Infantile Neuroaxonal Dystrophy

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Infantile neuroaxonal dystrophy is a disorder that primarily affects the nervous system.

Keywords: genetic conditions

1. Introduction

Individuals with infantile neuroaxonal dystrophy typically do not have any symptoms at birth, but between the ages of about 6 and 18 months they begin to experience delays in acquiring new motor and intellectual skills, such as crawling or beginning to speak. Eventually they lose previously acquired skills (developmental regression). In some cases, signs and symptoms of infantile neuroaxonal dystrophy first appear later in childhood or during the teenage years and progress more slowly.

Children with infantile neuroaxonal dystrophy experience progressive difficulties with movement. They generally have muscles that are at first weak and "floppy" (hypotonic), and then gradually become very stiff (spastic). Eventually, affected children lose the ability to move independently. Lack of muscle strength causes difficulty with feeding. Muscle weakness can also result in breathing problems that can lead to frequent infections, such as pneumonia. Seizures occur in some affected children.

Rapid, involuntary eye movements (nystagmus), eyes that do not look in the same direction (strabismus), and vision loss due to deterioration (atrophy) of the nerve that carries information from the eye to the brain (the optic nerve) often occur in infantile neuroaxonal dystrophy. Hearing loss may also develop. Children with this disorder experience progressive deterioration of cognitive functions (dementia), and they eventually lose awareness of their surroundings.

Infantile neuroaxonal dystrophy is characterized by the development of swellings called spheroid bodies in the axons, the fibers that extend from nerve cells (neurons) and transmit impulses to muscles and other neurons. In some individuals with infantile neuroaxonal dystrophy, abnormal amounts of iron accumulate in a specific region of the brain called the basal ganglia. The relationship of these features to the symptoms of infantile neuroaxonal dystrophy is unknown.

2. Frequency

Infantile neuroaxonal dystrophy is a very rare disorder. Its specific incidence is unknown.

3. Causes

Mutations in the *PLA2G6* gene have been identified in most individuals with infantile neuroaxonal dystrophy. The *PLA2G6* gene provides instructions for making a type of enzyme called an A2 phospholipase. This type of enzyme is involved in breaking down (metabolizing) fats called phospholipids. Phospholipid metabolism is important for many body processes, including helping to keep the cell membrane intact and functioning properly. Specifically, the A2 phospholipase produced from the *PLA2G6* gene, sometimes called PLA2 group VI, helps to regulate the levels of a compound called phosphatidylcholine, which is abundant in the cell membrane.

Mutations in the *PLA2G6* gene impair the function of the PLA2 group VI enzyme, which may disrupt cell membrane maintenance and contribute to the development of spheroid bodies in the nerve axons. Although it is unknown how changes in this enzyme's function lead to the signs and symptoms of infantile neuroaxonal dystrophy, phospholipid metabolism problems have been seen in both this disorder and a similar disorder called pantothenate kinase-associated neurodegeneration. These disorders, as well as the more common Alzheimer disease and Parkinson disease, also are associated with changes in brain iron metabolism. Researchers are studying the links between phospholipid defects, brain iron, and damage to nerve cells, but have not determined how the iron accumulation that occurs in some individuals with infantile neuroaxonal dystrophy may contribute to the features of this disorder.

A few individuals with infantile neuroaxonal dystrophy have not been found to have mutations in the *PLA2G6* gene. The genetic cause of the condition in these cases is unknown; there is evidence that at least one other unidentified gene may be involved.

3.1. The gene associated with Infantile neuroaxonal dystrophy

- PLA2G6

4. 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.

5. Other Names for This Condition

- INAD
- NBIA, PLA2G6-related
- neurodegeneration with brain iron accumulation, PLA2G6-related
- Seitelberger disease
- Seitelberger's disease

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