



## Chudley-McCullough Syndrome

### Alternative Names

CMCS

Deafness, Sensorineural, with Partial Agenesis of the Corpus Callosum and Arachnoid Cysts

Deafness, Autosomal Recessive 82

DFNB82

### Record Category

Disease phenotype

### WHO-ICD

Congenital malformations, deformations and chromosomal abnormalities > Other congenital malformations

### Incidence per 100,000 Live Births

0-1

### OMIM Number

604213

### Mode of Inheritance

Autosomal recessive

### Gene Map Locus

1p13.3

### Description

Chudley-McCullough Syndrome is an extremely rare condition characterized by the association of sensorineural hearing loss with partial corpus callosal agenesis and interhemispheric arachnoid cysts. The sensorineural hearing loss is profound, bilateral, and progressive. Brain abnormalities associated with the condition include hydrocephalus, agenesis of the corpus callosum, frontal polymicrogyria enlarged cisterna magna with cerebellar dysplasia, and nodular heterotopias.

CMCS is an extremely rare condition, with less than 10 families having been reported so far. Diagnosis is made based on BERA evaluation and neuroimaging studies. Posterior collosal agenesis with colpocephaly is the most common neuroimaging finding. Early diagnosis and intervention is important for better prognosis in

terms of psychomotor, speech and mental development. Hearing aids can help salvage some auditory function.

### Molecular Genetics

Chudley-McCullough Syndrome is an autosomal recessive condition. Mutations in the G protein Signaling Modulator 2 (GPSM2) gene on chromosome 1 have recently been implicated in the pathogenesis of this condition. Animal studies have supported a role for the GPSM2 protein in cell fate determination during early neurogenesis within the cerebral cortex. Mutations in GPSM2 have been shown to disrupt the process of mitotic spindles adapting the right planar orientation during neurogenesis.

### Epidemiology in the Arab World

#### Palestine

Shahin et al. (2010) and Walsh et al. (2010) reported a large consanguineous Palestinian kindred in which seven individuals had severe to profound prelingual, bilateral, non-syndromic sensorineural deafness. Vision and vestibular functions were normal, and there were no other findings on ophthalmic testing and clinical exam. Shahin et al. (2010) found linkage to a 3.1-Mb region on chromosome 1p13.3 (lod score of 5.16) between markers rs17542571 and rs1936942, which they designated DFNB82. Later, Walsh et al. (2010) identified a homozygous mutation in the GPSM2 gene (c.875C>T, R127X) in affected members of this family. All unaffected parents were heterozygous for the mutation.

#### United Arab Emirates

See Yemen > Hamzeh et al, 2016

#### Yemen

Hamzeh et al (2016) reported a family with two brothers affected with Chudley McCullough Syndrome. The two children were born to healthy consanguineous Yemeni parents. Both had bilateral severe sensorineural hearing loss and had cochlear implants placed in their right ears. Both had



moderate speech delay and mild developmental delay. They had hyperextensible elbow and knee joints. Brain CT in the older brother revealed posterior third ventricular cystic lesion, suggestive of an arachnoid cyst, along with partial agenesis of the corpus callosum. In the younger brother, CT brain showed the presence of a large posterior third ventricular arachnoid cyst extending to the left of the midline, compressing the left hemisphere and lateral ventricles. Partial agenesis of the corpus callosum was also seen. There was a positive family history of hearing loss and speech delay in the family, with the two of the parents' maternal cousins being affected. Molecular analysis identified a novel homozygous mutation in the GPSM2 gene in the two affected siblings.

### References

Hamzeh AR, Nair P, Mohamed M, Saif F, Tawfiq N, Al-Ali MT, Bastaki F. A novel nonsense GPSM2 mutation in a Yemeni family underlying Chudley-McCullough syndrome. *Eur J Med Genet.* 2016; 59(6-7):337-41. PMID: 27180139

Shahin H, Walsh T, Rayyan AA, Lee MK, Higgins J, Dickel D, Lewis K, Thompson J, Baker C, Nord AS, Stray S, Gurwitz D, Avraham KB, King MC, Kanaan M. Five novel loci for inherited

hearing loss mapped by SNP-based homozygosity profiles in Palestinian families. *Eur J Hum Genet.* 2010; 18(4):407-13. PMID: 19888295

Walsh T, Shahin H, Elkan-Miller T, Lee MK, Thornton AM, Roeb W, Abu Rayyan A, Loulus S, Avraham KB, King MC, Kanaan M. Whole exome sequencing and homozygosity mapping identify mutation in the cell polarity protein GPSM2 as the cause of nonsyndromic hearing loss DFNB82. *Am J Hum Genet.* 2010; 87(1):90-4. PMID: 20602914

### Related CTGA Records

G Protein Signaling Modulator 2

### External Links

<http://www.wohproject.org/disorders/chudley-mcculloughsyndrome/>

<https://rarediseases.info.nih.gov/diseases/86/chudley-mccullough-syndrome>

### Contributors

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