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MODERN CONCEPTS OF THE MECHANISMS OF ATHEROSCLEROSIS DEVELOPMENT

Muydinov J.I.
Fergana institute of public health medicine

Abstract

Atherosclerosis is a chronic disease resulting from a disorder of lipid and protein metabolism, characterized by damage to the integrity of the vascular wall of elastic and muscular-elastic arteries in the form of progressive focal deposition of lipids and proteins in the intima, as well as overactivation of fibrocytes with subsequent reactive proliferation of connective tissue. The main morphological expression of atherosclerosis is an atherosclerotic plaque (atheroma). An atherosclerotic plaque, narrowing the lumen of the artery, leads to insufficient vascularization (ischemia) with subsequent development of dystrophic and necrotic changes.

Keywords: atherosclerosis, atherogenesis, cardiology, cholesterol.

ATEROSKLEROZ RIVOJLANISH MEXANIZMLARINING ZAMONAVIY TUSHUNCHALARI

Muydinov J.I.
Farg'ona sog'liqni saqlash tibbiyot instituti

Annotatsiya

Ateroskleroz-lipid va oqsil almashinuvining buzilishi natijasida kelib chiqadigan surunkali kasallik bo'lib, intimadagi lipidlar va oqsillarning progressiv fokal cho'kishi shaklida elastik va mushak-elastik arteriyalarning qon tomir devorining yaxlitligiga zarar etkazish, shuningdek, biriktiruvchi to'qimalarning keyingi reaktiv proliferatsiyasi bilan fibrotsitlarning haddan tashqari faollashishi bilan tavsiflanadi. Aterosklerozning asosiy morfologik ifodasi aterosklerotik blyashka (ateroma). Arteriyaning bo'shlig'ini toraytiruvchi aterosklerotik blyashka distrofik va nekrotik o'zgarishlarning keyingi rivojlanishi bilan vaskulyarizatsiyaning (ishemiya) etishmasligiga olib keladi.

Kalit so‘zlar: ateroskleroz, aterogenez, kardiologiya, xolesterin.

СОВРЕМЕННЫЕ ПРЕДСТАВЛЕНИЯ О МЕХАНИЗМАХ РАЗВИТИЯ АТЕРОСКЛЕРОЗА

Муйдинов Ж.И.
Ферганский институт общественного здравоохранения

Аннотация

Атеросклероз - хроническое заболевание, возникающее в результате нарушения липидного и белкового обмена, характеризующееся повреждением целостности сосудистой стенки эластичных и мышечно-упругих артерий в виде прогрессирующего очагового отложения липидов и белков в интиме, а также гиперактивацией фиброцитов с последующей реактивной пролиферацией соединительной ткани. Основным морфологическим проявлением атеросклероза является атеросклеротическая бляшка (атерома). Атеросклеротическая бляшка, сужая просвет артерии, приводит к недостаточной васкуляризации (ишемии) с последующим развитием дистрофических и некротических изменений.

Ключевые слова: атеросклероз, атерогенез, кардиология, холестерин.

To date, the mechanism of atherogenesis has not been precisely established, but there are many theories, such as receptor, metabolic, immunogenic, damage response theory, etc., but in modern cardiology it is generally accepted that all theories are acceptable to some extent in the development of atherosclerosis, which confirms the multifactorial origin of atherosclerosis [1]. The causes of atherosclerosis have been studied in sufficient detail and are classified as risk factors, which is the subject of study in preventive cardiology [2, 3].

Risk factors for atherosclerosis are:

- Hyperlipidemia. Hyperlipidemia, in particular hypercholesterolemia, is a leading risk factor manifested by an imbalance in the blood of LDL and VLDL (low and very low density lipoproteins, the so-called proatherogenic potential) with HDL and HDLP (high and very high density lipoproteins, antiatherogenic potential). This ratio in atherosclerosis is 5:1, while the norm is 4:1 [5]. It is worth noting that 65% of registered cases of atherosclerosis are associated with an increase in the content of LDL and VLDL (bad lipoproteins) in the blood, while a decrease in the proportion of HDL and VLDL (good lipoproteins) accounts for about 35%. Moreover, it was found that an excessive increase in HDL can also lead to atherogenesis, that is, atherosclerosis develops with any type of dyslipidemia. Hyperlipidemia (hypercholesterolemia) is necessarily combined with dyslipoproteinemia, i.e. a violation of the content of LP in the blood plasma and a change in the ratio between their fractions. There are three types of hyperlipidemia: genetic/primary (familial hypo-alpha-lipoproteinemia, familial hypercholesterolemia, cholesterol ester storage

disease, familial hyperlipidemia), secondary (in diabetes mellitus, hypothyroidism, nephrotic syndrome and in diseases in which it is present in the symptom complex), and alimentary [4].

Materials and methods. Age. The age limit for atherosclerosis is certainly of certain clinical interest, since the increase in the frequency and severity of atherosclerosis with age is beyond doubt, which allows us to consider atherosclerosis not as a disease, but as a natural problem of age.

– Gender. It is worth noting that the incidence of atherosclerosis among men begins earlier than among women, moreover, this disease is more severe in males, therefore, complications of atherosclerosis in men are more common. However, in postmenopausal women and men of this age, the intersexual coefficient is equalized, and according to some studies, it even slightly shifts towards the female sex [1].

– Genetic factor. At the time of writing, the exact genes responsible for the inheritance of this pathology have not been established; the risk of developing atherosclerosis increases unprecedentedly in such genetic diseases as, for example, type 1 diabetes. - Arterial hypertension. Increased blood pressure of any genesis leads to systemic vasculitis. Consequently, increased blood pressure leads to a violation of the integrity and, thus, to an increase in the permeability of the vascular walls, including for the LP, which contributes to damage to the intimal endothelium. Increased permeability is achieved by successive disorganization of the structure and integrity of the connective tissue framework (mucoid swelling, fibrinoid swelling, fibrinoid necrosis, sclerosis, hyalinosis). Hypertension is also associated with the appearance of atherosclerotic plaques in vessels that are not typical for atherosclerosis, for example, in the pulmonary artery in pulmonary hypertension, in the portal vein in portal hypertension. - Smoking. Atherosclerosis of the coronary arteries and aorta is expressed in smokers 2 times more intensely and occurs 2 times more often than in non-smokers. Therefore, myocardial infarction and other complications of atherosclerosis in smokers develop significantly more often than in non-smokers [3]. Smoking is a risk factor for all cardiac diseases, the cardiotoxicity of which is manifested by a violation of the rheology of the microcirculatory bed. In this case, the harm of smoking is associated with the fact that nicotine stimulates blood clotting, promotes thrombus formation in the area of the atherosclerotic plaque, causes spasm of the arteries, including v.vasorum, thereby disrupting the trophism of the vessels themselves.

- Hormonal factors. Endocrinopathies contribute to atherosclerotic occlusion of blood vessels. These include hypothyroidism, type 2 diabetes, etc.

- Oral contraceptives. This factor is close to hormonal risk factors. Taking such contraceptives for 3-5 years leads to an increased risk of developing atherosclerosis.

- Stressful situations. Stress is an important factor, since any psychoemotional disorders lead to disruption of the regulation of fat-protein metabolism and vasomotor disorders. It is also worth noting that, thanks to the Dachau research during the Second World War, the possibility of stress acting as the main etiological factor in the development of atherosclerosis was proven. Dachau studied the condition of the vascular walls of prisoners in concentration camps during the Second World War. The prisoners' food contained virtually no fat, therefore, they did not have hypercholesterolemia and obesity, but due to the fact that they lived in a state of chronic psychoemotional overstrain, this became the trigger for atherogenesis. The leading mechanism of the atherogenic effect of negative emotions is the activation of the sympathoadrenal system with an increase in the concentration of catecholamines in the blood, as a result of which lipolysis processes in fat depots are enhanced and fatty acids are mobilized, which in normal quantities provide the body with a sufficient amount of energy. When released in excess quantities, they are not utilized, but are used to synthesize cholesterol and atherogenic lipoproteins [4].

Results and discussion. Obesity and physical inactivity. Poor nutrition and a sedentary lifestyle contribute to the disruption of fat-protein metabolism. Excess weight contributes to a significant (≈ 2-6 times) increase in the risk of hypertension, which is due to the development of metabolic syndrome, which underlies severe endothelial dysfunction. Since the endothelium is, to some extent, an active "endocrine" organ, it releases many substances into the circulatory bed, both vasoconstrictors and vasodilators, thereby regulating vascular tone and rheological properties of the blood. Metabolic syndrome is one of the main risk factors in the development of endothelial dysfunction, that is, in the shift in the regulation of vascular tone towards the pressor effect. – Viruses. Of clinical interest are patients infected with various types of viruses that exhibit tropism for the endothelial lining of the intimal layer of the vascular wall. Viruses, with their "aggression" factors, exert their destructive influence on the endothelium. By destroying endothelial cells, viruses lead to endothelial dysfunction.

– Gout. This disease affects not only the joints, but also the vessels (mainly the kidneys, heart and lungs), which can create additional conditions for the accelerated development of atherosclerotic plaques.

– Hyperhomocysteinemia. Homocysteine is a product of methionine metabolism. As a result of increased homocysteine levels, oxidative stress increases, endothelial function is impaired, blood pressure increases and thrombosis occurs. Homocysteine increases the risk of atherosclerosis, coronary heart disease, cerebral vascular disease and peripheral vascular disease. In terms of its severity, it can be compared with hypercholesterolemia and smoking. Elevated homocysteine levels are

a risk factor for congestive heart failure in individuals who have not previously suffered from heart attacks. Cyanocobalamin (vitB12) and folate (vitB9) reduce homocysteine levels by promoting its conversion to methionine or cysteine. - Osteonectin. There is evidence that bone marrow stem cells of the hematopoietic and stromal lineages are involved in atherogenesis. It is assumed that cells proliferating in the vascular intima are of bone marrow origin and that bone marrow colony-forming stem cells of the hematopoietic and stromal lineages circulating in the bloodstream penetrate into the vascular intima at sites of lipid concentration and development of atherosclerotic lesions. Stromal stem cells carry on their surface the marker osteonectin, a non-collagenous glycoprotein of bone tissue that selectively binds calcium and phosphorus salts to collagen. Osteonectin is intensely expressed by cells present in the vessel wall during the progression of atherosclerosis, namely during calcification of the atherosclerotic plaque. According to some researchers, a high content of osteonectin-positive cells in the peripheral bloodstream may reflect the presence of a productive stage of the inflammatory process in the vascular wall [5].
According to the latest recommendations, a modern clinician should consider risk factors not as a diagnostic sign, but as a prognostic, predisposing factor, which to one degree or another can lead to destructive changes in the integrity of the vascular wall of an atherogenic nature. It is also worth noting that risk factors are divided into two large groups, namely correlated/reversible (for example, an unhealthy lifestyle) and uncorrelated/irreversible (for example, metabolic disorders, both endocrine and non-endocrine origin with their organic disorders).

Conclusion. As already noted, under physiological conditions the endothelium plays an important homeostatic role, providing adequate lumen and low thrombogenicity of vessels. But under the influence of various damaging factors it perceives the situation as an emergency. Such an impact can be left by glycation products in diabetes mellitus, cytokines and active components of complement in systemic inflammation, viral particles, etc. As a result, the “angry” endothelial cells change their “product profile”: instead of prostacyclin and nitric oxide desirable in peacetime, adhesion molecules, proinflammatory cytokines, procoagulants and vasoconstrictors corresponding to “wartime” conditions prevail. Normally, the vasoconstrictor activity of the endothelium slightly prevails over the vasodilator. It is these phenotypic changes in the endothelium that form an important link in the pathogenesis of atherosclerosis – endothelial dysfunction.

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