Homocystinuria – Amino Acid Disorder

What are amino acid disorders?

The amino acid disorders are a class of inherited metabolic conditions that occur when certain amino acids either cannot be broken down or cannot be produced by the body, resulting in the toxic accumulation of some substances and the deficiency of other substances.

What is homocystinuria?

Homocystine accumulates in the urine in people with homocystinuria. It is caused most commonly by a deficiency in an enzyme called CBS (cystathionine beta-synthase). If CBS is not working well or is missing, methionine and homocystine build up to toxic levels in the body.

What is its incidence?

Homocystinuria is a very rare disease that affects about 1 out of every 200,000 babies born in BC. Although homocystinuria occurs in all ethnic groups, it is more common in certain populations. Its incidence has been reported as high as 1 in 20,000 to 1 in 60,000 in the Irish, Danish, German, and Australian populations.

What causes the disease?

Mutations in the gene for CBS result in an enzyme that is not working well or is deficient.

What are the clinical features of the disease?

Although babies with homocystinuria are normal at birth, without treatment they begin to have developmental delays and failure to thrive. They may also develop eye problems such as nearsightedness and dislocation of the lens, skeletal differences such as scoliosis and osteoporosis, and have a higher chance to develop blood clots. People with homocystinuria may also have long arms, legs, and fingers, which is sometimes described as a “Marfanoid” habitus. The risk of stroke and heart disease due to thrombophilia can be life-threatening.

How is the diagnosis confirmed?

The diagnosis is confirmed by measuring the levels of amino acids in the blood and urine. Levels of total homocystine and methionine will be elevated while the level of cystine will be decreased. CBS enzyme testing and genetic testing of the CBS gene may also be used to confirm the diagnosis. Diagnostic testing is arranged by specialists at BC Children’s Hospital.

What is the treatment of the disease?

A diet low in methionine and a special medical formula is often recommended in children with homocystinuria. Dietary supplementation with vitamins B6, B12, betaine, and folic acid may be considered. Treatment is coordinated by specialists at BC Children’s Hospital.

What is the outcome of treatment?

The special diet can lower the risk of developmental delays and other problems associated with homocystinuria.

The BC Newborn Screening Program is a collaboration of BC Women’s Hospital & Health Centre, BC Children’s Hospital and the BC Perinatal Health Program, all part of the Provincial Health Services Authority.

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Can a family have more than one child with homocystinuria?

Homocystinuria is inherited as an autosomal recessive disorder. The parents of a child who has homocystinuria are assumed to be carriers for the disorder and have a 1 in 4 (25%) chance, in each pregnancy, of having another child with the disorder. Prenatal testing for homocystinuria can be done as early as 10-12 weeks of pregnancy. Genetic counselling to discuss the benefits of prenatal testing options in more detail is recommended.

Unaffected siblings of a child with homocystinuria have a 2/3 chance of being carriers. Carriers are healthy and do not have symptoms of homocystinuria.

Resources

http://www.newbornscreening.info/Parents/aminoaciddisorders/CBS.html
http://www.orpha.net/data/patho/GB/uk-CbS.pdf
http://www.geneclinics.org

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