Heart and Brain Malformation Syndrome

Alternative Name
HBMS

Record Category
Disease phenotype

WHO-ICD
Congenital malformation of heart, unspecified

Incidence per 100,000 Live Births
NA

OMIM Number
616920

Mode of Inheritance
Autosomal recessive

Gene Map Locus
19q13.31

Description
Heart and Brain Malformation Syndrome (HBMS) is an extremely rare and severe multiple congenital anomaly syndrome. This syndrome is characterized by delayed psychomotor development, facial dysmorphism, cardiac defects and brain malformation. Facial dysmorphism may consist of microcephaly, microphthalmia, low, set and malformed ears, depressed nasal bridge, highly arched palate, and cleft lip. Patients are hypotonic with hyperactive limb reflexes. Cardiac abnormalities include interrupted aortic arch, hypoplastic valves, and ventricular septal defect. Cranial imaging in patients shows various abnormalities, including Dandy Walker malformation, decreased myelination, and thinning of corpus callosum.

Diagnosis is made through clinical and radiological evaluation. Treatment is supportive.

Molecular Genetics
HBMS follows an autosomal recessive pattern of inheritance. Mutations in the SMG9 gene, located on the long arm of chromosome 19, have been shown to be causal for this condition. This gene encodes an essential component of nonsense-mediated mRNA decay.

Epidemiology in the Arab World

Qatar
See Saudi Arabia > [Shaheen et al., (2016)].

Saudi Arabia
Shaheen et al., (2016) enrolled two families in which affected patients shared a similar pattern of malformations. The patient from the first family was a girl born by elective caesarean section to consanguineous parents. She was found to have craniofacial dysmorphism, microphthalmia, and major brain and heart malformations and died at 7-weeks. There was a positive family history with similar pattern of malformation in a sibling who died at age of one year and a stillborn. The second family was a Qatari family in which an affected girl was born to consanguineous parents. The proband also presented with craniofacial dysmorphism, congenital heart disease, and brain malformation. There was positive family history in a first cousin with similar pattern of malformations. Linkage analysis and exome sequencing were performed and revealed mutations in the SMG9 gene. The authors concluded that mutations in the SMG9 gene caused a distinctive congenital anomaly and that more studies were needed to further delineate the associated phenotypes.

References
Shaheen R, Anazi S, Ben-Omran T, Seidahmed MZ, Caddle LB, Palmer K, Ali R, Alshidi T, Hagos S, Goodwin L, Hashem M, Wakil SM, Abouelhoda M, Colak D, Murray SA, Alkuraya FS. Mutations in SMG9, Encoding an Essential Component of Nonsense-Mediated Decay Machinery, Cause a Multiple Congenital Anomaly Syndrome in Humans and Mice. Am J Hum Genet. 2016; 98(4):643-52. PMID: 27018474

Related CTGA Records
SMG9 Nonsense-Mediated mRNA Decay Factor

External Links

http://disorders.eyes.arizona.edu/handouts/heart-and-brain-malformation-syndrome

Pratibha Nair: 20.12.2016
Ameera Balobaid: 2.11.2016

Contributor