Case Report

Meckel-gruber syndrome: a case report

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Abstract Meckel-Gruber syndrome is a rare and lethal syndrome characterized by occipital encephalocele, postaxial polydactyly, and dysplastic cystic kidneys. The highest incidence is reported in the Gujarati Indians and individuals of Finnish descent.
Keywords: Occipital encephalocele, polycystic kidney, polydactyly.

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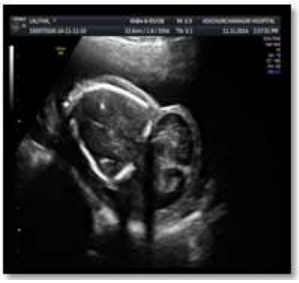
INTRODUCTION

Meckel-Gruber syndrome is an autosomal recessive syndrome characterized by a variety of systemic malformations with the most consistent features being occipital encephalocele, multicystic dysplasia of kidney, polydactyly. The worldwide incidence of MKS varies from 1 in 13,250 to 1, 40,000 live births. Antenatal ultrasound examination can establish the correct diagnosis by identifying at least two of the major features described. We report a rare case of Meckel-Gruber Syndrome identified by antenatal ultrasound.

CASE REPORT

A 24 old primigravida with 23 weeks amenorrhea was referred for a second trimester ultrasonogram to detect fetal anomalies. Pedigree analysis revealed a history of first degree consanguinity between the parents. Family history was non-corroborative. There was no history of intake of teratogenic drugs and other relevant past illness. She was on regular folic acid supplementation since beginning of conception. Ultrasonography was done using Voluson Pro 360 USG equipment, with a 4MHz Curvilinear transducer. The B mode scan revealed parieto-occipital encephalocele [fig 1], enlarged cystic left kidney [fig 2], micrognathia [fig 3] and hypertelorism.3D scan of the face showing micrognathia and hypertelorism was well appreciated [fig 4]. Though there was no oligohydramnios the fetal urinary bladder was not visualised. Considering the syndromic association between these features a possibility of Meckel Gruber's syndrome was hinted and the situation with its possible outcome explained to the parents.



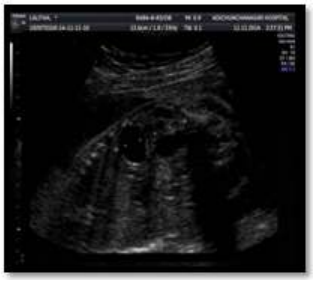


Figure 1: Transverse section of fetal head showing parieto-occipital encephalocele **Figure 2:** Coronal section of the enlarged cystic left kidney.

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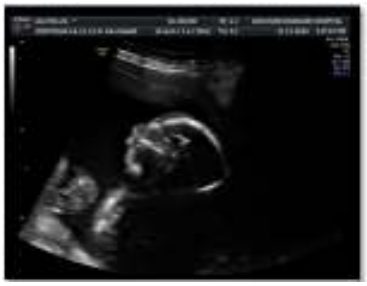

Figure 3: Sagittal view of fetal face showing micrognathia

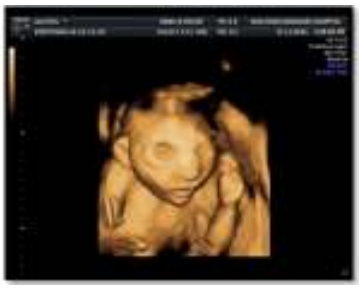

Figure 4: Face profile on 3D USG showing micrognathia and hypertelorism

The couple decided to terminate the gestation and the pregnancy was terminated two days later. Post-mortem examination of the fetus revealed a small head with a small cranium with a boggy swelling over the occipital region [fig 5], micrognathia, hypertelorism [fig 6] and micropenis [fig 7]. Autopsy revealed bilateral dysplastic left kidney and parieto-occipital cephalocele. Urinary bladder and both ureters were identified.

Figure 5: Boggy swelling in the occipital region suggestive occipital encephalocele and micrognathia.

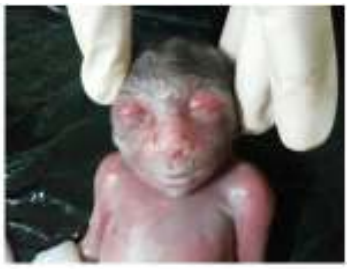

Figure 6: Profile view of face with evident hypertelorism and micrognathia.

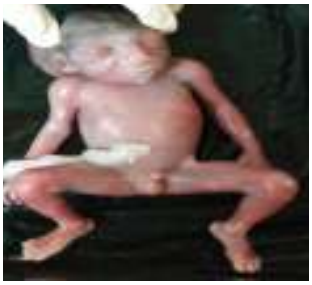

Figure 7: Micropenis with length of 0.6cm

DISCUSSION

Meckel -Gruber syndrome was first described by Johann Friedrich Meckel in 1822 in two siblings who died of identical malformations of occipital encephalocele, polycystic kidneys, and polydactyly. George B Gruber, in 1934, reported many familial cases with similar features and coined the term "dysencephalia splanchnocystica." In 2006, Opitz *et al*. gave the detailed review of developmental pathology of Meckel syndrome.[1] Worldwide, the incidence of Meckel-Gruber syndrome is 1 per 13,250-140,000 live births. The highest incidence is reported in the Gujarati Indians, with 1 affected birth per 1,300 (carrier rate, 1 in 18). Individuals of Finnish descent have a higher incidence (1 per 9000 live births, one person in 50 is a carrier. Cases of Meckel-Gruber syndrome have been reported in North America, Europe, Israel, Indonesia, India, Kuwait, and Japan.[2] It belongs to the ciliopathies, a category of diseases thought to be caused by dysfunction of cilia and flagella. Disruption of the homeo-box B (*HOXB*) region in 17q21-22. leads to malformations.[3] A second locus (*MKS2*) has been mapped to band 11q13, demonstrating the clinical and genetic heterogeneity of Meckel-Gruber syndrome.[4] A third MKS locus (*MKS3*) has been localized to chromosome 8q21.3-q22.1. Polydactyly (and possibly encephalocele) appear less common in *MKS3* -linked families.[5] Mutations in the *RPGRIP1L* gene in chromosome 16q12.2 (MKS5) have also been identified in patients with clinical features consistent with Meckel-Gruber syndrome.[6] A gene on chromosome 4p15 (*CC2D2A*) was recently considered as the most likely candidate for the clinical features of Meckel syndrome in

probands from 11 Finnish families (MKS6).[7] Central nervous system features include occipital encephalocele is characterized by extrusion or herniation of rhombic roof elements, cerebellar vermis, and caudal third ventricle and distended fourth ventricle through a widened posterior fontanelle. Arnold-Chiari malformation and Dandy-Walker malformation may be noted.[8] Cardiac including Atrial septal defect, coarctation of aorta, and pulmonary stenosis may be present. Cystic dysplasia of the kidneys is the most constant and characteristic feature of Meckel-Gruber syndrome.[9] Lung hypoplasia is secondary to oligohydramnios. Postaxial polydactyly is the most variable feature of the classic triad of major abnormalities. However, in some cases, preaxial polydactyly is present or not exhibited at all. Cleft lip and cleft palate may be present. Microphthalmia and micrognathia may be observed. Genital ambiguity secondary to incomplete development of internal/external genitalia can cause confusion in sex assignment of the fetus or infant. Cryptorchidism might be present in males. Urethral atresia may be present.[10]

DIFFERENTIAL DIAGNOSIS

MKS has to be differentiated from trisomy 13 (holoprosencephaly, cleft lip/palate, congenital heart diseases, and polydactyly), trisomy 18 (Choroid plexus cyst, congenital heart/kidney disease, rocker bottom feet, and polydactyly), Joubert Syndrome (hypoplasia/dysplasia of vermis, facial abnormalities, cystic renal diseases, polydactyly, and cleft palate), Bardet-Biedl syndrome (vision loss, mental retardation, renal diseases, polydactyly, and cleft palate), and Smith-Lemli-Opitz syndrome (Microcephaly, Mental retardations, and polydactyly).[11,12,13]

CONCLUSION

MKS is a rare neural tube defect associated with wide variety of malformations. Neonatal autopsy and genetic studies are gold standard for the diagnosis and to document the anomalies. When available, chromosomal analysis is done to confirm the diagnosis. USG and maternal serum alpha fetoprotein level estimation can be used to know the recurrence in subsequent pregnancy.

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