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My46 Trait Profile

Methylmalonic acidemia

Other Names: Methylmalonic aciduria

Methylmalonic acidemia is a rare genetic condition characterized by the body's inability to process certain proteins and fats. It is caused by mutations in the MUT, MMAA, MMAB, MMADHC, and MCEE genes.

Characteristics of Methylmalonic acidemia

Methylmalonic acidemia (MMA) is a rare inherited metabolic disorder in which the body is unable to metabolize (process) certain proteins and fats properly. As a result, other compounds can build up in blood, urine, and tissues. Too much of these compounds can be harmful to the body and cause health problems. People with MMA have difficulty breaking down certain amino acids called methionine, threonine, isoleucine and valine.

Signs and symptoms of MMA usually appear in early infancy, and they can range from mild to life-threatening. Infants with MMA may have vomiting, weak muscle tone (hypotonia), developmental delay, excessive tiredness (lethargy), and an enlarged liver (hepatomegaly). Seizures, inflammation of the brain (encephalopathy), and strokes can also appear in early infancy. As affected infants get older, they may have difficulty gaining weight. This is sometimes described as "failure to thrive." Individuals with MMA can also face problems later in life, including intellectual disability, chronic kidney disease, and inflammation of the pancreas (pancreatitis). It is very important that individuals with MMA get access to treatment. Failure to do so can lead to coma and sometimes, death. In general, the earlier the individual is diagnosed and treated, the better the outcomes.

Diagnosis/Testing

Individuals with MMA have changes or mutations in a group of genes known to make or influence an enzyme called methylmalonyl CoA mutase. Sometimes the specific mutations an individual has can determine the spectrum of health problems seen in individuals with MMA, ranging from mild to more severe. For example, individuals with severe MMA are more likely to have mutations that cause the methylmalonyl CoA mutase to not be made at all.

Many babies with MMA are diagnosed early in life through newborn screening (NBS). NBS tests a spot of blood from the baby's heel, and looks to see if the methylmalonyl CoA mutase enzyme is working properly. NBS test results are confirmed with additional blood and urine chemical tests, and possibly genetic testing of the MMA genes.

Management/Surveillance

Individuals with MMA are typically managed by a team of specialty providers that can include: geneticists, genetic counselors, primary care doctors, nutritionists, and social workers. The amino acids isoleucine, valine, threonine and methionine are found in many of the foods we eat (i.e., "protein-rich foods"), as well as breast milk and infant formulas. This means it is very important for individuals with MMA to follow a customized low-protein diet. This diet usually includes a medical formula specially made to provide all amino acids except for isoleucine, valine, threonine and methionine to ensure good nutrition. Specific medications and vitamin supplements (i.e., L-carnitine and B12) are also often prescribed. These are all examples of treatments, but because many individuals with MMA may have different needs, specific treatment plans can vary. It is usually recommended that an emergency treatment plan, often documented by an "Emergency Letter" is made to ensure that during times of illness or other metabolic stress, an individual with MMA

will be assessed for signs and symptoms of a metabolic crisis (e.g., poor feeding, vomiting, lethargy, excessive sleepiness, neurological signs, irritability) and given appropriate medical attention. It is of upmost importance that individuals with MMA adhere to their specific diet and treatment plans to avoid metabolic stress and/or crisis.

Mode of inheritance

Mutations in the MUT, MMAA, MMAB, MMADHC, and MCEE genes cause methylmalonic acidemia. MMA is inherited in an autosomal recessive pattern. This means that an individual has to inherit two gene mutations (i.e., one from each parent) to be affected with MMA. If both parents are carriers of gene mutation, they have a 1 in 4 (25%) chance with each pregnancy of having a child with MMA. Babies born in the United States are usually screened for MMA by newborn screening.

Risk to family members

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

Special considerations

None

Resources

Genetics Home Reference: Methylmalonic Acidemia
http://ghr.nlm.nih.gov/condition/methylmalonic-acidemia
Organic Acidemia Association
http://www.oaanews.org

References

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