Hypomyelination with brainstem and spinal cord involvement and leg spasticity

Description

Hypomyelination with brainstem and spinal cord involvement and leg spasticity (HBSL) is a condition that affects the brain and spinal cord (central nervous system). In particular, the condition affects nerves in specific regions (called tracts) within the spinal cord and the brainstem, which is the part of the brain that connects to the spinal cord. HBSL is a form of leukodystrophy, which is a group of conditions that involve abnormalities of the nervous system's white matter. The white matter consists of nerve fibers covered by a fatty substance, called myelin, that insulates the fibers and promotes the rapid transmission of nerve impulses. In HBSL, the nervous system has a reduced ability to form myelin (hypomyelination).

In HBSL, early development of motor skills (such as rolling over and sitting) may be normal, but movement problems typically begin within the infant's first year. However, in some individuals, these problems do not appear until adolescence. The characteristic feature of HBSL is muscle stiffness (spasticity) in the legs that worsens over time. Most people with HBSL are unable to walk independently. Other neurological problems in affected individuals can include abnormal side-to-side movements of the eyes (nystagmus), weak muscle tone (hypotonia) in the torso, and mild intellectual disability.

Distinct changes in the brains of people with HBSL can be seen using magnetic resonance imaging (MRI). These characteristic abnormalities typically involve specific regions (called tracts) within the brainstem and spinal cord, especially the pyramidal tract, lateral corticospinal tract, and the dorsal column.

Frequency

HBSL is a rare condition. Its prevalence is unknown.

Causes

HBSL is caused by mutations in a gene called *DARS1*, which provides instructions for making an enzyme called aspartyl-tRNA synthetase. This enzyme is important in the production (synthesis) of proteins.

During protein synthesis, building blocks (amino acids) are connected together in a

specific order, creating a chain of amino acids that forms the protein. Aspartyl-tRNA synthetase plays a role in adding the amino acid aspartate at the proper place in proteins.

Mutations in the *DARS1* gene result in decreased aspartyl-tRNA synthetase enzyme activity, which hinders the addition of aspartate to proteins. It is unclear how the *DARS1* gene mutations lead to the signs and symptoms of HBSL. Researchers do not understand why reduced activity of aspartyl-tRNA synthetase affects myelination or why specific parts of the brainstem and spinal cord are involved.

Learn more about the gene associated with Hypomyelination with brainstem and spinal cord involvement and leg spasticity

- DARS1

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

- Aspartyl-tRNA synthetase deficiency
- HBSL
- Hypomyelination with brain stem and spinal cord involvement and leg spasticity

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Hypomyelination with brain stem and spinal cord involvement and leg spasticity (https://www.ncbi.nlm.nih.gov/gtr/conditions/C4755254/)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- HYPOMYELINATION WITH BRAINSTEM AND SPINAL CORD INVOLVEMENT AND LEG SPASTICITY; HBSL (https://omim.org/entry/615281)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28hypomyelination+with+brainstem+and+spinal+cord+involvement+and+leg+spasticity%5BTIAB%5D%29+OR+%28%28DARS%5BTIAB%5D%29+AND+%28hypomyelination%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+%22last+3600+days%22%5Bdp%5D)

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