LATE DIAGNOSIS OF HOMOCYSTINURIA (CASE REPORT)

Krumina, Z., Vevere, P., Lace, B., Lugovska, R.
State Medical Genetics Center Of Latvia, Riga, Latvia

Homocystinuria is an autosomal recessive disease. Constant findings are myopia, dislocation of the lens, and a tendency to develop venous and arterial clots (thrombi). There is no specific cure for homocystinuria, however, many people respond to high doses of vitamin B6. A diet low in methionine may also be helpful. The treatment for homocystinuria is aimed to prevent complications.

The patient is 10 years old girl with epilepsy, mental retardation, behavior disorders, severe myopia and lens dislocation, kyphoscoliosis, arachnodactyly and generalised osteoporosis. Her height is 144 cm (75%), she has fine, brittle hair. She receives special education.

Early symptoms were severe myopia at the age of 3 years; later diagnosed also dislocation of the lens and mental retardation. The girl was examined regularly in hospital with diagnosis: mild mental retardation, epilepsy, the damage of CNS, myopia and lens dislocation. The geneticist saw her only at the age of 10 years and homocystinuria was suspected. Increased methionine and homocysteine in plasma confirmed the diagnosis. The treatment with high doses of vitamin B6, folic acid was started and proposed methionine-restricted diet. There are only 3 weeks from the beginning of therapy, so it's hard to evaluate the efficiency of treatment.

Our report wants to show that late diagnosis of homocistinuria in most cases leads to severe irreversible complications. ◆

INBORN ERRORS OF METABOLISM IN KOREA – 10 YEARS EXPERIENCE OF 1991–2000

Lee, H. J.[1], Lee, D. H.[2]
[1] Dept. of Pediatrics. Hallym University Hospital, 153 kyodong, Chunchon, 200-060 Korea
[2] Dept. of Pediatrics, Soonchunhyang University Hospital, Hannamdong, Yongsangu, Seoul, 140-743 Korea

Purpose and Method: To know the distribution of inborn errors of metabolism in Korea, we have done a retrospective study using questionnaire, covering all hospitals (439) in Korea. The study period was from 01 Jan 1991 to 31 Dec 2000, 10 years.

Result: 1,019 patients of IEM (84 cases of disorders of carbohydrate metabolism, 139 cases of aminoacidopathies, 39 cases of urea cycle disorders, 220 cases of organic acidopathies, 9 cases of FAOD, 14 cases of purine and pyrimidine metabolism, 252 cases of mineral metabolism, 27 cases of peroxisomal disorders, 69 cases of sphingolipidosis, 131 cases of mucopolysaccharidosis, 2 cases of oligosaccharidosis, 1 case of mucolipidosis, 13 cases of membrane transport disorders and 3 other cases) was diagnosed durine the study period. Disorders of mineral metabolism is the most frequently diagnosed disease group followed by organic acidopathies and aminoacidopathies and mucopolysaccharidosis. The most frequently diagnosed disease is Wilson disease (201 cases) followed by PKU (98 cases) and Hunter disease (69 cases). Diseases diagnosed more than 20 cases during the study period were 3-ketothiolase deficiency, GSD I, Gaucher disease, mitochondrial respiratory chain disorders, hemochromatosis, PDH deficiency, galactosemia, GA II, MPS I, and ALD. Many other disease were diagnosed and some of them were diagnosed only 1 or 2 cases during the study period. ◆

MITOCHONDRIAL FATTY ACID OXIDATION (FAO) DEFICIENCIES: AN OVERVIEW

Lehnert, W.[1], Matern, D.[2]
[1] University Children's Hospital, Metabolic Unit, Mathildenstr. 1, D-79106 Freiburg, Germany
[2] Devision of Laboratory Genetics, Mayo Clinic, Rochester, Mn 55905, USA

During periods of prolonged fasting causing depletion of glycogen stores, mitochondrial FAO, closely associated with ketone body formation, becomes an important source of energy for the brain. Furthermore 60–70% of the energy requirement of the heart muscle is provided by FAO under normal and even more under diseased condition. Consequently defects in this important pathway result in severe clinical disturbances affecting mainly the brain, liver, heart and skeletal muscle.

Mitochondrial FAO is a complex process involving transport of activated fatty acids into the mitochondria and successive removal of acetyl-CoA units. These are in turn metabolized by the tricarboxylic acid cycle or converted in the liver into ketone bodies. The resulting "reducing equivalents" are then used as fuel for the respiratory chain to produce ATP. Each step in FAO requires an enzyme or depends on a transport protein. At least 22 different disease causing inborn errors of fatty acid ß-oxidation have been identified so far. Diagnosis is not straight forward because clinical symptoms may be very similar in different diseases and in many cases pathognomonic urinary organic acid profiles may be absent during asymptomatic periods. Recently the recognition of FAO defects has been greatly facilitated by additionally investigating blood acylcarnitine pattern using tandem mass spectrometry. For further confirmation and characterization biochemical and molecular genetic methods are applied. ◆

TWO NOVEL MUTATIONS, 1034C>A AND IVS9+1G>T, OF GALACTOSE-1-PHOSPHATE URIDYLTRANSFERASE (GALT) GENE IDENTIFIED IN CHINESE GALACTOSEMIA

Liu, T. T.[1], Lin, C. H.[2], Liu, M. Y.[3], Chern, S. R.[4], Chiang, S. H.[2], Hsiao, K. J.[2,3]
[1] Genome Research Center, National Yang-Ming University
[2] Department of Medical Research and Education, Taipei Veterans General Hospital
[3] Institute of Genetics, National Yang-Ming University
[4] Department of Medical Research, Mackey Memorial Hospital; Taipei, Taiwan

Galactose-1-phosphate uridyltransferase (GALT; EC 2.7.7.12) catalyzes the second step of galactose-glucose interconversion. Deficiency of GALT leads to galactosemia (MIM 230400), and its incidence in Taiwan is determined to be around 1 in 400,000. Partial deficiency of GALT activity, either a heterozygote or the Duarte variant, can also be detected in the newborn period because of the galactose is elevated transiently. In this study, mutations in GALT gene were determined in Chinese galactosemia patients with full or partial deficient GALT activity in order to investigate the prevalence of GALT mutations in Chinese by PCR-based sequencing analysis from the Guthrie cards used in neonatal screening. Four galactosemia patients, 12 partial deficient patients (GALT activity <50% of normal) were analyzed. Three alterations, namely 940A>G (N314D), 1034C>A (A345D) and IVS9+1G>T, were identified. The 940A>G Duarte allele was found to occur as homozygote in 2 partial deficient patients. Two classical galactosemia patients were found to be compound heterozygote of 1034C>A

ND. 215