TASHKENT MEDICAL ACADEMY

Journal of Educational and Scientific Medicine

Issue 4 (2) | 2023

OAK.uz

Google Scholar

ISSN: 2181-3175

Journal of Education & Scientific Medicine

ISSN 2181-3175

Tashkent Medical Academy

Research Article

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Clinical Case of Biotinidase Deficiency

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ABSTRACT

Biotinidase deficiency is an autosomal recessively inherited metabolic disease. If left untreated, patients with biotinidase deficiency typically develop neurological and skin symptoms that can lead to coma and death. This article examined a clinical case of a patient with biotinidase deficiency. The article is aimed at increasing the attention of neurologists to the possible causes of symptomatic epilepsy against the background of a hereditary autosomal recessive metabolic disease - biotinidase deficiency.

Keywords: biotinidase deficiency, hereditary disease, neurometabolic disease, nervous system

INTRODUCTION

Biotinidase is an enzyme needed to process the vitamin biotin. Biotinidase deficiency is an autosomal recessively inherited metabolic disorder. [1]

Clinically untreated patients with biotinidase deficiency may present with a variety of neurological and dermatological signs, such as seizures, hypotonia, feeding problems, developmental delay, hearing loss, ataxia, optic atrophy, alopecia and skin rash [2], hearing and vision loss [3].

If untreated, patients with biotinidase deficiency develop neurological and skin symptoms that can lead to coma and death.

Symptomatic patients may improve markedly when treated with therapeutic doses of biotin, but some clinical features may be irreversible.

Fortunately, almost all symptoms can be prevented if treatment is started at birth or before symptoms develop. [1]

Clinical data from patients with partial biotinidase deficiency presented in the literature show that clinical symptoms of the disease can appear at any period of a person's life: occurring from infancy to adulthood. Results from newborn screening programs support the fact that biotin treatment started after birth prevents the development of symptoms in patients with biotinidase deficiency.

The presence of late-onset cases with varying clinical manifestations indicates that there is still much to learn about biotinidase deficiency. [2]

Purpose of the work: To analyze a clinical case of biotinidase deficiency, draw clinical and neurophysiolog-

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ical parallels, and evaluate the effectiveness of the amount of therapy provided.

MATERIALS AND METHODS

A patient aged 11 years and 7 months, together with her parents, sought medical help with complaints of seizures, frequent colds, and fatigue. According to her parents, the girl is capricious and irritable. The age at the time of manifestation of the first clinical signs is 7 years.

Family history:

Marriage is consanguineous (the spouses are first cousins). The parents of the proband's father are also consanguineous! At the time of the birth of the child, the mother is 20 years old, the father is 26 years old. The parents are healthy, the phenotype is without any special features.

The family history is burdened:

The father's niece (from a related marriage) suffered febrile convulsions from the age of one year and six months, and takes anti-epileptic drugs (AED); the father's nephew (from a related marriage) – convulsions since 9 months, takes AEDs; mother's nephew (from an unrelated marriage) – convulsions since 9 months, takes AEDs).

Siblings of the proband:

I pregnancy – proband, born in 2010. Pregnancy II – boy, 2012, birth weight 3400 g, with delayed motor development (started walking at the age of 2), hypotonic, late teething, frequent colds, rickets, allergies, congenital hydronephrosis (operated);

From the anamnesis:

Proband from the first pregnancy, first birth. Pregnancy with second degree anemia (hemoglobin 60-65 g/l); suffered from acute respiratory viral infection in the third trimester, severe toxicosis in the first trimester. Fetal movements are sluggish.

Ultrasound:

No pathological changes. The birth was on time, physiological, birth weight was 3100 g, the waters were cloudy, the cry was immediate, loud, she was attached to the breast on the first day, active sucking, the umbilical cord healed on the 10th day, there was no newborn jaundice. During the first 2 days – temperature. Discharged on the fourth day of life. She was breastfed until 12 months, sucking was active. Regular stool from birth.

Early psychomotor development:

She held her head from 8 months, began to sit from 9 months, began to walk from 12 months. From birth she was lethargic, hypotonic, inactive, easily tired, rolled up when crying, and cyanosis.

From birth:

Frequent colds, fatigue, late teething.

The first convulsions at the age of 7 years - there was an increase in temperature for two days, speech was lost, nocturnal enuresis was observed, vision began to deteriorate, for a month generalized tonic-clonic convulsions, combined with focal seizures, were repeated every 2-3 days. She started taking the drug valproic acid, but the seizures did not stop, and therefore it was replaced with levetiracetam; however, during the treatment, absence seizures with an average frequency of 8-10 per month are noted.

On examination:

Normosthenic physique, dolichocephaly, flattening of the chest, hypermobility of the joints, pale, tendon reflexes are reduced, muscle tone is preserved, there are no pathological signs, Govers' symptom is negative, stable in the Romberg position, finger-nose test is performed, motor activity is in full, clinodactyly of both little fingers on the hands, academic performance is low. Peaceful sleep. Currently taking levetiracetam on a regular basis, generalized seizures have stopped, but focal paroxysms of moderate frequency are repeated (simple absence seizures). Of the prescribed treatment, she took only levetiracetam, took 60 mg of biotin and stopped taking it a month before treatment, and also took potassium iodide. She did not receive the rest of the prescribed medications. According to the mother, while taking levetiracetam and biotin, fatigue decreased, the patient became less irritable, sleep became restful, there were no seizures, and no colds were noted.

Laboratory research:

1) Biochemical blood test: CPK – 396↑ u/l; LDH – 525 ↑ u/l; ALT – 159↑ u/l; AST – 85↑ u/l; ALP – 270↑ U/l; Ca – 2.6 mmol/l; P – 1.8 mmol/l; magnesium – 0.87 mmol/; urea – 3.5 mmol/l; creatinine – 44 μmol/l; ammonium – 48↑ μmol/l; homocysteine – 7.79↑ μmol/l; lactate – 1.9 mmol/l; vitamin B12 – 873 pg/ml; FC – 10.3 ng/ml; vitamin D – 22↓ ng/ml; glucose – 4.5 mmol/l.

2) Clinical exome sequencing: a homozygous mutation of the BTD gene was identified.

Instrumental research and consultations with specialists:

1) EEG night video monitoring: ZDR 8-9 Hz. Sleep was cyclical, modulated by phases and stages, and physiological patterns were pronounced. Stage II of the slow-wave sleep phase is the most represented. There was no convincing evidence for the presence of epileptic seizures, patterns of epileptic seizures and epileptiform activity while taking levetiracetam at a dose of 500 mg 2 times a day.

2) Consultation with an ophthalmologist: moderate myopia. Complex myopic astigmatism. Optic neuropathy. Moderate amblyopia.

3) Ultrasound of the liver and gallbladder: echo picture of moderately diffuse changes in the liver parenchyma. Moderate thickening of the gallbladder walls. Minor hepatomegaly.

4) Ultrasound of the kidneys and bladder: moderate thickening of the kidneys. Pyeelectasia of the kidneys.

5) Ultrasound of the uterus and appendages: without echopathology.

6) MRI of the Brain: MRI signs of moderate atrophy of the cerebral cortex in the convexital regions of both frontal areas. A slight expansion of the subarachnoid space (development option) of the posterior cranial fossa. Non-contrast MR angiography revealed no pathological changes. Parietal (reactive) thickening of the mucous membrane in both maxillary sinuses.

7) Consultation with a geneticist: genetically determined biotinidase deficiency.

Taking into account the family history, clinical course of the disease, instrumental, laboratory and molecular genetic studies, a diagnosis was made: Hereditary autosomal recessive metabolic disease - biotinidase deficiency (ICD 10 - E53.8). Complication: Symptomatic epilepsy with focal epileptic seizures of medium frequency.

The patient was recommended:

Biotin-rich diet therapy: liver; beans and soybeans; almond; rice bran; whole grains; egg yolks; sardines; cauliflower; mushrooms. fermented milk products enriched with bifid additives.

Physiotherapy, physical therapy, massage, swimming. Observation by a neurologist, epileptologist, hepatologist, paediatrician, ophthalmologist. Drug therapy: biotin 60 mg (60,000 mcg) per day on an ongoing basis.

Cholecalciferol 10 drops 1 time per day in the morning for 3 months. Potassium iodide 200 mcg, 1 tablet 1 time per day in the morning for 3 months.

Biotin 60 mg (60,000 mcg) per day on an ongoing basis. L – Arginine L-Aspartate 5 ml once a day for a month. Carnis (L-carnitine 500 mg, Coenzyme Q10 5 mg, Cyanocobalamin 0.5 mcg) 10 ml orally once a day for a month.

RESULTS AND DISCUSSION

After taking levetiracetam, generalized seizures stopped, but rare focal seizures were observed. We presented this clinical case at training courses on neurometabolic diseases organized by the European Society of Child Neurologists and colleagues from Austria and the Netherlands suggested reducing the biotin dose from 60 mg to 12 mg and continuing to monitor the patient.

CONCLUSION

Follow-up with a clinical geneticist or metabolic specialist is required annually for individuals with profound biotinidase deficiency and every two years for individuals with partial biotinidase deficiency. If symptoms return after biotin therapy, urine organic acid testing should be considered to assess compliance with biotin therapy. Measure growth parameters, assess for new manifestations (seizures, changes in tone, movement disorders), monitor developmental progress and educational needs, and assess skin manifestations (eczematous rash, alopecia, thrush and/or candidiasis) at each visit. Ophthalmological and audiological examinations should be performed annually for individuals with profound biotinidase deficiency and every two years for individuals with partial biotinidase deficiency. Agents to avoid: raw eggs should be avoided as they contain avidin, an egg white protein that binds biotin, thereby reducing its bioavailability. However, thoroughly cooked eggs are not a problem because heat inactivates avidin, making it unable to bind biotin. [4]

Because treatment is inexpensive and readily available, it is critical to detect this disease before symptoms appear, especially findings related to central nervous system damage, hearing loss, and vision loss. In patients with suspected enzyme deficiency, the diagnosis should be definitively confirmed by genetic testing.[3]

CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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BIOTINIDAZA ETMASHISHINI KLINIK HOLATI

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ABSTRAKT

Biotinidaza etishmovchiligi autosomal retsessiv irsiy metabolik kasallikdir. Agar davolanmasa, biotinidaza etishmovchiligi bo'lgan bemorlarda odatda koma va o'limga olib keladigan nevrologik va teri belgilari paydo bo'ladi. Ushbu maqolada biotinidaza etishmovchiligi bo'lgan bemorning klinik holati ko'rib chiqildi. Maqola nevrologlarning e'tiborini irsiy autosomal retsessiv metabolik kasallik - biotinidaza etishmovchiligi fonida simptomatik epilepsiyaning mumkin bo'lgan sabablariga qaratilgan.

Kalit so'zlar: biotinidaza etishmovchiligi, irsiy kasallik, neyrometabolik kasallik, asab tizimi

КЛИНИЧЕСКИЙ СЛУЧАЙ БИОТИНИДАЗНОЙ НЕДОСТАТОЧНОСТИ

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АБСТРАКТ

Дефицит биотинидазы является аутосомно-рецессивно наследуемым метаболическим заболеванием. При отсутствии лечения у больных с дефицитом биотинидазы обычно развиваются неврологические и кожные симптомы, которые могут привести к коме и летальному исходу. В данной статье был рассмотрен клинический случай заболевания больной с биотинидазной недостаточностью. Статья направлена на повышение внимания врачей-неврологов на возможные причины симптоматической эпилепсии на фоне наследственного аутосомно-рецессивного заболевания обмена - дефицита биотинидазы.

Ключевые слова: биотинидазная недостаточность, наследственное заболевание, нейрометаболическое заболевание, нервная система