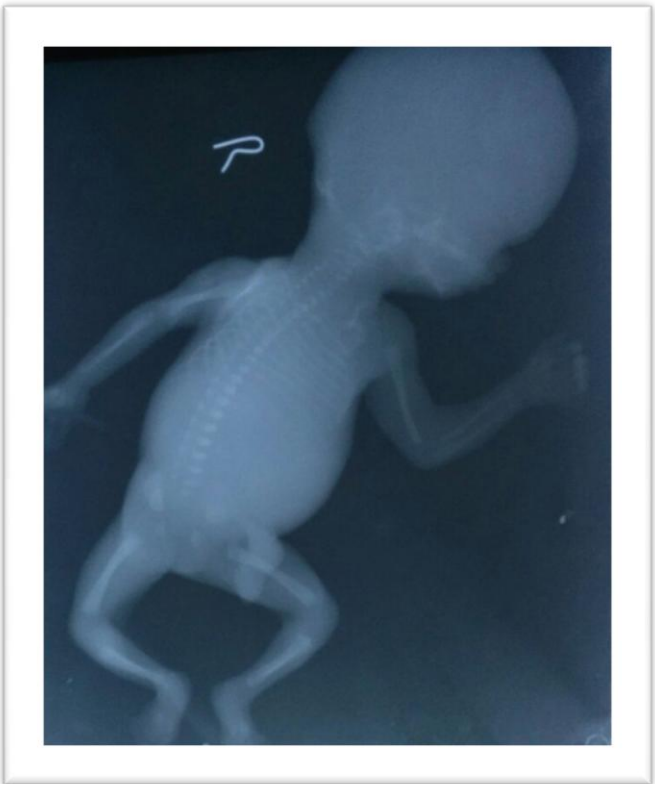


Fig :7- 20 weeks gestation- post abortus radiograph

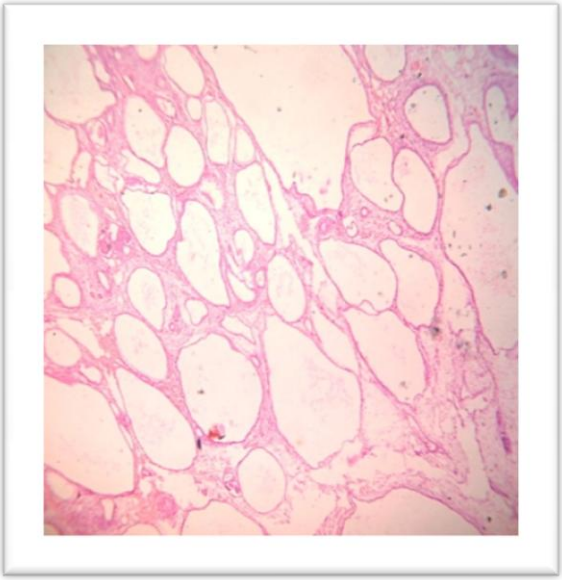


Fig: 8-20 weeks gestation- Multicystic dysplastic kidney

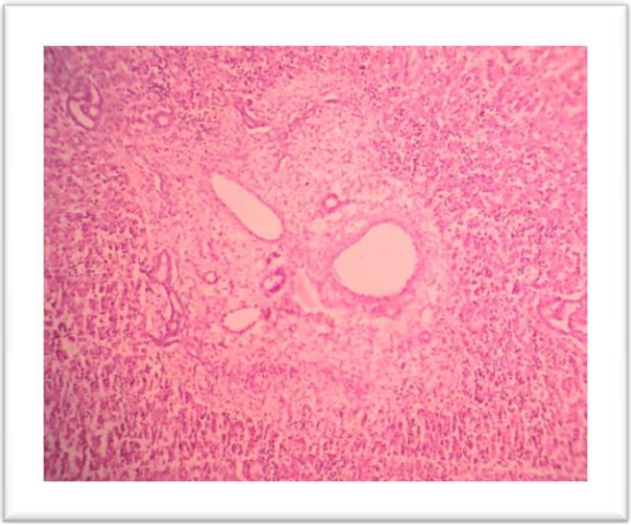
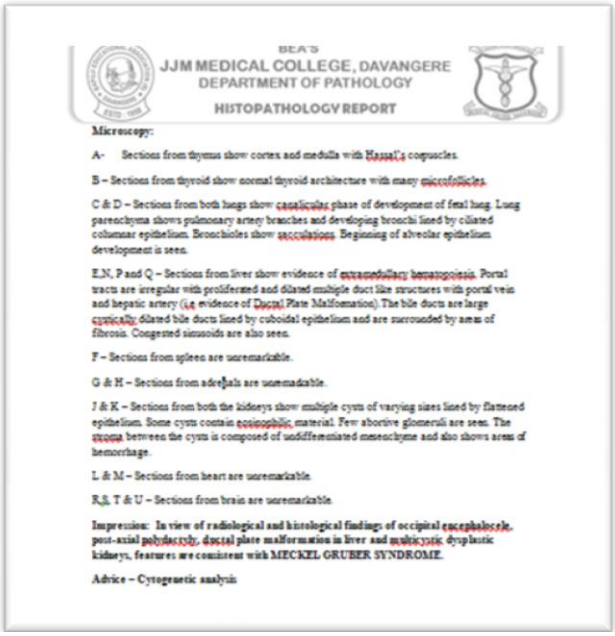


Fig : 9 - 20 weeks gestation ,liver- ductal plate malformation



BEATS

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DEPARTMENT OF PATHOLOGY
HISTOPATHOLOGY REPORT

Microscopy:

A- Sections from thymus show cortex and medulla with Hassal's corpuscles.

B – Sections from thyroid show normal thyroid architecture with many microfollicles.

C & D – Sections from both lungs show canalicular phase of development of fetal lung. Lung parenchyma shows pulmonary artery branches and developing bronchi lined by ciliated columnar epithelium. Bronchioles show sacculations. Beginning of alveolar epithelium development is seen.

E,N, P and Q – Sections from liver show evidence of extramedullary hematopoiesis. Portal tracts are irregular with proliferated and dilated multiple duct like structures with portal vein and hepatic artery (i.e evidence of Ductal Plate Malformation). The bile ducts are large cystically dilated bile ducts lined by cuboidal epithelium and are surrounded by areas of fibrosis. Congested sinusoids are also seen.

F – Sections from spleen are unremarkable.

G & H – Sections from adrenals are unremarkable.

J & K – Sections from both the kidneys show multiple cysts of varying sizes lined by flattened epithelium. Some cysts contain eosinophilic material. Few abortive glomeruli are seen. The stroma between the cysts is composed of undifferentiated mesenchyme and also shows areas of hemorrhage.

L & M – Sections from heart are unremarkable.

R,S, T & U – Sections from brain are unremarkable.

Impression: In view of radiological and histological findings of occipital encephalocele, post-axial polydactyly, ductal plate malformation in liver and multicystic dysplastic kidneys, features are consistent with MECKEL GRUBER SYNDROME.

Advice – Cytogenetic analysis

III. Discussion:

The disease affects all races with males and females being equally affected .Once diagnosed the chances of Meckel Gruber Syndrome (MKS) in subsequent pregnancy are 1 in 4 (25%).The diagnostic criteria for MKS is presence of at least two of the three classic features like dysplastic cystic kidney, occipital encephalocele and polydactyly , which are observed in 100% , 90% and 83.5% respectively. In our case , on antenatal ultrasonography bilateral kidneys were dysplastic, occipital encephalocele and polydactyly were seen .

The spectrum of central nervous system malformation observed in MKS are occipital encephalocele, anencephaly , absences of olfactory lobes and tract , holoprosencephaly ,cerebellar hypoplasia , Dandy Walker malformation, Arnold Chiari M alformation , scizencephly and agnesis of corpus callosum. Other congenital malformations include hepatic fibrosis , ductal agnesis , portal fibrosis , cleft lip and cleft palate, hypo/hypertelorism , pulmonary hypoplasia , atrial septal defect , coarctation of aorta , pulmonary stenosis , club feet , syndactyly, clinodactyly, micrognathia , genital anomalies.

Molecular testing for MKS should be done to differentiate MKS from trisomy 13, trisomy 18, Joubert syndrome , Bardet- Biedl syndrome and Smith-Lemli Opitz syndrome. The most likely syndrome to be confused with MKS is trisomy 13 , since 30% of fetuses with trisomy 13 will have enlarged cystic kidney and many of them also have polydactyly and neural tube defects[6,7].

Meckel Gruber Syndrome can be diagnosed by ultrasonography at 11 to 14 weeks of gestational age .Maternal and aminiotic fluid alpha feto protein may be elevated in associated encephalocele or anencephaly. A karyotype examination is required to exclude chromosomal aberrations.MKS is a lethal syndrome , generally results in intrauterine death or neonatal death within few hours of life .

IV. Conclusion:

Meckel Gruber syndrome is a rare lethal autosomal recessive disorder , and is associated with wide variety of malformations. Antenatal ultrasonogrphy and measurement of alphafetoprotein levels in the amniotic fluid help in diagnosing MKS . Neonatal autopsy and genetic studies are helpful in diagnosis. Parents should be counseled of likely recurrence of MKS in subsequent gestations.

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