International Science Group

ISG-KONF.COM

ABOUT THE PROBLEMS OF SCIENCE AND PRACTICE, TASKS AND WAYS TO SOLVE THEM

VI

SCIENTIFIC AND PRACTICAL CONFERENCE

26-30 October

Milan, Italy

DOI 10.46299/ISG.2020.II.VI

ISBN 978-1-63649-928-4

ABOUT THE PROBLEMS OF SCIENCE AND PRACTICE, TASKS AND WAYS TO SOLVE THEM

Abstracts of VI International Scientific and Practical Conference

Milan, Italy
October 26-30, 2020

ABOUT THE PROBLEMS OF SCIENCE AND PRACTICE, TASKS AND WAYS TO SOLVE THEM

Library of Congress Cataloging-in-Publication Data

UDC 01.1
The VI th International scientific and practical conference «About the problems of science and practice, tasks and ways to solve them» (October 26-30, 2020). Milan, Italy 2020. 596 p.

ISBN - 978-1-63649-928-4
DOI - 10.46299/ISG.2020.II.VI

EDITORIAL BOARD

MUKOLIPIDOZ II TYPE: MEDICO-GENETIC CONSULTUATION

Lastivka Iryna,
PhD, AssociateProfessor
Bukovinian State Medical University»

Antsupova Vita,
PhD, AssociateProfessor,
Bogomolets National Medical University

Sheiko Larysa
PhD, Associate Professor
Shupyk National Medical Academy
of Postgraduate Education

A wide range of nosological forms of accumulation diseases, their phenotypic similarity, as well as insufficient knowledge of physicians of this large group of orphan diseases, usually lead to errors in diagnosis and incorrect medical and genetic counseling of families. Mucolipidosis (ML) deserves special attention - diseases caused by insufficient activity of hydrolases and which not only have similarities with mucopolysaccharidosis (MPS), but also rank second after them. The first reports of ML appeared in the literature in the late 60's of last century. The first classification of ML included only 4 types. Subsequent studies have led experts to classify type I ML as a group of sialidosis, and type IV ML as a group of gangliosidosis. Thus, ML today is represented by two types - ML II (I-cell disease) and ML III type (ML III A and ML III C) [1].

ML II is caused by mutations in the GNTAB gene, which encodes the enzyme N-acetylglucosamine-1-phosphotransferase (N-AG-1-FT), which is based on the membranes of the Golgi complex. The result is a violation of intralysosomal degradation of biopolymers - sphingolipids, glycosaminoglycans (GAG), glycoproteins. The activity of lysosomal enzymes is sharply reduced in cultured fibroblasts and increased in the culture fluid and serum of patients. It was found that the GNTAB gene is located on the long arm of chromosome 12 at locus 12q23.3, encodes α- and β-subunits of the enzyme N-AG-1-FT, mutations in the gene responsible for the formation of the clinical picture of ML II and ML IIIA types. To date, 169 mutations have been described, half of which are missense and nonsense mutations. The GNPTG gene is localized on the short arm of chromosome 16 at locus 16p13.3. Mutations in the GNPTG gene, which selectively encode the γ-subunit of the enzyme N-AG-1-FT, lead to the development of ML III C. Clinical symptoms of I-cell disease (ML II) are formed in the presence of a proband deletion c3503-3504delTS only in the homozygous state , and if the second mutation is represented by a nonsense

mutation or a mutation with a shift of the reading frame. The combination of deletion p.3503-3504delTS with missense mutation causes symptoms of ML III A type [1, 2].

Type II ML (I-cell disease) was first described by P. Demars and J. Leroy in 1967. The population frequency is 1: 200,000 [2,4,5]. The manifestation begins at birth. Clinical manifestations are similar to the symptoms of MPS type I (Gurler syndrome). Patients lag sharply behind in growth, have pronounced changes in the skull and skeleton (short neck and chest, congenital dislocations of the thighs, joint contractures, small orbits, which contribute to the increase of exophthalmos). Attention is drawn to rough facial features, eyelids with edema, gingival hyperplasia, inguinal, inguinal and umbilical hernias, profound mental retardation. Hepatosplenomegaly and corneal memory need to be expressed insignificantly. In most patients, the diagnosis is heart disease. In the impossibility of ML, the first sign of help is often cardiomegaly with the development of stable heart failure with gradual damage to the aortic and measuring valves. For I-cell disease is characterized by a progressive course. Children with this form die in the 2-3rd year of life from complications of the bronchopulmonary and cardiovascular systems. Due to the fact that ML is inherited autosomal recessively, the risk for the native sibling is 25%, the risk of carrier - 50% [2,3].

The diagnosis of ML is established on the basis of a set of phenotypic traits, the results of biochemical and molecular genetic research methods (mutations in the CNPTAB gene). The first stage of biochemical diagnosis of ML is based on the determination of renal excretion of GAG. The normal content of GAG in the urine excludes MPS and indicates the possibility of a diagnosis of ML. The second important step in the biochemical diagnosis of ML is to determine the activity of such lysosomal enzymes in blood plasma as β-D-glucuronidase, N-acetyl-alpha-D-glucosaminidase and total hexosaminidase. Increasing their activity by 5-15 times serves as a diagnostic marker of ML. The final stage of diagnosis is molecular genetic research - the search for mutations in the CNPTAB gene [1,4,5].

No specific treatment for type II ML has been developed to date.

Here is our own case of ML type II. A 3-year-old boy was referred to a geneticist for further examination and verification of the diagnosis due to mental and physical retardation. In the analysis of the pedigree it was established that the marriage is not blood related. The pedigree of the mother and father is burdened with cardiovascular pathology (myocardial infarction). The child's paternal grandfather had diabetes. Among the siblings of the father and mother there was no delay in physical and mental development. The mother suffers from myocarditis with myocardiosclerosis and mild myopia. The father is healthy.

From the anamnesis it is known that the child was born from the first pregnancy in young healthy parents at 38 weeks by cesarean section. Birth weight was 2800 g, length was 54 cm At birth there was fetal distress with cardiac arrhythmia. The patient had a history of low anthropometric data for gestational age, limited range of motion, muscular hypotension, and frequent acute respiratory diseases. He started walking at the age of 2, he has been talking since he was 3 years old.

The following phenotypic features were noted during the objective study: weight - 14 kg, height - 83 cm; rough facial features, hyperplasia of the gums, chest deformity,

stiffness in the knee and elbow joints, gait on bent knees. Face flat with full cheeks, small orbits, slight exophthalmos, depressed nose, epicanthus. The voice is hoarse, breathing is stridor. Phrase language is represented by simple sentences, hyperactive behavior. The child is sent for additional examination on suspicion of MPS. The normal level of GAG excretion was revealed; increase of activity of enzymes in blood plasma: iduronate sulfatase to 2961 nmol/h/mg/protein (norm 161-268 nmol/h/mg/protein) and arylsulfatase A to 1030 nmol/h/mg/protein (norm 40-65 nmol/h/mg/protein); found a mutation in the gene CNPTAB, on the basis of which it was concluded that the child has type II ML. The child was given the status of "Child with a disability" and a set of rehabilitation measures was determined. In 2015, surgical treatment was performed (achyloplasty on the left). Today the child is 9 years old. The boy has progressive flexion contractures of the joints, metabolic cardiomyopathy, growth retardation and psycholinguistic development.

Thus, ML belong to the groups of orphan diseases of accumulation that require the attention of pediatricians, geneticists, cardiologists, neurologists, orthopedists and doctors of other specialties. The main clinical manifestations are perceived by very special, developed diagnostic algorithms that allow early suspicion, differentiation from MES and diagnosis of the disease.

References:

1. Cathey S.S., Leroy J.G., Wood T., Eaves K. et al. Phenotype and genotype in mucolipidoses II and III alpha/beta: a study of 61 probands. J. Med. Genet, 2010. V. 47. P. 38-48.

2. Ghosh P., Dahms N.M., Kornfeld S. Mannose 6-phosphate receptors: new twists in the tale. Nat. Rev. Mol. Cell. Biol, 2003. V.4. P. 202-212.

3. McElligott F., Beatty E., O'Sullivan S., Hughes J. et al. Incidence of I-cell disease (mucolipidosis type II) in the irish population. J. Inherit. Metab. Dis., 2011. V.34. Suppl. 3. P. 206.

4. Okada S., Owada M., Sakiyama T., Yutaka T. et al. I-cell disease: clinical studies of 21 Japanese cases. Clin. Genet., 1985. V. 28. P. 207-215.

5. Tiede S., Storch S., Lübke T., Henri B. et al. Mucolipidosis II is caused by mutations in GNPTA encoding the α/β GlcNAc-1-phosphotransferase. Nat Med, 2005. V. 11. P. 110-112.