Pelizaeus-Merzbacher-like disease type 1

Description

Pelizaeus-Merzbacher-like disease type 1 is an inherited condition involving the brain and spinal cord (central nervous system). This disease is one of a group of genetic disorders called leukodystrophies. Leukodystrophies are abnormalities of the nervous system's white matter, which consists of nerve fibers covered by a fatty substance called myelin. Myelin insulates nerve fibers and promotes the rapid transmission of nerve impulses. In particular, Pelizaeus-Merzbacher-like disease type 1 involves hypomyelination, which means that the nervous system has a reduced ability to form myelin. The signs and symptoms of this condition are very similar to another leukodystrophy called Pelizaeus-Merzbacher disease, but the two disorders have different genetic causes.

Beginning in the first few months of life, infants with Pelizaeus-Merzbacher-like disease type 1 typically experience weak muscle tone (hypotonia), involuntary movements of the eyes (nystagmus), and delayed development of speech and motor skills, such as sitting or grasping objects. As children with Pelizaeus-Merzbacher-like disease type 1 get older, hypotonia changes to muscle stiffness (spasticity).

During childhood, individuals with Pelizaeus-Merzbacher-like disease type 1 develop problems with movement and balance (ataxia), difficulty with movements that involve judging distance or scale (dysmetria), tremors that occur mainly during movement (intention tremors), and head and neck tremors (titubation). People with this condition have an inability to perform quick, alternating movements (dysdiadochokinesia), such as quickly tapping different fingers. Some develop involuntary tensing of the muscles (dystonia) and jerking (choreiform) movements. Many people with Pelizaeus-Merzbacher-like disease type 1 develop skeletal issues such as an abnormal curvature of the spine (scoliosis) and require wheelchair assistance from childhood.

Muscle abnormalities can lead to difficulty swallowing and problems producing speech (expressive language), but affected individuals can understand speech (receptive language). Most individuals with Pelizaeus-Merzbacher-like disease type 1 have normal intelligence. Rarely, hearing loss, optic atrophy, and recurrent seizures (epilepsy) can occur.

Frequency

The prevalence of Pelizaeus-Merzbacher-like disease type 1 is unknown, but it is thought to be rare.

Causes

Pelizaeus-Merzbacher-like disease type 1 is caused by mutations in the *GJC2* gene. This gene provides instructions for making a protein called connexin-47. This protein plays a role in forming channels called gap junctions between cells. Gap junctions made with connexin-47 facilitate communication between nervous system cells called oligodendrocytes or between oligodendrocytes and another type of nervous system cell called astrocytes. Communication between these cells is necessary for the formation of myelin.

GJC2 gene mutations that cause Pelizaeus-Merzbacher-like disease type 1 reduce the production of connexin-47, prevent the connexin-47 protein from reaching the cell membrane, or decrease the function of the protein in the gap junction. All of these *GJC2* gene mutations disrupt the communication between nerve cells that normally occurs at gap junctions and impair myelin formation. These changes lead to nerve damage in the brain and spinal cord that impairs nervous system function, resulting in the signs and symptoms of Pelizaeus-Merzbacher-like disease type 1.

Learn more about the gene associated with Pelizaeus-Merzbacher-like disease type 1

- GJC2

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- HLD2
- Hypomyelinating leukodystrophy 2
- Pelizaeus Merzbacher like disease
- Pelizaeus-Merzbacher-like disease
- PMLD - Pelizaeus Merzbacher like disease
- PMLD1

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Hypomyelinating leukodystrophy 2 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1837355/)

Genetic and Rare Diseases Information Center

- Pelizaeus-Merzbacher-like disease (https://rarediseases.info.nih.gov/diseases/12300/index)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- LEUKODYSTROPHY, HYPOMYELINATING, 2; HLD2 (https://omim.org/entry/608804)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28Pelizaeus-Merzbacher-like+disease%5BTIAB%5D%29+OR+%28hypomyelinating+leukodystrophy+2%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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