Congenital Disorder of Glycosylation, Type In

Alternative Names
CDG1N
CDG In
CDGIn

Record Category
Disease phenotype

WHO-ICD
Endocrine, nutritional and metabolic diseases > Metabolic disorders

Incidence per 100,000 Live Births
Unknown

OMIM Number
612015

Mode of Inheritance
Autosomal recessive

Gene Map Locus
3p21.1

Description
As the name suggests, Congenital Disorders of Glycosylation (CDGs) are in-born errors of metabolism caused by enzymatic defects in the highly conserved biochemical process of N-linked glycosylation. This process involves the synthesis and processing of (N)-linked glycans or oligosaccharides on glycoproteins. CDGs are classified into two types: type I CDGs are concerned with defects in the synthesis of the lipid-linked oligosaccharide (LLO) chain or its transfer to the protein, while type II CDGs involve disruptions in the terminal portion of the glycosylation pathway, namely the processing of the LLO chain bound to the protein.

CDG1N is a type I disorder with an infantile-onset. Affected patients suffer from severe developmental delay, hypotonia, myoclonic jerks, seizures, ataxia, spasticity and hyperreflexia. Infants exhibit feeding difficulties and may fail to thrive. Other symptoms include respiratory insufficiency, short stature, microcephaly, micrognathia, sensorineural deafness, loss of visual acuity, adducted thumbs and valgus foot deformity. Some patients have been reported to suffer from coagulopathy and hepatomegaly.

The disorder is diagnosed based on isoelectric focusing studies or capillary electrophoresis to detect a type I pattern of transferrin isoforms. It is further confirmed by genetic analysis of the RFT1 gene. There is currently no cure for the condition and treatment is focused on symptomatic care and the prevention of secondary complications.

Molecular Genetics
CDG1N follows an autosomal recessive pattern of inheritance. It is caused by homozygous or compound heterozygous mutations in the RFT1 gene. This gene encodes an enzyme involved in N-linked glycosylation; specifically, it catalyzes the translocation of the Man(5)GlcNAc(2)-dolichylpyrophosphate intermediate from the cytoplasmic side of the endoplasmic reticulum (ER) membrane to the luminal side. RFT1 mutations associated with CDG1N are mainly missense variants that result in a non-functioning RFT1 enzyme.

Epidemiology in the Arab World
Saudi Arabia
Monies et al. (2017) studied the findings of 1000 diagnostic panels and exomes carried out at a next generation sequencing lab in Saudi Arabia. One patient, a 3-year-old male from a consanguineous family, presented with congenital microcephaly, global developmental delay, epilepsy and hematemesis. Using whole exome sequencing, a homozygous mutation (c.775+1G>C) was

identified in exon 7 of the patient's RFT1 gene, associated with CDG1N. Given the atypical presentation of the patient, this case helped in the phenotypic expansion of the disorder.

References

Monies D, Abouelhoda M, AlSayed M, Alhassnan Z, Alotaibi M, Kayyali H, Al-Owain M, Shah A, Rahbeeni Z, Al-Muhaizea MA, Alzaidan HI, Cupler E, Bohlega S, Faqeih E, Faden M, Alyounes B, Jaroudi D, Goljan E, Elbardisy H, Akilan A, Albar R, Aldhalaan H, Gulab S, Chedrawi A, Al Saud BK, Kurdi W, Makhseed N, Alqasim T, El Khashab HY, Al-Mousa H, Alhashem A, Kanaan I, Algoufi T, Alsaleem K, Basha TA, Al-Murshedi F, Khan S, Al-Kindy A, Alnemer M, Al-Hajjar S, Alyamani S, Aldhekri H, Al-Mehaidib A, Arnaout R, Dabbagh O, Shagrani M, Broering D, Tulbah M, Alqassmi A, Almugbel M, AlQuaiz M, Alsaman A, Al-Thihli K, Sulaiman RA, Al-Dekhail W, Alsaegh A, Bashiri FA, Qari A, Alhomadi S, Alkuraya H, Alsebayel M, Hamad MH, Szonyi L, Abaalkhail F, Al-Mayouf SM, Almojalli H, Alqadi KS, Elsiesy H, Shuaib TM, Seidahmed MZ, Abosoudah I, Akleh H, AlGhonaium A, Alkharfy TM, Al Mutairi F, Eyaid W, Alshanbary A, Sheikh FR, Alsohaibani FI, Alsonbul A, Al Tala S, Balkhy S, Bassiouni R, Alenizi AS, Hussein MH, Hassan S, Khalil M, Tabarki B, Alshahwan S, Oshi A, Sabr Y, Alsaadoun S, Salih MA, Mohamed S, Sultana H, Tamim A, El-Haj M, Alshahrani S, Bubshait DK, Alfadhel M, Faquih T, El-Kalioby M, Subhani S, Shah Z, Moghrabi N, Meyer BF, Alkuraya FS. The landscape of genetic diseases in Saudi Arabia based on the first 1000 diagnostic panels and exomes. Hum Genet. 2017 Aug;136(8):921-939. PMID: 28600779.

Related CTGA Records

RFT1, S. Cerevisiae, Homolog of (OMIM 611908)

External Links

https://rarediseases.org/rare-diseases/congenital-disorders-of-glycosylation/

https://www.ncbi.nlm.nih.gov/books/NBK1332/#cdg.Causes_of_Congenital_Disorders_of_Gl

http://cdgcare.com/what-is-cdg/

Contributors

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22.09.2017