Joubert Syndrome 16

Alternative Names
JBTS16

Record Category
Disease phenotype

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

Incidence per 100,000 Live Births
0-1

OMIM Number
614465

Mode of Inheritance
 Autosomal recessive

Gene Map Locus
11q12.2

Description
Joubert syndrome (JS) is an inherited multi-visceral disorder caused by aberrant primary cilia formation and function. JS is characterized by the Molar Tooth Sign (MTS), a mid-hindbrain malformation easily identifiable through an axial brain MRI scan. Neurological features include hypotonia, ataxia, and cognitive impairment. The clinical phenotype additionally includes retinal, renal, hepatic -and more rarely- orofacial, skeletal, cardiac, genital, and endocrinal defects. JS is thought to affect 1 in 100,000 births; however the incidence in consanguineous populations is thought to be much higher (e.g. ~1 in 5000 for UAE).

JS16 (JBTS16) is a subtype of JS very similar to JBTS2, involving characteristic neurological features with mainly ocular involvement; renal, skeletal (polydactyly), and genital (cryptorchidism) defects are additional albeit relatively rarely reported features. The ocular phenotype involves retinal dystrophy, oculomotor apraxia, reduced visual acuity, as well as chorioretnal and optic nerve coloboma. Renal involvement include cystic kidneys, nephronophthisis and nephrocalcinosis.

Molecular Genetics
JBTS16 is an autosomal recessive disorder caused by homozygous mutations in TMEM138, a ciliary gene involved in trafficking intracellular vesicles containing essential proteins to the cilium. The first screening for pathogenic TMEM138 variants reported 5 unique mutations (all in Arab and Pakistani families) including splice site and missense transition mutations.

Epidemiology in the Arab World

Egypt
See United Arab Emirates > [Lee et al., 2012]

Oman
See United Arab Emirates > [Lee et al., 2012]

United Arab Emirates
Lee et al., (2012) identified TMEM138 as a ciliary gene associated with JS (JBTS16), and performed the first mutation screening in a large group of JS cases. Three Emirati families, one Omani family, and two Egyptian families were reported, with affected members exhibiting the characteristic molar tooth sign. Among the Emirati families, 2 children from one family presented with ocular features including oculomotor apraxia (OMA) and coloboma. In the second family, 3 children presented with similar ocular features in addition to cystic kidneys and polydactyly each reported in 1 sibling; one sibling is deceased. In the third family, 3 adult siblings presented with retinal dystrophy. In the Omani family, 1 infant presented with OMA and coloboma, as well as cystic kidneys and hypertension; the family has 6 deceased siblings. Lastly, in the 2 Egyptian families only characteristic ocular features presented including OMA and coloboma presenting in 1 individual from 1 family, and OMA presenting in 1 individual in the other family.
Ben-Salem et al., (2014) reviewed the mutation spectrum for Joubert Syndrome in the Arab world. Among the cases, 3 individuals from 2 Emirati families were diagnosed with JBTS16 with unspecified clinical information. The Individuals harbored the same missense transversion mutation (p.Tyr130Cys) described by Lee et al. (2012).

Bizzari S et al., (2017) reported on two Emirati siblings with Joubert Syndrome 16 (JBTS16). The proband was born to consanguineous parents (1st cousins once removed); he was diagnosed at 17 months of age through identification of the molar tooth sign in brain imaging. He presented with hypotonia and global developmental delay. Additional symptoms involving ocular, renal, and genital defects included microphthalmia, nystagmus, minor coloboma, and esotropia, small renal subcortical cysts, as well as cryptorchidism. He exhibited a prominent forehead, an open normotensive anterior fontanelle, and pectus excavatum. His sister presented with similar symptoms. Whole Exome Sequencing identified a previously reported splice site mutation in TMEM138.

References


Related CTGA Records
TMEM138

External Links
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=EN&Expert=2318

Contributors
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