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My46 Trait Profile

Pantothenate Kinase-Associated Neurodegeneration

Other Names: Neurodegeneration with brain iron accumulation, Hallervorden-Spatz syndrome

Pantothenate kinase-associated neurodegeneration is a rare genetic condition characterized by progressive muscle dystonia (cramping) and abnormal iron accumulation in the brain. It is caused by mutations in the PANK2 gene which makes the protein called pantothenate kinase 2.

Characteristics of Pantothenate Kinase-Associated Neurodegeneration

Pantothenate kinase-associated neurodegeneration (PKAN) is a progressive disorder, meaning it worsens over time. Individuals with PKAN often first have trouble walking normally and have a tendency to fall. They develop worsening dystonia (constant muscle cramping) and spasticity (tightness) in their limbs that affect walking, writing, typing, and other activities of daily living. Retinal degeneration (i.e., deterioration of the retina – the tissue that lines the back of the eye) is also common and can impair night vision and/or cause tunnel vision (i.e., having a loss of peripheral vision). Dysarthria (speech difficulty) is frequent and can make affected individuals very difficult to understand. Individuals with PKAN usually have normal intellectual abilities. As the disease progresses, individuals eventually have difficulty with eating and managing their oral secretions, which can lead to additional complications such as choking. Some individuals have milder symptoms with slower progression. The features seen in PKAN are due to an abnormal buildup of iron in certain areas of the brain. Nearly all individuals with PKAN have a brain MRI finding called an “eye-of-the-tiger” sign, which describes the location and appearance of their iron accumulation.

Diagnosis/Testing

PKAN is most often diagnosed by the presence of an “eye-of-the-tiger” finding on brain MRI and genetic testing for changes or mutations in a gene called PANK2. This gene makes an enzyme called pantothenate kinase 2. This enzyme is involved in energy metabolism in the mitochondria (the “powerhouse” of the cell). It is not entirely understood how mutations in the PANK2 gene lead to abnormal iron accumulation in the brain.

Management/Surveillance

Management for PKAN is aimed at reducing symptoms. Medications such as baclofen and other treatments, such as Botox injections, are often used to reduce painful and debilitating dystonia and spasticity. As the condition progresses and symptoms worsen, other therapies such as deep brain stimulation (i.e., a treatment aimed to decrease dystonia) or an intrathecal baclofen pump (i.e., a devise that that delivers the baclofen medication directly into the spinal cord in an attempt to treat severe spasticity) may be considered. Management of PKAN often includes physical, occupational, and speech therapies, as well as nutritional assessment. A feeding tube may be useful during later disease to help maintain weight and avoid choking.

Mode of inheritance

PKAN is inherited in an autosomal recessive pattern. This means that an individual has to inherit two PANK2 mutations (i.e., one from each parent) to be affected with PKAN. If both parents are carriers of a PANK2 mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with PKAN.

Risk to family members

Parents of a child with PKAN are carriers of PKAN. If a sibling of a child with PKAN is unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of PKAN.

Special considerations

None

Resources

Neurodegeneration with Brain Iron Accumulation Disorders Association
http://www.nbia.org/
Treat Iron-Related Childhood Onset Neurodegeneration (TIRCON)
http://www.tircon.eu
Genetics Home Reference: Pantothenate kinase-associated neurodegeneration
http://ghr.nlm.nih.gov/condition/pantothenate-kinase-associated-neurodegeneration

References

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