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STAGES OF ATHEROSCLEROTIC FOCUS DEVELOPMENT AND TYPES OF UNSTABLE PLAQUES – PATHOPHYSIOLOGICAL AND HISTOLOGICAL CHARACTERISTICS

Muydinov J.I.
Fergana institute of public health medicine

Abstract

The literature review is devoted to the current state of the problem of atherosclerotic plaque, the stages of its formation from a lipid spot to an unstable atherosclerotic plaque and different types of instability (lipid, inflammatory, dystrophic-necrotic), including pathophysiological (mechanisms of formation and development) and pathomorphological (histological description with illustrations) characteristics of the process.

Keywords: unstable plaque, pathophysiology, atherosclerotic lesions of coronary arteries, types of instability, histology.

ATEROSKLEROTIK FOKUSNING RIVOJLANISH BOSQICHLARI VA BEQAROR BLYASHKA TURLARI-PATOFIZIOLOGIK VA GISTOLOGIK XUSUSIYATLAR

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

Annotatsiya

Adabiyotlarni ko'rib chiqish aterosklerotik blyashka muammosining hozirgi holatiga, uning lipid nuqtasidan beqaror aterosklerotik blyashka hosil bo'lish bosqichlariga va beqarorlikning turli turlariga (lipid, yallig'lanish, distrofik-nekrotik), shu jumladan patofiziologik (shakllanish va rivojlanish mexanizmlari) va patomorfologik (gistologik tavsif bilan) bag'ishlangan. illyustratsiyalar) jarayonning xususiyatlari.

Kalit so‘zlar: beqaror blyashka, patofiziologiya, koronar arteriyalarning aterosklerotik shikastlanishi, beqarorlik turlari, gistologiya.

СТАДИИ РАЗВИТИЯ АТЕРОСКЛЕРОТИЧЕСКОГО ОЧАГА И ТИПЫ НЕСТАБИЛЬНЫХ БЛЯШЕК – ПАТОФИЗИОЛОГИЧЕСКИЕ И ГИСТОЛОГИЧЕСКИЕ ХАРАКТЕРИСТИКИ

Муйдинов Ж.И.
Ферганский институт общественного здравоохранения

Аннотация

Обзор литературы посвящен современному состоянию проблемы атеросклеротической бляшки, этапам ее формирования от липидного пятна до нестабильной атеросклеротической бляшки и различным типам нестабильности (липидной, воспалительной, дистрофически-некротической), включая патофизиологические (механизмы образования и развития) и патоморфологические (гистологическое описание с указанием иллюстрации) характеристики процесса.

Ключевые слова: нестабильная бляшка, патофизиология, атеросклеротические поражения коронарных артерий, типы нестабильности, гистология.

Introduction. According to many studies, the development of atherosclerosis is based on the consistent interaction of many etiopathogenetic factors, ultimately leading to the formation of an atherosclerotic plaque [1, 3]. The initial stage of atherosclerosis is characterized by the appearance of spots and stripes containing lipids in the intima of the arteries [5, 6]. Lipid spots appear in the arteries from early childhood. At the age of 10, lipid spots occupy about 10% of the aortic intima, and by the age of 25 – from 30% to 50%. In the coronary arteries, lipoidosis occurs from 10–15 years, in the arteries of the brain – at the end of the third decade of life (by 35–45 years) [2, 4].

Materials and methods. Lipid spots are small yellowish areas (up to 1.0–1.5 mm) in the intima of the aorta or large arteries. Lipid spots consist mainly of foam cells containing a large amount of lipids, especially cholesterol (CS), and T-lymphocytes (T-LY). Macrophages (MF) and smooth muscle cells (SMC) are also present in lipid spots. Lipid spots are characterized by predominantly intracellular accumulation of CS esters. Connective tissue formation is observed around lipid spots. As the pathological process progresses, connective tissue grows in the areas of lipid deposition, which leads to the formation of fibrous plaques, in the center of which a lipid core is formed. This is facilitated by an increase in the amount of lipids released as a result of apoptosis of SMC, MF and foam cells overloaded with

cholesterol. Extracellularly located lipids impregnate the intima, forming a lipid core, which is an accumulation of atheromatous masses (lipid-protein detritus). Around the lipid core, a zone of connective tissue appears, initially rich in cellular elements (MF, foam cells, SMC, T-LF), collagen and elastin.

Results and discussion. A modern concept of 6 successive stages of atherosclerotic plaque development has been formulated [1]. The initial stages are characterized by gradual accumulation of lipids (stage 1), first intracellularly (stage 2), then extracellularly and formation of a lipid spot/strip (stage 3) and, further, a young atherosclerotic plaque (stage 4); then comes stage 5, characterized by development of fibrous plaque stroma with formation of fibrous capsule and fibrous cap of plaque; then stage 6 develops – unstable vulnerable plaque, which, in case of unfavorable outcome, is complicated by crack, rupture or rupture of fibrous cap and development of thrombosis with acute clinical manifestations. At the initial stage of formation of an atherosclerotic lesion, modification and, in general, dysfunction of endothelial cells occurs, manifested by: a) an increase in the permeability of the endothelium, especially for atherogenic, cholesterol-rich low-density lipoproteins (LDL), b) an increase in the adhesive properties of the endothelium, enhancing chemotaxis and migration of monocytes into the subendothelial space, c) a decrease in the vasodilating properties of the endothelium, which leads to a violation of local hemodynamics.

At the stage of lipid spot development, monocytes that have migrated to the subendothelial space are gradually transformed into MFs, which are activated and, via scavenger receptors, unregulatedly capture oxidized LDLs rich in cholesterol. The subsequent transformation of macrophages into cholesterol-loaded foam cells (FCs) leads to a gradual increase in first intracellular and then extracellular lipid accumulation in the subendothelial space, which is the morphological basis of the lipid spot/stripe [2]. At the stage of young plaque development, a lipid core is formed, which is then isolated from the surrounding tissues by a fibrous capsule containing collagen, proteoglycans, and activated SMCs that synthesize them. The area of the fibrous plaque capsule covering it from the side of the vessel lumen and called the “fibrous cap of the plaque” is the most vulnerable area in terms of the development of thinning, cracks, rupture and rupture. The progressive increase in the plaque collagenization process, observed at the next stage of the development of the atherosclerotic lesion – the stage of the fibrous plaque, occurs in parallel with the progressive accumulation of PC in the plaque core and the beginning of the development of their apoptosis. Activated MFs play an important role in the development of inflammation in fibrous plaque and the formation of unstable plaque, since they: a) secrete a significant amount of inflammatory cytokines that trigger a

cascade of inflammatory changes in the lesion, b) themselves actively produce and stimulate the production of tissue factor by endothelial cells, which enhances the penetration of monocytes, T-LF, neutrophils and other cells into the subendothelial space and into the plaque, c) produce a large number of active oxygen metabolites that activate oxidative changes in the plaque, especially the processes of lipid oxidation, cholesterol, through cytokines and chemokines, and also by increasing apoptosis processes in the plaque core, contribute to a decrease in the resistance of the fibrous cap of the plaque [3].

At the stage of development of unstable vulnerable plaque, the secretion of destructive metalloproteinases, which break down collagen and elastin of the fibrous cap of the plaque and aggravate destructive processes in the plaque core, becomes the dominant function of activated macrophages. The clinical and prognostic significance of the formed atherosclerotic plaque largely depends on the structure of its fibrous cap and the size of the lipid core. According to modern concepts [4], mature, formed atherosclerotic plaques are divided depending on their morphological structure into stable and unstable. Stable plaques are characterized by the presence of a well-defined dense fibrous cap, without its thinning throughout the entire length of the plaque and a small atheromatous core. Some plaques have calcium salt deposits at their base instead of an atheromatous core. A thickened fibrous cover of the plaque indicates a good reparative function of the intimal SMC. The cover of stable plaques consists of dense connective tissue, a significant part of which is made up of compactly located collagen fibers with a small amount of lipids and cellular elements - monocytes/MF, T-LF, SMC [5]. It is believed that the fibrous component of a stable plaque stenotic to the lumen of the artery predominates in volume over the lipid part and makes up more than 70% of the plaque [3]. There is data on a linear relationship between the degree of stenosis of the vessel lumen and the % content of acellular fibrous tissue and the lipid core of the plaque. Over time, a stable plaque can become fibrotic across almost its entire thickness, leading to critical stenosis of the vessel lumen.

A vulnerable unstable atherosclerotic plaque is a plaque in which a thrombogenic site is likely to form [4]. An unstable plaque or a plaque with a tendency to ulcerate and rupture has a cap of less than 65 μm with infiltration of MF and T-LF, a large lipid core relative to the entire plaque area of more than 40%. Increased neovascularization and a large number of PCs are observed around the core [2]. Currently, several histological types of vulnerable unstable plaques are distinguished [4], including fibroatheroma with a thin fibrous cap (lipid type), plaques with an increased content of proteoglycan or inflammation leading to erosion and thrombosis (inflammatory-erosive type) and plaques with necrosis/calcification

(dystrophic-necrotic type). In the work of Naghavi M. et al., the results on different types of instability of atherosclerotic plaques are summarized and presented, among which, nevertheless, three main types are clearly distinguished - lipid, inflammatory and dystrophic-necrotic [5]. The lipid type of unstable plaques is characterized by the presence of a large atheromatous core (circular or eccentrically located) and thinning of the fibrous cap from 15 to 45 μm. The atheromatous core, occupying from 39.3% to 85.4% of the plaque area, is represented by atheronecrotic detritus with a high content of lipids, cholesterol crystals and accumulation of PC at the periphery. The fibrous cap often contains a significant amount of inflammatory cells (MF and T-LF) and single SMCs [6]. The degree of cap infiltration by inflammatory cells can vary widely from case to case and in different plaques in the same deceased. In the lipid type of unstable plaques, the most frequently observed degree of inflammatory cell infiltration of the fibrous cap is moderate and severe. The uneven distribution of MF and T-LF in different areas of the plaque, revealed by immunomorphological research methods, indicates the activity of the inflammatory process in those areas of the fibrous cap where its ruptures are most frequently observed. The content of collagen fibers (the main component of the extracellular matrix, which determines the strength of the fibrous cap) in lipid type plaques is reduced. In most cases, an abundance of inflammatory cellular elements is observed between the loosely located and thinned collagen fibers [2].

Conclusion. Thus, an atherosclerotic plaque goes through a number of stages in the process of its development – from a lipid spot to atheromatosis, calcification and fibrosis with the development of complications in the form of ulceration, hemorrhage, thrombosis. In this case, the size of the plaque and the degree of stenosis of the vessel lumen can fluctuate significantly, regardless of its internal structure. At the same time, an indication for surgical treatment, regardless of the morphological heterogeneity of the atherosclerotic plaque, which determines its stability or instability, is the degree of stenosis of the vessel of more than 50%, causing significant local and systemic hemodynamic disturbances. In this regard, the morphology of an atherosclerotic plaque can determine not only the development of early postoperative complications, but also their nature (rupture, vessel thrombosis, embolic syndrome), as well as the possibility of carrying out differentiated corrective therapy in the rehabilitation period after surgical treatment [6].

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