Hypermethioninemia

Description

Hypermethioninemia is an excess of a particular protein building block (amino acid), called methionine, in the blood. This condition can occur when methionine is not broken down (metabolized) properly in the body.

People with hypermethioninemia often do not show any symptoms. Some individuals with hypermethioninemia exhibit intellectual disability and other neurological problems; delays in motor skills such as standing or walking; sluggishness; muscle weakness; liver problems; unusual facial features; and their breath, sweat, or urine may have a smell resembling boiled cabbage.

Hypermethioninemia can occur with other metabolic disorders, such as homocystinuria, tyrosinemia, and galactosemia, which also involve the faulty breakdown of particular molecules. It can also result from liver disease or excessive dietary intake of methionine from consuming large amounts of protein or a methionine-enriched infant formula. The condition is called primary hypermethioninemia when it is not associated with other metabolic disorders or excess methionine in the diet.

Frequency

Primary hypermethioninemia that is not caused by other disorders or excess methionine intake appears to be rare; only a small number of cases have been reported. The actual incidence is difficult to determine, however, since many individuals with hypermethioninemia have no symptoms.

Causes

Primary hypermethioninemia that is not associated with other metabolic disorders can be caused by variants (also known as mutations) in the *MAT1A*, *GNMT*, or *AHCY* gene. These genes provide instructions for making enzymes that each carry out one step of the multistep process to break down methionine. The reactions involved help supply some of the amino acids needed for protein production. These reactions are also involved in transferring methyl groups, consisting of a carbon atom and three hydrogen atoms, from one molecule to another (transmethylation), which is important in many cellular processes.

The *MAT1A* gene provides instructions for producing the enzyme methionine

adenosyltransferase. This enzyme converts methionine into a compound called S-adenosylmethionine, also known as AdoMet or SAMe.

The *GNMT* gene provides instructions for making the enzyme glycine N-methyltransferase. This enzyme starts the next step in the process, converting AdoMet to a compound called S-adenosyl homocysteine (also known as AdoHcy).

The *AHCY* gene provides instructions for producing the enzyme S-adenosylhomocysteine hydrolase. This enzyme converts AdoHcy into the compound homocysteine. Homocysteine may be converted back to methionine or into another amino acid, cysteine.

Variants in one of these genes result in a shortage (deficiency) of an enzyme involved in breaking down methionine. A deficiency of any of these enzymes leads to a buildup of methionine in the body, which may cause signs and symptoms related to hypermethioninemia.

Learn more about the genes associated with Hypermethioninemia

- AHCY
- GNMT
- MAT1A

Inheritance

Hypermethioninemia can have different inheritance patterns. This condition is usually 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 mutated gene, but do not show signs and symptoms of the condition.

Hypermethioninemia is occasionally inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In these cases, an affected person usually has one parent with the condition.

Other Names for This Condition

- Deficiency of methionine adenosyltransferase
- Glycine N-methyltransferase deficiency
- GNMT deficiency
- Hepatic methionine adenosyltransferase deficiency
- MAT deficiency
- MET
- Methionine adenosyltransferase deficiency
- Methioninemia

- S-adenosylhomocysteine hydrolase deficiency

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Hypermethioninemia with deficiency of S-adenosylhomocysteine hydrolase (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3151058/)
- Genetic Testing Registry: Glycine N-methyltransferase deficiency (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1847720/)
- Genetic Testing Registry: Hepatic methionine adenosyltransferase deficiency (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268621/)

Genetic and Rare Diseases Information Center

- Brain demyelination due to methionine adenosyltransferase deficiency (https://rarediseases.info.nih.gov/diseases/8397/index)
- Hypermethioninemia due to glycine N-methyltransferase deficiency (https://rarediseases.info.nih.gov/diseases/10764/index)
- S-adenosylhomocysteine hydrolase deficiency (https://rarediseases.info.nih.gov/diseases/13177/index)

Patient Support and Advocacy Resources

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

Catalog of Genes and Diseases from OMIM

- METHIONINE ADENOSYLTRANSFERASE I/III DEFICIENCY (https://omim.org/entry/250850)
- GLYCINE N-METHYLTRANSFERASE DEFICIENCY (https://omim.org/entry/606664)
- HYPERMETHIONINEMIA WITH S-ADENOSYLHOMOCYSTEINE HYDROLASE DEFICIENCY (https://omim.org/entry/613752)

Scientific Articles on PubMed

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

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