Published on *My46* (https://www.my46.org) 01/23/2022

My46 Trait Profile

Propionic acidemia

Other Names: Propionic Aciduria, Propionyl-CoA carboxylase deficiency

Propionic acidemia is a genetic condition characterized by a deficiency in the protein propionyl-CoA carboxylase. It is caused by mutations in the PCCA or PCCB genes that make the propionyl-CoA carboxylase protein.

Characteristics of Propionic acidemia

Propionic acidemia (PA) is a genetic condition in which the body cannot metabolize (break down or use) propionic acid properly. It is caused by a deficiency (lack or shortage) of the protein propionyl-CoA carboxylase. As a result, propionic acid can build up in the body and be harmful to many tissues.

There are many different health problems that can occur in individuals with PA. Developmental delay and intellectual disability are common due to changes in the brain. Seizures, poor growth, and osteoporosis (which can lead to fractures) can also occur. Individuals with PA are at higher risk of developing acute and recurrent pancreatitis (inflammation of the pancreas). Some affected children have large livers (hepatomegaly) which can resolve with treatment. Long term complications include optic atrophy (damage to the optic/eye nerve), especially in males, hearing loss, premature ovarian failure (in women) and chronic kidney failure. Additionally, many children with PA have similar facial features with a prominent forehead, flat nasal bridge, long philtrum (grove above upper lips), and an upward curve to the lips.

PA may be diagnosed at birth (neonatal onset) or later in childhood (late-onset). Neonatal onset is most common and presents within the first few days of life with poor feeding, vomiting, and drowsiness. If left untreated, an affected child may develop lethargy, seizures, coma and death. Metabolic acidosis (too much acid in body fluids) is common because the body produces too much or cannot get rid of acid. Children with late-onset PA can have loss of developmental skills (regression), chronic vomiting, inability to tolerate protein, failure to thrive, low muscle tone (hypotonia), brain findings leading to abnormal movements (choreoathetosis) or sustained muscle contractures (dystonia), and an enlarged heart (cardiomyopathy).

The prognosis of people with PA depends on the initial presentation and any neurological or brain damage that may have occurred. Children can have developmental delays that improve with time and therapy. Later in life, pancreatitis, cardiomyopathy and kidney failure can cause serious problems.

Diagnosis/Testing

Most individuals with PA have changes or mutations in the PCCB (50-60%) or the PCCA (35-50%) genes. These genes make the propionyl-CoA carboxylase enzyme that is responsible for breaking down propionic acid. Mutations in these genes that cause the enzyme to not be made, or not be made properly, result in many of the health problems seen in individuals with PA.

Many babies with PA 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 propionyl-CoA carboxylase enzyme is working properly. NBS test results are confirmed with additional blood or urine chemical tests and usually testing of the PCCA or PCCB genes. Unfortunately, many children may show symptoms before the NBS results are reported. Routine lab tests often show decreased platelets, white blood cells and red blood cells.

Management/Surveillance

Individuals with PA are typically managed by a team of specialty providers that can include: geneticists, nurse practitioners, genetic counselors, primary care doctors, dietitians, and social workers. Management of PA focuses on fast and effective emergency treatment. Acute attacks occur in times of stress like infection, injury or surgery. The first symptom is usually vomiting; though seizures can also occur. The cause of the attacks, such as an infection, should be treated quickly. Individuals should be treated with increased calories and fluids to stop the breakdown of their muscles and flush the build up of harmful substances out of the kidneys. The intake of protein (in foods) may be stopped or reduced for a couple of days. Medications to treat acidosis, low blood sugar or high ammonia may be used. Affected individuals should be given an emergency protocol letter which details the treatment that should be started.

Day to day management of PA focuses on restricting the amino acids that make propionic acid. This means it is very important for individuals with PA to follow a customized low-protein diet. It is of upmost importance that individuals with PA adhere to their specific diet and treatment plans to avoid metabolic stress and/or crisis. The diet usually includes a medical formula specially made to provide protein and calories needed for growth and development and to ensure good nutrition. Specific medications (e.g.metronidazole) and vitamin supplements (e.g. carnitine) are also often prescribed. Many children need feeding tubes because of low muscle tone. Avoidance of fasting is also necessary. Liver transplantation is a treatment option for children with many acute attacks, frequent high ammonia levels, and poor growth.

Mode of inheritance

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

Risk to family members

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

Special considerations

None

Resources

Genetics Home Reference: Propionic acidemia
http://ghr.nlm.nih.gov/condition/propionic-acidemia
Medical Home Portal: Propionic acidemia
http://www.medicalhomeportal.org/newborn/propionic-acidemia
Organic Acidemia Association
http://www.oaanews.org/
Rare Connect: Propionic Acidemia
https://www.rareconnect.org/en/community/propionic-acidemia

References

Carillo-Carrasco N, Venditti C. (Updated 17 May 2012). Propionic Acidemia. In: GeneReviews at Genetic Testing Registry (database online). Copyright, University of Washington, Seattle. 1993-2013. Available at http://www.ncbi.nlm.nih.gov/books/NBK92946/. Accessed [03/16/3024].

Hoffman, GF. & Schulze, A. (2009). Organic acidemias. In K. Sarafoglou, G.F. Hoffmann & K.S. Roth (Eds.), Pediatric endocrinology and inborn errors of metabolism (83-118). New York, NY: McGraw Hill Medical. Print.

Created: Mar-14
Updated: mm/yyyy
Created by: Ashley Vollenweider, MSN, CPNP; Karin Dent, MS, LCGC