Congenital Disorder of Glycosylation, Type IIi

Alternative Names
CDG2I
CDG IIi
CDGIIi

Record Category
Disease phenotype

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

Incidence per 100,000 Live Births
Unknown

OMIM Number
613612

Mode of Inheritance
Autosomal recessive

Gene Map Locus
7q22.3

Description
CDG2I belongs to a group of phenotypically and genetically heterogeneous Congenital Disorders of Glycosylation (CDGs) caused by enzymatic defects in the synthesis and processing of glycans or oligosaccharides on glycoproteins. While type 1 CDGs involve defects in the assembly of the dolichol lipid-linked oligosaccharide (LLO) chain and its transfer to the nascent protein, type 2 CDGs are a result of defects in the trimming and processing of the protein-bound glycans either in the endoplasmic reticulum or the Golgi apparatus.

CDG2I is characterized by intellectual disability, developmental delay, atrophy of the cerebellum and brain stem, truncal ataxia and hypotonia. Affected patients exhibit decreased O-glycosylation of APOC3 and decreased N-glycosylation of serum transferrin and alpha-1-acid glycoprotein. The disorder affects both men and women equally. However, the exact prevalence of this condition is yet to be determined.

Diagnosis of CDG2I is done by isoelectric focusing, which allows the detection of abnormal transferrin patterns. Currently, enzyme replacement therapy is being investigated as a possible treatment for CDG. Patients also require symptomatic support and may benefit from physical, occupational and speech therapy.

Molecular Genetics
The disorder follows an autosomal recessive pattern of inheritance and is caused by mutations in the COG5 gene. COG5 is involved in the intra-Golgi and ER to Golgi vesicle-mediated transport of proteins, particularly the enzymes responsible for glycosylation. At least 8 mutations in the COG5 gene have been identified to result in CDG2I. The homozygous intronic transition 1669-15T-C results in altered splicing and a transcript lacking the 58 amino acids of exons 15 and 16.

Epidemiology in the Arab World
Saudi Arabia
Anazi et al. (2016) investigated the effectiveness of genomic tools in diagnosing Intellectual Disability (ID) cases. The authors carried out molecular karyotyping, exome sequencing and sequencing by a neurological gene panel. Genomic tools were found to have a higher diagnostic yield than standard clinical evaluations (58% vs 16%) in a cohort of 337 ID patients. In one such patient, the genomic approach uncovered a homozygous c.1120-12T>A intronic mutation in the COG5 gene. Although the gene is associated with the disorder CDG2I, the patient showed atypical features such as a cleft lip and palate, perforated bowel, microcephaly, severe spasticity, squint, simplified ears, microphthalmus, down-slanting palpebral fissure, bi-temporal narrowing, small mouth, absence of corpus callosum, absence of cingulate gyrus and colpocephaly.

References
Anazi S, Maddirevula S, Faqeih E, Alsedairy H, Alzahrani F, Shamseldin HE, Patel N, Hashem M, Ibrahim N, Abdulwahab F, Ewida N, Alsaif HS, Al

Sharif H, Alamoudi W, Kentab A, Bashiri FA, Alnaser M, AlWadei AH, Alfadhel M, Eyaid W, Hashem A, Al Asmari A, Saleh MM, AlSaman A, Alhasan KA, Alsughayir M, Al Shammari M, Mahmoud A, Al-Hassnan ZN, Al-Husain M, Osama Khalil R, Abd El Meguid N, Masri A, Ali R, Ben-Omran T, El Fishway P, Hashish A, Ercan Sencicek A, State M, Alazami AM, Salih MA, Altassan N, Arold ST, Abouelhoda M, Wakil SM, Monies D, Shaheen R, Alkuraya FS. Clinical genomics expands the morbid genome of intellectual disability and offers a high diagnostic yield. Mol Psychiatry. 2016 Jul 19. PMID: 27431290.

Related CTGA Records

Component of Oligomeric Golgi Complex 5 (OMIM 606821)

Congenital Disorder of Glycosylation, Type Ia (OMIM 212065)

Congenital Disorder of Glycosylation, Type Il (OMIM 608776)

External Links

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

http://cdgcare.com/

Contributors

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