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MODERN APPROACHES TO DIAGNOSTICS AND TREATMENT OF OPTIC NEUROPATHY

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Abstract. *Leber optic neuropathy is a genetic disease that causes progressive atrophy of the optic nerve and loss of vision. The pathology occurs when a mutation in mitochondrial DNA occurs, which is transmitted to children through the maternal line. The main symptom of the disease is a sharp decrease in visual acuity from normal to light perception, which most often occurs between the ages of 18 and 30. For diagnosis, ophthalmoscopy, OCT, and visual potential tests are prescribed. The diagnosis can be confirmed using molecular genetic testing. Treatment of Leber neuropathy includes neurometabolic drugs and long-term rehabilitation.*

Keywords: *Causes, Pathogenesis, Symptoms, Complications, Diagnostics, Treatment of Leber's optic neuropathy, Conservative therapy, Experimental treatment, Rehabilitation, Prognosis and prevention.*

Introduction: The disease is named after the German ophthalmologist Theodor Leber, who first described 15 cases of sudden vision loss in patients from four families. The molecular genetic basis of the disease was established in 1988 by the American biochemist D. Wallace.

Leber's hereditary optic neuropathy (LHON) occurs with a frequency of 1 case per 50 thousand people, but every ten thousandth person on the planet is a carrier of the mutation. In Russia, the disease is more common among the population of Siberia. Men suffer from optic neuropathy 5 times more often than women.

The disease develops as a result of mutations in mitochondrial DNA, which lead to a disruption of the energy supply of the optic nerves and lead to their death. Up to 95% of cases are associated with 3 types of hereditary anomalies: 3460G>A in the ND1 gene, 11778GC (ND6). The mutation of the ND4 gene is the most common in clinical practice. Leber optic neuropathy can also be caused by other variants of anomalies that are not well understood due to their rarity.

Mitochondrial DNA mutations are characterized by complete penetrance, so some people with an abnormal gene develop a pronounced clinical picture, while others remain asymptomatic carriers throughout their lives. External triggers play a role in the development of the disease.

The most important of them are:

When the nucleotide sequence in mitochondrial DNA is disrupted, the structure of the proteins encoded by these genes changes. Since Leber's optic neuropathy affects the ND genes encoding proteins of complex I (NADH-ubiquinone reductase), the pathology occurs at the stage of formation of ATP molecules. The cells of the nervous system are sensitive to the lack of energy molecules, which leads to damage to the optic nerve.

The molecular basis of the disease is a decrease in ATP transport to the distal parts of the axons, which leads to the initiation of apoptosis processes from the periphery. ATP deficiency is most pronounced in the thin unmyelinated fibers that make up the optic nerve, therefore vision is primarily affected in Leber's neuropathy. The development of pathology is facilitated by the congenital multiplicity of axons in the optic nerve head and the special structure of the cribriform plate.

Research methods and materials: Leber's optic neuropathy is characterized by 3 successive stages: preclinical, acute, chronic (atrophic). The first stage is asymptomatic, but when the patient is examined by an ophthalmologist for another reason, swelling of the optic nerve and the appearance of telangiectasias in it are detected. The duration of this stage is not regulated, since the disease is detected very rarely in the preclinical stage.

The acute stage of Leber's optic neuropathy most often occurs in young men aged 18 to 30 years. Patients complain of a sharp decrease in vision, similar to a central scotoma. Within 1-1.5 months, a person loses the ability to distinguish small objects, sometimes even counting fingers up to a hundred, and only the sensation of light remains. Pathology affects both eyes simultaneously or sequentially with an interval of 6-8 weeks.

After 6 months, the disease becomes chronic, when visual acuity is reduced to several thousandths. During this period, nerve atrophy continues, after which the function of the eyeball cannot be restored. The ophthalmological picture is characterized by pallor of the optic disc. However, there are cases of reverse development of symptoms, when after some time patients partially restore vision.

Extraocular manifestations are possible with optic neuropathy. Nerve damage can affect more than just the optic tract, so some patients experience peripheral neuropathy, myopathy, and muscular dystonia. If the disease manifests itself in early childhood, there is a risk of developing

subacute necrotizing encephalomyopathy (Leigh syndrome). Sometimes, symptoms of NONLS and MELAS syndrome overlap.

The main problem of Leber's neuropathy is loss of vision, which is especially difficult for young patients. Against the background of blindness, severe depression develops, which can end in suicide attempts. Since even partial restoration of vision does not occur in everyone, in the future patients become disabled and are forced to undergo rehabilitation to adapt to new living conditions.

In some women, Leber's neuropathy occurs in the form of multiple sclerosis, with alternating periods of exacerbation and remission. In such patients, vision loss alternates with episodes of incomplete recovery of vision. It is characterized by the secondary development of neurological symptoms in combination with blindness, known as Harding's disease. The pathology is accompanied by foci of demyelination in the brain, which aggravates the clinical course.

Progressive vision loss is a reason for a comprehensive examination of the patient by an ophthalmologist. Diagnostically important criteria: central scotoma, absence of pain syndrome, the presence of similar symptoms in close relatives on the maternal line. The following tests are used to confirm Leber's optic neuropathy:

Results: Ophthalmoscopy. Fundus examination reveals swelling and waxy pallor of the optic disc. Central disc excavation is within normal limits. In the early stages of the disease, retinal hemorrhages are clearly visible during examination.

Visometry. It is impossible to assess visual acuity using standard tables, since this indicator does not exceed 0.001. In practice, this corresponds to the ability to "count fingers near the face" and distinguish silhouettes. In addition, perimetry is performed, which confirms the loss of central visual fields.

Optical coherence tomography. Targeted examination of the macula of the retina shows thinning and poor differentiation of all layers, flattening of the foveolar contour, and thickening of the internal limiting membrane. OCT is the most informative method for diagnosing ON atrophy.

Visual acuity testing. Electrophysiological diagnostics of visual evoked potentials show a decrease in nerve conduction in the preoptic area. The severity of these changes depends on the degree of visual loss.

Molecular genetic testing. To confirm the diagnosis of Leber neuropathy, isolation of the mitochondrial mutation is necessary. Patients are offered targeted testing for the 3 most common point mutations and, if indicated, a multigene panel or complete mtDNA sequencing is performed.

In the acute stage, NONL should be differentiated from inflammatory diseases of the optic nerve: retrobulbar neuritis, Devic optic myelitis, optic neuritis in rheumatic diseases. Ischemic

optic neuropathy, which is characteristic of increased intraocular pressure, should be excluded. The chronic stage of the disease is distinguished by compression of the optic nerve by tumors of the orbit and chiasmatic-sellar region.

1. Ophthalmological examination
2. Ophthalmological examination
3. Treatment of Leber's optic neuropathy
4. Conservative therapy

Discussion: For people with visual impairments, social and psychological adaptation is of primary importance. The rehabilitation program consists of teaching independent movement, spatial orientation, and self-care skills. All patients receive training in Braille, which allows them to continue reading and studying. At the request of the person, labor rehabilitation and training in skills (carving, music, sculpture) are carried out.

NONL with the 14484T>C mutation is considered prognostically favorable, with patients having a chance of complete recovery of vision. The 3460G>A mutation has a very unfavorable course and quickly leads to blindness. Anomaly 11778G<A has an intermediate prognosis. To prevent the disease, patients with severe heredity are recommended to avoid provoking factors.

Conclusion: In practical ophthalmology, there is no effective treatment regimen that would improve the visual function of patients. Coenzyme Q10, levocarnitine, and cytochrome preparations are prescribed as adjuvant and pathogenetic therapy. They are often combined into "mitochondrial cocktails" to enhance their therapeutic effect. However, even long-term use of drugs does not significantly affect clinical indicators.

Since drug therapy has not restored vision, scientists have placed great hopes in genetic engineering technologies. Their essence is based on the transformation of mutant mitochondrial DNA to a normal state in order to increase the ATP content in the axons of the visual pathway and prevent nerve atrophy. Today, such methods are at the experimental stage, and some are undergoing the first phase of clinical trials.

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