Glutaric Acidemia Type I (GAI) – Organic Acid Disorders

What are organic acid disorders?

Organic acid disorders (also sometimes called organic acidemias) are a class of inherited metabolic disorders that occur when the body cannot break certain components of proteins (for example, branched-chain amino acids) and other substances. This leads to an accumulation of harmful substances in the blood and urine, which can cause serious health problems.

What is GAI?

In the body, the breakdown of protein produces the amino acids lysine, hydroxylysine, and tryptophan, among others. These are further processed into a substance called glutaric acid. An enzyme called Glutaryl-CoA dehydrogenase is then responsible for breaking down glutaric acid. Glutaric Acidemia Type I (GAI) occurs when the glutaryl-CoA dehydrogenase enzyme is not working well or is deficient.

What is its incidence?

GAI is a rare disease. The incidence is not well documented but there will likely be less than 1 diagnosis every 3 years in BC.

What causes the disease?

Mutations in the gene for glutaryl-CoA dehydrogenase, called GCDH, results in enzyme that is not working well or is deficient.

What are the clinical features of the disease?

Although babies with GAI are usually normal at birth, some may have a larger than average head (macrocephaly). They may also have hypotonia and seem jittery and irritable. Without treatment, they may have an episode of metabolic crisis with encephalopathy, which can progress to coma and death. The first episode usually occurs in infancy and can be triggered by events such as an illness or a fever. Other symptoms can include hypotonia, progressive muscle spasms, poor balance and poor coordination, and neurological problems. Increased amounts of acidic substances may be found in the blood (acidemia). As the child grows older, the risk of crises and symptoms decrease. The presentation of GAI is variable and there may be individuals with the disorder who are asymptomatic.

How is the diagnosis confirmed?

The diagnosis of Glutaric Acidemia Type I is confirmed by measuring urine organic acids. The glutaric acid levels are elevated and the finding of 3-OH-glutaric acid is typical. However, levels may rise and fall and may not be consistently abnormal. Enzyme testing and/or mutation analysis of the GCDH gene may assist in confirming the diagnosis. Diagnostic testing is arranged by specialists at BC Children's Hospital.

What is the treatment of the disease?

The mainstay of treatment is to prevent fasting, especially when a child is ill. In an acute symptomatic episode, IV glucose and fluids can be given, along with other medications that can help the body to get rid of harmful substances. In the long term, a low protein diet and a special medical

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.

Provincial Health Services Authority
Province-wide solutions. Better health.

formula may be recommended. Supplementation with carnitine and riboflavin may also be considered. This can prevent metabolic crises and their sequelae. Treatment is coordinated by specialists at BC Children's Hospital.

What is the outcome of treatment?

If treatment is able to prevent episodes of metabolic crisis, children with GAI have a good prognosis. However, response to treatment and therefore the outcome is variable.

Can a family have more than one child with GAI?

GAI is inherited as an autosomal recessive disorder. The parents of a child who has GAI 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 GAI 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 GAI have a 2/3 chance of being carriers. Carriers are healthy and do not have symptoms of GAI.

Resources

http://www.newbornscreening.info/Parents/organicaciddisorders/GA1.html
http://www.glutaricacidemia.org/
http://www.oaanews.org/
http://www.geneclinics.org

Revised November 2009

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.

Provincial Health Services Authority
Province-wide solutions. Better health.