Meckel Syndrome 8

Alternative Names
MKS8

Record Category
Disease phenotype

WHO-ICD
Congenital malformations, deformations and chromosomal abnormalities > Congenital malformations of the urinary system

Incidence per 100,000 Live Births
N/A

OMIM Number
613885

Mode of Inheritance
Autosomal recessive

Gene Map Locus
12q24.31

Description
Meckel Syndrome 8 (MKS8) is an autosomal recessive multisystem disorder that represents a severe form of ciliopathy in humans. It is defined by the tetrad of encephalocele, polydactyly, and renal and biliary ductal dysplasia, although clinical heterogeneity is known to exist even within the same families. Because of their serious health problems, most individuals with MKS8 die before or shortly after birth.

MKS8 is particularly prevalent with a reported incidence as high as 1:3,500 in newborns. It is inherited in an autosomal recessive pattern with six genes described to date. It is suggested by studies in mice that the type I membrane protein that belongs to the tectonic family may be involved in hedgehog signaling, and essential for ciliogenesis.

Molecular Genetics
MKS8 is an autosomal recessive multisystem disorder. A splice site mutation in the TCTN2 gene has been identified by homozygosity mapping in a family with MKS8 that completely abolished normal splicing and created two aberrant transcripts. The mutation was found to segregate with disease in the family in homozygosity and was not observed in 192 ethnically matched controls.

Epidemiology in the Arab World

Saudi Arabia
Shaheen et al. (2011) identified a new MKS locus in a consanguineous family of Arab origin affected with Meckel Syndrome. The family had several affected members, all born to consanguineous parents. One of these patients died at 2-hr of age and was found to have encephalocele, polydactyly, and renal anomalies by report. Another affected member of this family was delivered at 36-weeks gestation. Antenatal ultrasound scan revealed anhydromnios, grossly enlarged echogenic kidneys, polydactyly, and encephalocele. Apgar score was 3 and 2 at 1 and 5 min, respectively. Examination showed dysmorphic features consisting of occipital encephalocele, broad forehead, flat hypoplastic nose, anophthalmia, cleft lip and palate, low-set malformed ears, short neck, polydactyly of both hands and feet with equinovarus deformity, grossly distended abdomen due to bilateral renal enlargement, and normal female genitalia. She expired at 30-min of age. The third patient was born at term and by history there was genital ambiguity, large encephalocele, four limb polydactyly, and renal anomalies and died within 1-hr of delivery. His brother was diagnosed antenatally at 23 weeks with severe microcephaly, large occipital encephalocele, abnormal intracranial structures, bilateral enlarged polycystic kidneys, narrow chest, and four-limb polydactyly. Mother was induced and baby was delivered dead at 24

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weeks. Examination revealed severe microcephaly, microphthalmia, cleft palate, large occipital encephalocele, distended abdomen, and four-limb polydactyly. An affected sibling was terminated at 15-weeks of gestation following the ultrasonographic finding of occipital encephalocele, bilateral polycystic kidneys, pericardial effusion, fixed lower limbs, and polydactyly. DNA samples from two of the several affected members revealed a splice site mutation (c.1506_2A4G; NM_024809.3) in the TCTN2 gene. The mutation identified was found to segregate with the disease in the family and was not observed in 192 ethnically matched controls.

References

Shaheen R, Faqeih E, Seidahmed MZ, Sunker A, Alali FE, AlQahtani K, Alkuraya FS. A TCTN2 mutation defines a novel Meckel Gruber syndrome locus. Hum Mutat. 2011; 32(6):573-8. PMID: 21462283

Related CTGA Records

Tectonic Family, Member 2

External Links

https://ghr.nlm.nih.gov/condition/meckel-syndrome
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=GB&Expert=564

Contributors

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