Glutaric aciduria

Glutaric aciduria type I (GA I) is an organic aciduria , caused by the body's inability to process the amino acids lysine and tryptophan due to glutaryl-CoA dehydrogenase deficiency. The enzyme glutaryl coenzyme A dehydrogenase is stored in mitochondria. It catalyzes the oxidative decarboxylation of glutaryl-CoA to crotonyl-CoA in the liver, kidney, fibroblasts and leukocytes. Deficiency of this enzyme increases the level of toxic glutaric acid and its metabolites. Flooding of the organism by toxic metabolites occurs at each load with increased amounts of lysine and tryptophan (eg during normal weight loss in the neonatal period, in the breakdown of the child 's body proteins during fever and starvation, during common infections, after operations and in similar stressful situations).

GA1 is caused by deficient or dysfunctional glutaryl-CoA dehydrogenase

GA 1 is an AR inherited disease (GCDH- gene at 19p13.2, OMIM # 231670). Since October 1, 2009, it has been a part of nationwide neonatal screening in the Czech Republic. Elevated C5-DC acylcarnitine indicates the presence of GA I. If GA I is suspected, analysis of organic acids in the urine is performed immediately to show elevated levels of glutaric acid and 3-hydroxyglutaric acid to confirm the diagnosis. If the analysis does not confirm the diagnosis, the DMP specialist will consider analysis of urinary glutarylcarnitine and 3-hydroxyglutaric acid in blood and cerebrospinal fluid, analysis of enzymes in fibroblasts, and molecular analysis of the GCDH gene.

Incidence of GA I : 1: 40,000 in Caucasian populations and 1:30,000 in Sweden.

Child with glutaric aciduria

Clinical manifestations

- neonates : macrocephaly (70% of patients), otherwise asymptomatic
- later metabolic acidosis , failure to thrive and sudden onset of dystonia and athetosis due to irreversible striatal damage
- prognosis: with appropriate care, 60–70% of patients will not suffer from a neurodegenerative disorder

- onset of symptoms typically between the second month and the third year of life
- There are several different clinical presentations:
    1. Affected children appear to be normal until they suffer from an acute metabolic crisis, usually between 6 and 18 months of age, with residual neurological findings that improve slightly at rest. Specific changes in the basal ganglia, especially atrophy and gliosis of the putamen and caudate nerve, occur within days to weeks after an encephalopathic episode.
    2. After a period of normal development, affected children have an acute crisis with residual neurological findings similar to the previous case, but continue to develop with recurrent episodes of ketosis, vomiting, hepatomegaly, and encephalopathy during infections.
    3. Approximately 25% of children gradually develop motor delay, hypotension, dystonia, and dyskinesia during the first few years of life without any apparent acute crisis.
    4. Individuals can be completely asymptomatic without any crisis and with normal development. This fact was documented by testing carriers and finding 5% of asymptomatic members of the Amish community with GAI. Changes in white matter were later diagnosed in some of these adults.

- physical examination: macrocephaly, cerebral palsy , dystonia

Treatment

- riboflavin treatment and dietary restriction of lysine and tryptophan (A protein-restricted diet consists of consuming a permitted amount of special low-protein foods, which each patient provides for their own nutrition and is not reimbursed by health insurance companies.)
- with each common viral or bacterial infection, it is necessary in the early stages of the disease to reduce protein intake even more in the short term and to provide more energy in the form of glucose with insulin by intravenous

infusion

- immediate treatment of catabolic conditions with aggressive treatment of fever
- Glucose , insulin and carnitine can prevent neurological impairment in patients without basal ganglia damage
- admission to hospital is necessary for any illness accompanied by vomiting

Forecast

Untreated course of the disease: Most symptomatic patients die without treatment during the first decade of life. Patients may have recurrent fevers of unclear origin. Two cases of children who died of hyperthermia are described, so fever control is necessary. The patient can also sweat profusely, either centrally or peripherally.

Course of the disease with treatment: Presymptomatic diagnosis showed better results than identification of patients after the first encephalopathic attack. Even during treatment, 35% of patients suffer from neurological disabilities and delayed psychomotor development.

Examination of relatives

In other children who have the same father and mother as the affected child, the risk of this disease is 1/4 (25%). Prenatal diagnosis is possible by enzyme analysis by amniocyte analysis or CVS.

Links

Related Articles

- Neonatal screening
- Isovaleric aciduria
- Leucinosis

References

1. ↑Jump up to:a b c d e f g h i j k DOC. MUDR. VOTAVA, Felix, CSc., Tomas, PhD. DOC. RNDR. ADAM and Jiří, DrSc. PROF. MUDR. ZEMAN, et al. *Neonatal screening* [online]. © 2009. Last revision 2009, [cited. December 17, 2009]. < http://www.novorozeneckyscreening.cz/nemoci >.

External links

- OMIM # 231670

Hereditary metabolic disorders (DMPs)	
In general	DMP of complex molecules • DMP of small molecules • Neonatal screening • Screening of hereditary diseases • Examination methods at DMP
DMP amino acids	Alkaptonuria
Organic aciduria	-
DMP urea cycle	Alcaptonuria • Ornithine transcarbamylase deficiency • Prolidase deficiency • Phenylketonuria • Glutaric aciduria • Hyperphenylalaninemia • Hyperornitinemia • Isovaleric aciduria • Leucinosis • Non-ketotic hyperglycemia • Cystinosis • Tyrosinemia
DMP propionate, biotin and cobalamin	Biotinidase deficiency • Methylmalonic acidemia • Propionic acidemia
DMP purines and pyrimidines	Liver porphyria • Skin porphyria • Mitochondrial neurogastrointestinal encephalomyopathy
DMP sugars	Glycogenoses • Fructosealdolase deficiency • Fructose-1,6-bisphosphatase deficiency • Essential fructosuria • Galactokinase deficiency • Galactose-1-phosphate uridyltransferase deficiency
DMP mitochondria	Phosphoenolcarboxykinase Deficiency • LCHAD Deficiency • MCAD Deficiency • Pyruvate Dehydrogenase Deficiency • Pyruvate Carboxylase Deficiency • SCAD Deficiency • Chronic Progressive External Ophthalmoplegia • Leber's Hereditary Optic Neuropathy • Leigh Syndrome • Maternally Hereditary Diabetes and Deafness • SayLC Syndrome
DMP peroxisomes	Neonatal adenodystrophy • Refsum's disease • Rhizomelic chondrodystrophia punctata • X-linked adrenoleukodystrophy • Zellweger syndrome
DMP of lysosomes	Fabry disease • Gaucher disease • Krabbe disease • Danon's disease • Mucolipidosis II • Metachromatic leukodystrophy • Mucopolysaccharidosis III • Niemann-Pick disease • Cystinosis • Tay-Sachs disease
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