ATHEROSCLEROSIS

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Abstract: *Atherosclerosis (from the Greek αθήρα - "gruel" + σκλήρωσις - "hardening"[2]) is a chronic disease of the arteries of the elastic and muscular-elastic type, resulting from a violation of lipid and protein metabolism and accompanied by the deposition of cholesterol and some fractions of lipoproteins in the lumen vessels. Deposits form in the form of atheromatous (cholesterol) plaques. Subsequent growth of connective tissue in them (sclerosis), and calcification of the vessel wall lead to deformation and narrowing of the lumen, up to obstruction (blockage of the vessel). It is important to distinguish atherosclerosis from Mönckeberg arteriosclerosis, another form of sclerotic lesions of the arteries, which is characterized by the deposition of calcium salts in the medial lining of the arteries, diffuseness of the lesion (absence of plaques), and the development of aneurysms (rather than blockages) of blood vessels. Atherosclerosis of the heart vessels leads to the development of coronary artery disease.*

Key words: *Atherosclerosis, blockages, sclerosis, cholesterol, ischemic heart disease.*

Epidemiology

Video with subtitles

According to WHO, the first two places in the list of causes of mortality for the population of our planet are occupied by heart attack and stroke - cardiovascular diseases, which are usually a consequence of generalized atherosclerosis [3]. In the Russian Federation in 2020, the standardized mortality rate from diseases of the circulatory system amounted to 48% of all deaths[4].

Etiology

At the moment, there is no single theory of the occurrence of this disease. The following options are put forward, as well as their combinations:

• theory of lipoprotein infiltration - primary accumulation of lipoproteins in the vascular wall,

• theory of endothelial dysfunction - primary violation of the protective properties of the endothelium and its mediators,

• autoimmune - primary dysfunction of macrophages and leukocytes, their infiltration of the vascular wall,

• monoclonal - primary occurrence of a pathological clone of smooth muscle cells,

• viral - primary viral damage to the endothelium (herpes, cytomegalovirus, etc.),

• peroxide – primary violation of the antioxidant system,

• genetic - primary hereditary defect of the vascular wall,

• chlamydia - primary damage to the vascular wall by chlamydia, mainly Chlamydia pneumoniae.

• hormonal - an age-related increase in the level of gonadotropic and adrenocorticotropic hormones leads to increased synthesis of the building material for hormones - cholesterol.

Risk factors

• smoking (the most dangerous factor)

• alcohol consumption

• hyperlipoproteinemia (total cholesterol > 5 mmol/l, LDL > 3 mmol/l, Lp(a) > 50 mg/dl)

• arterial hypertension (systolic blood pressure > 140 mm Hg. diastolic blood pressure > 90 mm Hg. art.)

• diabetes

• obesity

• sedentary lifestyle (hypodynamia)

• emotional stress

• poor nutrition

• hereditary predisposition

• postmenopause

• hyperfibrinogenemia

• homocysteinuria and homocysteinemia

• hypothyroidism[5]

• irregular sleep[6].

According to the European Guidelines on Cardiovascular Disease Prevention, the leading risk factors are assessed based on the SCORE (Systematic COronary Risk Evaluation) scale.[7][8]

The pathogenesis of atherosclerosis is called atherogenesis. It occurs in several stages. The development of atherosclerotic lesions is a set of processes of lipoproteins and leukocytes entering and exiting the intima, cell proliferation and death, formation and restructuring of the intercellular substance, as well as vascular proliferation and calcification. These processes are controlled by many signals, often in different directions. More and more data are accumulating on the complex pathogenetic relationship between changes in the function of the cells of the vascular wall and the leukocytes that migrated into it and risk factors for atherosclerosis. Accumulation and modification of lipoproteins

Normally, the intimacy of the arteries is formed by a unicellular endothelial layer, under which there are smooth muscle cells, immersed in the intercellular substance. The first manifestations of the disease are the so -called lipid spots. Their appearance is

associated with the local deposition of lipoproteins in intimacy. Not all lipoproteins have atherogenic properties, but only low (LDL) and very low density (LOPP). Initially, they accumulate in intima mainly due to the binding with the components of the intercellular substance - proteoglycans. In places of formation of lipid spots, the predominance of heparan sulfates over two other glycosaminoglycans - keratan sulfates and chondroitin sulfates plays a large role.

In intima, lipoproteins, especially related to proteoglycans, can enter into chemical reactions. The main role is played by two: oxidation and non -enzymatic glycosylation. In intimacy, unlike plasma, there are few antioxidants. A mixture of oxidized LDLs is formed, and both lipids and the protein component are oxidized. During the oxidation of lipids, hydraulic transmission, lysophilipids, oxisterins and aldehydes are formed (with peroxidation of fatty acids). The oxidation of apoproteins leads to a rupture of peptide bonds and the combination of the side chains of amino acids (usually β-aminogroups of lysine) with products of the breakdown of fatty acids (4-hydroxynonenal and melonov dyalldehyde). Persistent hyperglycemia in diabetes contributes to non -enzymatic glycosylation of apoproteins and own proteins of intimacy, which also disrupts their functions and accelerates atherogenesis.

Migration of leukocytes and the formation of xantomic (foamy) cells.

Migration of leukocytes, mainly monocytes and lymphocytes, is the second stage of development of a lipid spot. Their migration in intima is provided by the receptors located on endothelia - adhesion molecules. Molecules VCAM-1 and ICAM-1 (from the super-family of immunoglobulins) and P-Selectin deserve special attention. The synthesis of adhesion molecules can increase cytokines. So, Interlayykin-1 (IL-1) and the factor of tumor necrosis (FNOα) cause or enhance the synthesis of VCAM-1 and ICAM-1 endothelial cells. In turn, the release of cytokines with the cells of the vascular wall is stimulated by modified lipoproteins. A vicious circle is formed.

The character and nature of blood flow plays. In most sections of the unchanged artery, blood flows laminarly, and the emerging forces reduce the expression (manifestation) on the surface of endothelial cells of adhesion molecules. Also, laminar blood flow contributes to the formation of nitrogen nitrogen oxide in the endothelium. In addition to the vasodilating action, in a low concentration supported by endothelium, NO has anti-inflammatory activity, reducing, for example, the synthesis of VCAM-1. But in the branches of branching, the laminar current is often disturbed, it is there that atherosclerotic plaques usually occur.

After adhesion, leukocytes pass through the endothelium and fall into intimacy. Lipoproteins can directly strengthen migration: oxidized LDLs contribute to chemotaxis leukocytes.

Monocytes are involved in the further formation of the lipid spot. In intimacy, monocytes become macrophages, from which, due to the lipoprotein endocytosis mediated by receptors, xantomic (foamy) cells are filled with lipids. Previously, it was

assumed that well -known LDL receptors are involved in endocytosis, but with a defect in these receptors both in experimental animals and patients (for example, with family hypercholesterolemia), there are still numerous xanthoms and atherosclerotic plaques filled with xantomic cells. In addition, exogenous cholesterol slows down the synthesis of these receptors, and with hypercholesterolemia there are few. Now it is supposed to be the role of the macrophages regions-receptors (binding mainly modified lipoproteins) and other receptors for oxidized LDLs and small atherogenic lonspances. Some xantomic cells that absorb lipoproteins from intercellular substance leave the artery wall, thereby preventing lipids in it. If the receipt of lipoproteins in intima prevails over their excretion with macrophages (or other ways), lipids accumulate and an atherosclerotic plaque is formed. In a growing plaque, some xantomic cells are apoptosis or necrosis. As a result, in the center of the plaque, a cavity is formed, filled with rich lipid masses, which is characteristic of the late stages of atherogenesis.

Pros- and anti-arterogenic factors

With the absorption of modified lipoproteins, macrophages are distinguished by cytokines and growth factors that contribute to the development of plaques. Some cytokines and growth factors stimulate the division of smooth muscle cells and the synthesis of the intercellular substance that accumulates in the plaque. Other cytokines, especially interferon-γ from activated T-lymphocytes, inhibit the division of smooth muscle cells and collagen synthesis. Factors such as IL-1 and FNOα cause the production of the platelet factor of growth and the growth factor of fibroblasts in the intimacy that play a role in the further fate of plaques. Thus, there is a complex interaction of factors, both accelerating and inhibiting atherogenesis. The role is great and non -nonsense mediators. Activated macrophages and vascular wall cells (endothelial and smooth muscle) produce free oxygen radicals, which stimulate the sodium of smooth muscle cells, enhance the synthesis of cytokines, and also bind NO. On the other hand, activated macrophages are capable of the synthesis of induced No-syntase. This high-acting enzyme produces NO in high, potentially toxic concentrations-in contrast to a small concentration of NO created by the constitutive form of the enzyme-endothelial No-syntase.

In addition to macrophages, high -density lipoproteins (HDLP), which provide the so -called valuable transport transport of cholesterol, participate in the removal of cholesterol from the affected intima. A clear reverse dependence between the concentration of HDL cholesterol and the risk of IBS has been proved. In women of childbearing age, the concentration of HDL cholesterol is higher than that of male peers, and in many ways, women are less likely to suffer from atherosclerosis. In the experiment, it is shown that LDP can remove cholesterol from xantomic cells.

Participation of smooth muscle cells

Atherosclerotic plaques develops from a lipid spot, but not all spots become plaques. If lipid spots are characterized by the accumulation of xantomic cells, then for plaques - fibrosis. The intercellular substance in the plaque is mainly synthesized by smooth muscle cells, the migration and proliferation of which is probably a critical moment in the formation of a fibrous plaque at the site of the accumulation of xantomic cells.

Migration in a lipid spot of smooth muscle cells, their proliferation and synthesis of intercellular substance is caused by cytokines and growth factors distinguished under the influence of modified lipoproteins and other substances by macrophages and vascular wall cells. Thus, the platelet growth factor, secreted by activated endothelial cells, stimulates the migration of smooth muscle cells from media to intima. The growth factors formed by local factors cause the division of both their own smooth muscle cells of intimacy and cells that came from media. One of the powerful stimulants of the synthesis with these collagen cells is a transforming river growth factor. In addition to paracrine (factors come from neighboring cells), autocrine (the factor is produced by the cell itself) regulation of smooth muscle cells. As a result of the changes taking place with them, the transition of a lipid spot to an atherosclerotic plaque containing a lot of smooth muscle cells and intercellular substance is accelerated. Like macrophages, these cells can enter into apoptosis: it is caused by cytokines that contribute to the development of atherosclerosis.

The development of complicated plaques

In addition to the usual risk factors and the above cytokines in the later stages of atherosclerosis, an important role belongs to changes in the blood coagulation system. For the appearance of lipid spots, the endothelium damage or descending is not required. But in the future, microscopic tears can occur in it. On a naked basal membrane, platelets adhesion occurs, and small platelet thrombi forms in these places. Activated platelets distinguish a number of substances that accelerate fibrosis. In addition to the platelet factor of growth and the transforming factor of growth P, low molecular weight mediators, such as serotonin, are acting on smooth muscle cells. Usually these blood clots dissolve without causing any symptoms, and the integrity of the endothelium is restored.

As the plaques develops, vasa vasorum (blood vessels) begin to grow abundantly in it. New vessels affect the fate of plaques in several ways. They create an extensive surface for the migration of white blood cells both inside the plaque and from it. In addition, new vessels are a source of hemorrhage in plaques: as with diabetic retinopathy, they are brittle and prone to break. The emerging hemorrhage leads to thrombosis, thrombin appears. It not only participates in hemostasis, but also affects intimacy cells: it stimulates the division of smooth muscle cells and the production of cytokines, and also causes the synthesis of the endothelium of growth factors. As a result of hemorrhages, plaques often contain fibrin and hemosiderin.

Atherosclerotic plaques are often used. The plaques contain calcium -binding proteins of osteocalcin and osteopomontin and some other proteins characteristic of bone tissue (in particular, proteins are bone morphogenesis regulators).

Gangrene of the right lower limb due to thrombosis of the femoral artery against the background of atherosclerosis

Clinic

Clinical manifestations often do not correspond to morphology. With pathological autopsy, an extensive and pronounced atherosclerotic lesion of blood vessels may turn out to be a find. And vice versa, the organ of ischemia of the organ can appear with moderate spinning of the lumen of the vessel. The predominant damage to certain arterial pools is characteristic. The clinical picture of the disease also depends on this. The defeat of the coronary arteries gradually leads to coronary failure, manifested by coronary heart disease. Atherosclerosis of cerebral arteries causes either the transient ischemia of the brain or strokes. The defeat of the arteries of the extremities is the cause of intersecting chromium and dry gangrene. Atherosclerosis of the mesenteric arteries leads to ischemia and intestinal infarction (mesenteric thrombosis). It is also possible to defeat the renal arteries with the formation of Goldblatt's kidney. Even within individual arterial pools, focal lesions are characteristic - with the involvement of typical sites and the safety of the neighboring ones. So, in the vessels of the heart, occlusion most often occurs in the proximal section of the anterior interventricular branch of the left coronary artery. Another typical localization is the proximal renal artery and bifurcation of the carotid artery. Some arteries, for example, internal thoracic, are rarely affected, despite the proximity to coronary arteries both in arrangement and structure. Atheroscleic plaques often occur in bifurcation of arteries - where the blood flow is uneven; In other words, local hemodynamics plays a role in the location of the plaques (see Pathogenesis).

Diagnostics

Diagnosis of diseases associated with atherosclerosis includes:

• Patient survey and clarification of symptoms of the disease: symptoms of coronary heart disease, symptoms of cerebrovascular disorders, intersecting lameness, symptoms of the abdominal toad, etc.;

• General examination of the patient: signs of aging of the body, listening to systolic noise in the focus of aorta; Palpation of all arteries available to palpation: aorta, external iliac arteries, general femoral arteries, popliteal arteries, arteries of the rear of the foot and rear tibia artery, radiation and elbow arteries, carotid arteries.

• Determination of systolic noise over auscultative points of arteries.

• If you suspect the defeat of the arterial channel of the lower extremities, the determination of the capillary response.

• determination of the concentration of cholesterol in the blood and determining the lipid blood balance;

• X -ray examination of the organs of the chest, X -rayendovascular examination methods;

• ultrasound examination of the heart and organs of the abdominal cavity and retroperitoneal space;

• Dopplerography of the vessels of the limbs or, which may be better, ultrasound duplex and triplex scanning of the arteries of the brachiocephalic region, the arteries of the lower extremities, the aorto-illegal segment, as well as the transcranial doppler.

• Diagnostics of the rigidity of the arterial wall [9], including the method of voluminous sphigmography [10] and determination of the heart-lining vascular index (Cavi) [11]

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