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Case report

Meckel Gruber Syndrome

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ABSTRACT

The ciliopathies are a group of related inherited diseases characterized by malformation in organ development affecting multiple organ systems with kidney, skeleton and brain malformations frequently observed with abnormality of primary cilia, essentially sensory organelles. Meckel Gruber Syndrome is a rare autosomal recessive most severe lethal ciliopathies caused by the failure of mesodermal induction. It is characterized by classic triad of cystic dysplastic kidneys, occipital encephalocele and post axial polydactyly with pulmonary hypoplasia as commonest cause for death. Antenatal ultrasound can establish the correct diagnosis by identifying at least two of the major described features. The incidence is highest in Indian Gujarati and Finnish populations. We report this rare case in non Gujarati Indian diagnosed on antenatal ultrasound.

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Introduction

Meckel Gruber syndrome (MKS) is an autosomal recessive lethal syndrome characterized by combination of systemic malformations associated with mutations affecting ciliogenesis with abnormality mapped to six different chromosomes suggesting the genetic heterogeneity [1]. The most consistent anomaly is renal cystic dysplasia associated with anomalies of central nervous system (typically encephalocele), polydactyly, hepatic ductal dysplasia. Finding at least two of the three features of the triad makes the diagnosis.

Recognition of this syndrome is important, not only for managing the affected pregnancy but also for counselling future issues. Prenatal detection is particularly important among families not previously known to be at risk for MKS.

This case reporting highlights the diagnostic ultrasound features of this rare disorder emphasizing on the need of syndromic approach needed in complex anomalies.

CASE REPORT

A routine antenatal sonogram was performed on a 25 year old second gravida (G2P1L1) mother with no history of consanguineous marriage. Past and family histories were non contributory. She was not on any teratogenic drugs.

Ultrasound scan revealed single live fetus of 13 weeks 6 days maturity with microcephaly, large atretic occipital encephalocele, bilateral enlarged polycystic kidneys with pulmonary hypoplasia and reduced liquor (Image 1, 2). No feature of polydactyly. Based on presence of two major criteria antenatal diagnosis of Meckel Gruber Syndrome was made.

Patient was explained regarding the anomaly spectrum and lethal outcome of the disease and pregnancy was terminated after five days with informed written consent.

Abortus had small head with occipital bony defect, large encephalocele, overtly distended abdomen and clubfeet (Image 3). There was no polydactyly.

IMAGES AND LEGENDS

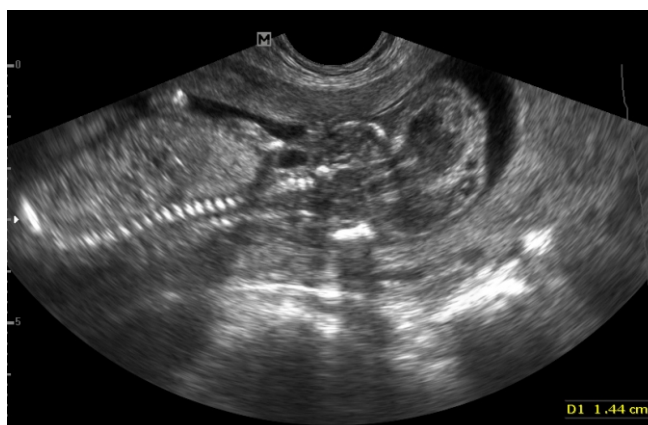


Image 1. Sagittal image of fetus showing small head (microcephaly), large occipital encephalocele with brain parenchyma protruding from skull and pulmonary hypoplasia.

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Image 2. Transverse image of fetal abdomen showing enlarged bilateral polycystic kidneys.



Image 3. Abortus showing distended abdomen, small head with occipital encephalocele and club feet.



DISCUSSION

Meckel Gruber syndrome (MKS) was first described by Johann Friedrich Meckel in 1822 in two sibling with occipital encephalocele, polycystic kidneys, polydactyly and microcephaly. George B Gruber, in 1934 reported similar familial cases and coined the term "dysencephalia splanchnocystica" [2].

Worldwide the incidence of MKS is 1 per 13,250 – 1, 40,000 live births with much higher incidence in Indian Gujarati families (1 in 3000) and in Finland (1 in 9000) [3].

The classic triad of MKS comprise of cystic renal dysplasia (seen in 100% cases), occipital encephalocele (60-85%) and polydactyly (55-83%) [4].

The kidney exhibits the most constant anomaly with presence of renal cystic dysplasia in all cases. Kidney might enlarge 10-20 times of normal size, polycystic kidneys and together with oligohydraminos leads to pulmonary hypoplasia which is commonest cause of mortality.

Detection of an occipital encephalocele is important because its concurrence with oligohydraminos and bilateral renal cystic dysplasia is important clue for the diagnosis. Additional central nervous system anomalies include microcephaly, agenesis of corpus callosum, cerebro-cerebellar hypoplasia, dandy-walker variant [5].

Polydactyly is most variable feature of the classic skeletal presentation of MKS [6]. Other skeletal features are club foot, short limbs, talipes, syndactyly.

Hepatic lesions are consistently important but hidden abnormalities noted on post mortem examination only includes portal fibrosis, reactive bile duct proliferation, bile duct dilatation, portal vascular obliterations [7].

Other occasional anomalies include craniosynostosis, hypoplastic optic nerve, cleft lip, cardiac defects, cryptorchidism, and single umbilical artery.

Our case had two classic features of enlarged bilateral polycystic kidneys with large occipital encephalocele. Polydactyly was absent which is seen only in 55-83% of cases. Club foot was present as skeletal manifestation. Patient was counselled about the disease and pregnancy was terminated after five days. Although there was no history of consanguinity, patient and her husband was informed regarding risk in future pregnancy and need of early ultrasound screening.

Natural history and management: this condition has 100 mortality with death in utero or soon after birth secondary to complications like pulmonary hypoplasia, liver and renal failure. Since there is no treatment it is preferable to diagnose the condition prenatally and abort the affected foetus. As MKS has a high risk (25%) of recurrence, parents should be counselled for future pregnancies [8].

Differential diagnosis of MKS includes Bardet-Biedl syndrome, Joubert syndrome, Larsen syndrome and Trisomy 13. Trisomy 13 is also associated with similar anomalies like in MKS, however presence of holoprosencephaly or other midline central nervous system anomalies favours Trisomy 13 and in these patients karyotyping is indicated.

CONCLUSION

The sonographic findings of severe oligohydraminos and bilateral renal anomalies should initiate a specific search for CNS anomalies to look for diagnosis of lethal MKS. Proper counselling is required for parents for risk in future pregnancy. Early Ultrasound examination and maternal serum alpha fetoprotein level estimation can be used to know the recurrence in subsequent pregnancy.

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