Perrault Syndrome 4

Alternative Names
PRLTS4

Record Category
Disease phenotype

WHO-ICD
Congenital malformations, deformations and chromosomal abnormalities > Other congenital malformations

Incidence per 100,000 Live Births
Unknown

OMIM Number
615300

Mode of Inheritance
Autosomal recessive

Gene Map Locus
3p21.31

Description
Perrault syndrome 4 is an autosomal recessive disorder that causes progressive sensorineural hearing loss in both males and females as well as premature ovarian failure in females. Hearing loss is more severe at lower frequencies and becomes milder at higher frequencies. This results in unusual upsloping audiograms. In females, ovarian failure is accompanied by increased gonadotropin levels. Patients may have a small prepubertal sized uterus and hypoplastic ovaries.

Prognosis of the disorder appears positive and patients affected by Perrault syndrome have a normal life expectancy. Perrault syndrome is a rare condition with less than 100 cases reported worldwide. However, the disorder is often underdiagnosed as in the absence of an affected sister, male patients are simply assumed to suffer from non-syndromic hearing loss.

Diagnosis is made based on hormone levels, pelvic ultrasound examinations and CT scans to ensure hearing loss is not caused by temporal bone malformations. Treatment requires a multidisciplinary approach involving audiologists and endocrinologists. Patients may benefit from hearing aids and cochlear implants.

Molecular Genetics
Perrault syndrome 4 follows an autosomal recessive pattern of inheritance. It is caused by mutations in the LARS2 gene. LARS2 encodes a leucyl-tRNA synthetase which is responsible for attaching the amino acid leucine to the appropriate tRNA during mitochondrial protein translation. The enzyme is hence believed to play an important role in mitochondrial energy production. Variants in the LARS2 gene associated with Perrault Syndrome 4 are generally homozygous and compound heterozygous missense mutations that reduce or eliminate LARS2 enzyme activity.

Epidemiology in the Arab World
Saudi Arabia
Anazi et al. (2016) recruited 337 Intellectual Disability (ID) patients to determine the feasibility of employing genomic tools as a first-tier diagnostic test. The genomic approach of molecular karyotyping, exome sequencing and sequencing by a neurological gene panel was found to have a higher diagnostic yield than standard clinical evaluations (58% vs 16%). In one patient, the analysis uncovered a homozygous c.457A>C (p.Asn153His) mutation in the LARS2 gene, which is associated with Perrault syndrome 4. However, the authors noted that the patient's features of ID short stature, T1DM, cirrhosis, thrombocytopenia, leukopenia, seizures, psoriasis, absent ovaries and uterus, vitiligo and osteoporosis were not typical presentations of this disorder.

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

Leucyl-tRNA Synthetase 2 (OMIM 604544)

External Links

https://ghr.nlm.nih.gov/condition/perrault-syndrome#

http://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=EN&Expert=2855

Contributors

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