Spastic Paraplegia 8, Autosomal Dominant

Alternative Names
SPG8

Record Category
Disease phenotype

WHO-ICD
Diseases of the nervous system > Systemic atrophies primarily affecting the central nervous system

Incidence per 100,000 Live Births
0-1

OMIM Number
603563

Mode of Inheritance
Autosomal dominant

Gene Map Locus
8q24.13

Description
Spastic paraplegia 8 is a neurologic disorder characterized by severe lower limb spasticity and weakness. Symptoms include hyperreflexia, extensor plantar responses, degeneration of the lateral corticospinal tracts, decreased vibratory sense in the lower limbs, pes cavus and atrophy of the shins. Patients also suffer from urinary urgency and incontinence.

Hereditary spastic paraplegias have a combined prevalence of about 1 to 18 in 100,000 and SPG8 forms only a small percentage of these cases. SPG8 is considered a ‘pure’ or ‘uncomplicated’ form of spastic paraplegia as it is not accompanied by other system involvement or other neurologic findings such as seizures, dementia, amyotrophy, extrapyramidal disturbance, or peripheral neuropathy. The disorder has an adult-onset and some affected individuals become wheelchair-bound as the disease progresses.

Management of spastic paraplegia includes regular physical therapy, assistive walking devices and ankle-foot orthotics. Antispasmodic drugs can help relieve muscle cramps and tightness. Affected patients must undergo regular neurological examinations to evaluate disease progression as well as urological analysis to prevent secondary complications such as urinary tract infections. Patients’ families may also benefit from genetic counselling.

Molecular Genetics
The disorder follows an autosomal dominant pattern of inheritance and is caused by heterozygous mutations in the KIAA0196 gene. This gene encodes the strumpellin protein, believed to be involved in inducing actin polymerization. So far only missense mutations have been associated with the disorder, the most common being Val626Phe caused by a 1956G-T transversion.

Epidemiology in the Arab World
Saudi Arabia
Anazi et al. (2016) studied a cohort of 337 Intellectual Disability patients to assess the feasibility of genomic tools as a first-tier diagnostic test. Patients were recruited based on IQ scores, delayed speech acquisition and other cognitive developmental delays. They were subjected to molecular karyotyping, exome sequencing and a multi-gene panel comprised of genes associated with neuro-genetic diseases. The tests helped uncover a de-novo mutation (c.1669G>A, p.Ala557Thr) in the KIAA0196 gene of one patient, suggesting a diagnosis of spastic paraplegia 8. However, it was noted that the subject exhibited features atypical of the disease such as ID, an infantile onset and a lack of spasticity.

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

KIAA0196 Gene (OMIM 610657)

Spastic Paraplegia 3, Autosomal Dominant (OMIM 182600)

External Links

https://ghr.nlm.nih.gov/condition/spastic-paraplegia-type-8#

https://rarediseases.org/rare-diseases/hereditary-spastic-paraplegia/

Contributors

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