HOMOCYSTINURIA AS THE CAUSE OF CEREBRAL VENOUS THROMBOSIS IN CHILDREN

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Classical homocystinuria due to cystathionine beta-synthase (CbS) deficiency is characterized by the multiple involvement of the eye, skeleton, central nervous system, and vascular system.

The disease is a disorder of methionine metabolism caused by mutations in the CBS gene (21q22.3). CbS normally converts homocysteine to cystathionine in the transsulfuration pathway of the methionine cycle and requires pyridoxal 5-phosphate as a cofactor. The other two cofactors involved in methionine remethylation include vitamin B12 and folic acid.

Synonym(s):
Cystathionine beta-synthase deficiency
Prevalence: 1-9 / 100000
Inheritance: Autosomal recessive
Age of onset: childhood
ICD-10: E72.1
OMIM: 236200
UMLS: C0751202
MeSH: -
GARD: 6667
MedDRA: 10071093

If the disease is diagnosed in the newborn infant, as ideally it should be, the aim of treatment must be to ensure the development of normal intelligence and prevent the development of other complications. Later, it aims at preventing life-endangering thromboembolic events and further escalation of the complications. There are currently three recognized modalities of treatment. For those that are pyridoxine responsive, the treatment includes pyridoxine in pharmacological doses in combination with folic acid and vitamin B12 supplements. In pyridoxine nonresponsive individuals, the recommended treatment is a methionine-restricted, cystine-supplemented diet in combination with the pyridoxine, folic acid and vitamin B12 supplementation. Betaine anhydrous is a methyl donor that may lead to lowering of homocysteine levels in these individuals and can be used as an adjunct to such a diet. It obtained EU marketing authorization as an orphan drug for the treatment of homocystinuria in 2007.

Register of child stroke

Average age of stroke depending on the type of stroke

The symptoms of the manifestation of stroke depending on stroke type

Confirming the diagnosis

Patients	Gene	Mutation
№1	CBS	p.Ile278Thr / p.Cys109Arg
№2	MTHFR	C337G>A(p.Ar-g113Thr) / c.780+1G>T
№3	MAT-1A	c.8-87A>G p.Tyr296Cys homozygous state
№4	CBS	c.785G>T(p.262M) / c.352G>gt A(p.V118M)
№5	CBS	c.904G>A (Glu302Lys) / c.847G>T (Glu283Term)
№6	CBS	c.904G>A (Glu302Lys) / c.847G>T (Glu283Term)
№7	CBS	c.904G>A (Glu302Lys) / c.847G>T (Glu283Term)

Patient	Age, years	Symptoms	thrombosis	treatment
№1	4	Occlusive hydrocephalus, epilepsy, psychomotor development delay The diagnosis was established in 2 months	+	Diet, betaine, methionine, Vit.B6 50mg/day and vitamin B12 1 mg 1 time a month, L-methylfolate 60mg/day, methionine 300mg/day
№2	11	Congenital cataract, artefacts, scoliosis The diagnosis was established in 11 years old	+	Diet, Fragmin, vitv6 150mg / day, Vit.V12 1000mg / m 1 time per month, folic acid 5 mg/ day
№3	17	Osteochondral exostoses, astigmatism, hyperhomocysteinemia, pigeon chest deformity, myopia, abnormal heart rhythm The diagnosis was established in 15 years old	+	Diet, warfarin, folic acid 5mg / day, Vit.B6 200mg/day, Vit B12 1000 mg / m 1 time in 3-4 months
№4	5	Violation of posture, myopia The diagnosis was established in 3 years old	+	Diet, Fragmin, Vit.V6 60mg/ day, Vit V12 1000mgv / m 1 time per month, folic acid (Angiovit)
№5	14	Congenital high myopia, mental retardation, poor coordination, skeletal deformation (feet, posture progressive) The diagnosis was established in 13 years old	-	Special nutrition (Betaine), (B6-insensitivity),twisted.B6 100mg/day, Vit B12 1 mg/day, folic acid 5mg/day, trombas

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