ROLE OF ENDOTHELIAL DYSFUNCTION IN THE PATHOGENESIS OF DIABETIC RETINOPATHY

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Relevance. According to the WHO, diabetic retinopathy develops in patients with type 2 diabetes, in average, 5–7 years after the onset of the disease and remains one of the most frequent prognostically unfavorable manifestations of systemic diabetic microangiopathy, leading to blindness in 74.2% of cases (Smirnova O.M).

Recent researches have confirmed that endothelial cell dysfunction plays a key role in vascular tone violation and structure in patients with diabetes mellitus. In this regard, the correction of endothelial function is the main goal of therapy and prevention of diabetes mellitus and its complications (Kravchun NA, Chernjavskaja IV; Semenko VV, Serdyuk VM). Main task of therapy is elimination of vasoconstriction and increase the availability of NO to the walls of vessels. Last one is achieved through the stimulation of NO-synthase or inhibition of fragmentation (Kravchun NA, Chernjavskaja IV). It is established that at the progression of DR, the synthesis of NO decreases. Several authors have found that the concentration of L – arginine in the lacrimal fluid in patients with DR is significantly diminish as the disease progresses. Reducing of free NO amount promotes the secretion of vasoconstrictor substances – endothelin, angiotensin II, prostaglandin PGI-2 and is accompanied by angiospazm, violation of hemodynamics and vasomotorics. Insufficiencyof NO also leads to the development of thrombogenic and vasoproliferative factors (Verbovaja NI, Lebedeva EA, Aleksandrovskij JaA). In the early stages of diabetic retinopathy development, NO can be used as a diagnostic marker for the severity of the pathological process and, if necessary, for the correction of the correlation between compensatory and pathological mechanisms (Semenko VV, Serdyuk VM).

ALKAPTONURIA

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Alkaptonuria is a hereditary metabolic disorder caused by a violation of the metabolism of tyrosine, characterized by the excretion in urine of a large amount (up to 4–8 g and more per day) of homogentisic acid (2,5-dihydrophenylacetic acid). Alkaptonuria develops as a result of a genetic enzymopathy. Alkaptonuria is marked by a violation of the homogentisic acid oxidase gene, which is located on the long arm of the third chromosome (3q 21–23). As a result, there is an incorrect production of the enzyme homogentisate 1,2-dioxygenase, which is involved in the cleavage of tyrosine and phenylalanine.

Homogentisic acid is an intermediate metabolite of tyrosine and phenylalanine metabolism, which, under the influence of homogentisate 1, 2-dioxygenase, is converted to maleacetoacetic acid, and then cleaved to acetoacetic and fumaric acids, which are involved in further biochemical cycles.

With alkaptonuria, due to the lack of an enzyme, the occurrence of homogentisic acid metabolism is not observed, as a result of which it is transformed into quinone polyphenols, which accumulate in the connective tissues and are excreted with urine in significant volumes.

In most cases, the diagnosis of alkaptonuria occurs as early as childhood, but in some cases the diagnosis is made only after the onset of the entire symptom complex. The pathogenetic diagnosis of alkaptonuria involves the biochemical examination of urine using the method of enzymatic spectrophotometry or liquid chromatography and the determination in it of homogentisinic and benzochoninoacetic acids.

An assessment of the color of urine makes it possible to notice its significant darkening when exposed to air, warming up and alkalinisation. The study of synovial fluid, in which there are no signs of inflammation, but contains particles of an ocronotic pigment, may be of some help. Specific changes in alkaptonuria are found in the synovial membrane obtained by joint biopsy.

The classic signs of alkaptonuria are staining of urine, tissue, and damage to the joints. Sometimes the first symptoms of the disease can be identified even in children. Due to the high concentration of homogentisic acid in the urine, it even after a short time settling takes on a dark brown color. In patients with alkaptonuria, the occurrence of a kidney disease, pyelonephritis and calculous prostatitis in men is quite often observed.

When the skin manifestations of the disease in patients, the appearance of brown-gray pigmentation in the face, palms, neck, abdomen, axillary and inguinal cavities. In addition, the classic symptoms are the sealing and staining of the auricles in a gray-deep color, as well as the occurrence of pigmentation on the conjunctiva and sclera. Sometimes there is a diffuse accumulation of pigment in the cartilage of the larynx, which causes hoarseness, pain when swallowing, shortness of breath and dysphagia. As the disease progresses, calcification of the aorta and the heart valves may form, with the result that atherosclerosis and the development of aortic and mitral defects are noted in such patients. In the case of a severe illness, the patient may accumulate in the tissues of the thyroid and pancreas, adrenal glands and spleen.

Today, a special treatment regimen for alkaptonuria has not yet been developed. Many experts advise low-protein diets to reduce over-production of homogentisic acid. To improve the quality of tyrosine metabolism, vitamin C administration is indicated. Intra-articular administration of hydrocortisone and hyaluronic acid can also be used.