CLN4 disease

Description

CLN4 disease is a condition that primarily affects the nervous system, causing problems with movement and intellectual function that worsen over time. The signs and symptoms of CLN4 disease typically appear around age 30, but they can develop anytime between adolescence and late adulthood.

People with CLN4 disease often develop seizures and uncontrollable muscle jerks (myoclonic epilepsy), a decline in intellectual function (dementia), problems with coordination and balance (ataxia), tremors or other involuntary movements (motor tics), and speech difficulties (dysarthria). The signs and symptoms of CLN4 disease worsen over time, and affected individuals usually survive about 15 years after the disorder begins.

CLN4 disease is one of a group of disorders known as neuronal ceroid lipofuscinoses (NCLs), which may also be collectively referred to as Batten disease. (The adult forms of NCLs, which includes CLN4 disease, are sometimes known as Kufs disease.) All the NCLs affect the nervous system and typically cause worsening problems with vision, movement, and thinking ability. The different NCLs are distinguished by their genetic cause. Each disease type is given the designation "CLN," meaning ceroid lipofuscinosis, neuronal, and then a number to indicate its subtype.

Frequency

CLN4 disease is a rare disorder, but its prevalence is unknown. Collectively, all forms of NCL affect an estimated 1 in 100,000 individuals worldwide.

Causes

Mutations in the *DNAJC5* gene cause CLN4 disease. The *DNAJC5* gene provides instructions for making a protein called cysteine string protein alpha (CSPα). This protein is found in the brain, where it plays a role in the transmission of nerve impulses, helping nerve cells communicate with each other. Specifically, CSPα is involved in recycling certain proteins that are involved in nerve impulse transmission by refolding misshapen proteins so that they can be used in additional transmissions.

DNAJC5 gene mutations lead to the production of an altered CSPα protein. The altered protein cannot perform its function, which reduces protein recycling, causing a shortage (

deficiency) of functional proteins needed for impulse transmission. Without normal communication between nerve cells, neurological functions are impaired, contributing to the features of CLN4 disease.

CLN4 disease, like other NCLs, is characterized by the accumulation of proteins and other substances in lysosomes, which are compartments in the cell that digest and recycle materials. These accumulations occur in cells throughout the body; however, nerve cells seem to be particularly vulnerable to their effects. The accumulations can cause cell damage leading to cell death. The progressive death of nerve cells in the brain and other tissues contributes to the decline of neurological function in CLN4 disease. However, it is unclear how mutations in the *DNAJC5* gene are involved in the buildup of substances in lysosomes.

Learn more about the gene associated with CLN4 disease

- DNAJC5

Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Some cases of this condition result from new (de novo) mutations in the gene that occur during the formation of reproductive cells (eggs or sperm) in an affected individual's parent or in early embryonic development. These cases occur in people with no history of the disorder in their family.

Other Names for This Condition

- Adult neuronal ceroid lipofuscinosis
- Ceroid lipofuscinosis, neuronal, 4B, autosomal dominant
- CLN4B
- Parry disease

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Ceroid lipofuscinosis, neuronal, 4 (Kufs type) (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1834207/)

Genetic and Rare Diseases Information Center

- Adult neuronal ceroid lipofuscinosis (https://rarediseases.info.nih.gov/diseases/10973/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22CLN4 disease%22)

Catalog of Genes and Diseases from OMIM

- CEROID LIPOFUSCINOSIS, NEURONAL, 4 (KUFS TYPE); CLN4 (https://omim.org/entry/162350)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28kufs+disease%5BTIAB%5D%29+OR+%28adult+neuronal+ceroid+lipofuscinosis%5BTIAB%5D%29+OR+%28CLN4+disease%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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