Pantothenate kinase-associated neurodegeneration

Pantothenate kinase-associated neurodegeneration (formerly called Hallervorden-Spatz syndrome) is a disorder of the nervous system. This condition is characterized by progressive difficulty with movement, typically beginning in childhood. Movement abnormalities include involuntary muscle spasms, rigidity, and trouble with walking that worsens over time. Many people with this condition also develop problems with speech (dysarthria), and some develop vision loss. Additionally, affected individuals may experience a loss of intellectual function (dementia) and psychiatric symptoms such as behavioral problems, personality changes, and depression.

Pantothenate kinase-associated neurodegeneration is characterized by an abnormal buildup of iron in certain areas of the brain. A particular change called the eye-of-the-tiger sign, which indicates an accumulation of iron, is typically seen on magnetic resonance imaging (MRI) scans of the brain in people with this disorder.

Researchers have described classic and atypical forms of pantothenate kinase-associated neurodegeneration. The classic form usually appears in early childhood, causing severe problems with movement that worsen rapidly. Features of the atypical form appear later in childhood or adolescence and progress more slowly. Signs and symptoms vary, but the atypical form is more likely than the classic form to involve speech defects and psychiatric problems.

A condition called HARP (hyporebetalipoproteinemia, acanthocytosis, retinitis pigmentosa, and pallidal degeneration), which was historically described as a separate syndrome, is now considered part of pantothenate kinase-associated neurodegeneration. Although HARP is much rarer than classic pantothenate kinase-associated neurodegeneration, both conditions involve problems with movement, dementia, and vision abnormalities.

Frequency

The precise incidence of this condition is unknown. It is estimated to affect 1 to 3 per million people worldwide.

Causes

Mutations in the PANK2 gene cause pantothenate kinase-associated neurodegeneration.

The PANK2 gene provides instructions for making an enzyme called pantothenate kinase 2. This enzyme is active in mitochondria, the energy-producing centers within cells, where it plays a critical role in the formation of a molecule called coenzyme A.
Found in all living cells, coenzyme A is essential for the body’s production of energy from carbohydrates, fats, and some protein building blocks (amino acids).

Mutations in the \textit{PANK2} gene likely result in the production of an abnormal version of pantothenate kinase 2 or prevent cells from making any of this enzyme. A lack of functional pantothenate kinase 2 disrupts the production of coenzyme A and allows potentially harmful compounds to build up in the brain. This buildup leads to swelling and tissue damage, and allows iron to accumulate abnormally in certain parts of the brain. Researchers have not determined how these changes result in the specific features of pantothenate kinase-associated neurodegeneration. Because pantothenate kinase 2 functions in mitochondria, the signs and symptoms of this condition may be related to impaired energy production.

\textbf{Inheritance Pattern}

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.

\textbf{Other Names for This Condition}

\begin{itemize}
  \item NBIA1
  \item neurodegeneration with brain iron accumulation type 1
  \item PKAN
\end{itemize}

\textbf{Diagnosis & Management}

\textbf{Genetic Testing Information}

\begin{itemize}
  \item What is genetic testing? \\
  \url{primer/testing/genetictesting}
  \item Genetic Testing Registry: Hypoprebetalipoproteinemia, acanthocytosis, retinitis pigmentosa, and pallidal degeneration \\
  \url{https://www.ncbi.nlm.nih.gov/gtr/conditions/C1846582/}
  \item Genetic Testing Registry: Neurodegeneration with brain iron accumulation \\
  \url{https://www.ncbi.nlm.nih.gov/gtr/conditions/CN043643/}
\end{itemize}

\textbf{Research Studies from ClinicalTrials.gov}

\begin{itemize}
  \item ClinicalTrials.gov \\
  \url{https://clinicaltrials.gov/ct2/results?cond=%22pantothenate+kinase-associated +neurodegeneration%22+OR+%22Hallervorden-Spatz+Syndrome%22}
\end{itemize}
Other Diagnosis and Management Resources

- GeneReview: Pantothenate Kinase-Associated Neurodegeneration
  https://www.ncbi.nlm.nih.gov/books/NBK1490
- MedlinePlus Encyclopedia: Hallervorden-Spatz Disease
  https://medlineplus.gov/ency/article/001225.htm
- MedlinePlus Encyclopedia: MRI
  https://medlineplus.gov/ency/article/003335.htm

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Hallervorden-Spatz Disease
  https://medlineplus.gov/ency/article/001225.htm
- Encyclopedia: MRI
  https://medlineplus.gov/ency/article/003335.htm
- Health Topic: Degenerative Nerve Diseases
  https://medlineplus.gov/degenerativenervediseases.html
- Health Topic: Movement Disorders
  https://medlineplus.gov/movementdisorders.html

Genetic and Rare Diseases Information Center

- Pantothenate kinase-associated neurodegeneration

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke
  https://www.ninds.nih.gov/Disorders/All-Disorders/Neurodegeneration-Brain-Iron-Accumulation-Information-Page

Educational Resources

- MalaCards: neurodegeneration with brain iron accumulation 1
  https://www.malacards.org/card/neurodegeneration_with_brain_iron_accumulation_1
- NBIAcure: PKAN
  http://nbiacure.org/learn/nbia-disorders/pkan/
- Orphanet: Neurodegeneration with brain iron accumulation
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=385
Patient Support and Advocacy Resources

• National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/pantothenate-kinase-associated-neurodegeneration/

• NBIAcure
  http://nbiacure.org/

Clinical Information from GeneReviews

• Pantothenate Kinase-Associated Neurodegeneration
  https://www.ncbi.nlm.nih.gov/books/NBK1490

Scientific Articles on PubMed

• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28pantothenate+kinase-associated+neurodegeneration%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

• HYPOPREBETALIPOPROTEINEMIA, ACANTHOCYTOSIS, RETINITIS PIGMENTOSA, AND PALLIDAL DEGENERATION
  http://omim.org/entry/607236

• NEURODEGENERATION WITH BRAIN IRON ACCUMULATION 1
  http://omim.org/entry/234200

Medical Genetics Database from MedGen

• Classic pantothenate kinase-associated neurodegeneration

Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16416393
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2117327/

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301663

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16437574
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12510040

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12614941

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14631201

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14638969

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15911822

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12510036

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11479594


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