Hyperprolinemia

Description

Hyperprolinemia is an excess of a particular protein building block (amino acid), called proline, in the blood. This condition generally occurs when proline is not broken down properly by the body. There are two forms of hyperprolinemia, called type I and type II.

People with hyperprolinemia type I often do not show any symptoms, although they have proline levels in their blood between 3 and 10 times the normal level. Some individuals with hyperprolinemia type I exhibit seizures, intellectual disability, or other neurological or psychiatric problems.

Hyperprolinemia type II results in proline levels in the blood between 10 and 15 times higher than normal, and high levels of a related compound called pyrroline-5-carboxylate. This form of the disorder is more likely than type I to involve seizures or intellectual disability that vary in severity.

Hyperprolinemia can also occur with other conditions, such as malnutrition or liver disease. In particular, individuals with conditions that cause elevated levels of a chemical called lactic acid in the blood (lactic acidosis) may have hyperprolinemia as well, because lactic acid stops (inhibits) the breakdown of proline.

Frequency

It is difficult to determine the prevalence of hyperprolinemia type I because most people with the condition do not have any symptoms. Hyperprolinemia type II is thought to be a rare condition; its prevalence is also unknown.

Causes

Hyperprolinemia is caused by variants (also known as mutations) in the *ALDH4A1* and *PRODH* genes. These genes provide instructions for enzymes that break down proline.

Hyperprolinemia type I is caused by variants in the *PRODH* gene, which provides instructions for producing an enzyme called proline dehydrogenase. This enzyme begins the process of breaking down proline by starting the reaction that converts proline to pyrroline-5-carboxylate.

Hyperprolinemia type II is caused by variants in the *ALDH4A1* gene, which provides

instructions for producing the enzyme pyrroline-5-carboxylate dehydrogenase. This enzyme helps to break down the pyrroline-5-carboxylate produced in the previous reaction, converting it to the amino acid glutamate.

The conversion of proline to glutamate (and the conversion of glutamate to proline, which is controlled by different enzymes) is important for maintaining a supply of amino acids needed for protein production, and for energy transfer within the cell.

Variants in either the *PRODH* or *ALDH4A1* gene can cause a reduction in proline dehydrogenase or pyrroline-5-carboxylate dehydrogenase function and a decrease in the breakdown of proline. As a result, there is a buildup of proline in the body, leading to hyperprolinemia.

Learn more about the genes associated with Hyperprolinemia

- ALDH4A1
- PRODH

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have variants. Most often, the parents of an individual with an autosomal recessive condition each carry one copy of the altered gene, but do not show signs and symptoms of the condition. In about one-third of cases, individuals carrying one copy of an altered *PRODH* gene have moderately elevated levels of proline in their blood, but these levels do not cause any health problems. Individuals with one altered *ALDH4A1* gene have normal levels of proline in their blood.

Other Names for This Condition

- Proline oxidase deficiency
- Prolinemia
- Pyrroline carboxylate dehydrogenase deficiency
- Pyrroline-5-carboxylate dehydrogenase deficiency

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Hyperprolinemia type 2 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C2931835/)
- Genetic Testing Registry: Proline dehydrogenase deficiency (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268529/)

Genetic and Rare Diseases Information Center

- Hyperprolinemia type 1 (https://rarediseases.info.nih.gov/diseases/2847/index)
- Hyperprolinemia type 2 (https://rarediseases.info.nih.gov/diseases/6710/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Hyperprolinemia%22)

Catalog of Genes and Diseases from OMIM

- HYPERPROLINEMIA, TYPE I; HYRPRO1 (https://omim.org/entry/239500)
- HYPERPROLINEMIA, TYPE II; HYRPRO2 (https://omim.org/entry/239510)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28hyperprolinemia%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

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Last updated August 27, 2021