Available online at www.jmpas.com

ISSN NO. 2320 – 7418

DOI:10.22270/jmpas.v9i4.967

REVIEW ARTICLE

STEPS OF ATHEROSCLEROSIS AND ITS COMPLICATION

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Keywords
Atherosclerosis, complications, formation, HDL, LDL

Received
15/09/2020
Reviewed
20/09/2020
Revised/ Accepted
27/09/2020

ABSTRACT

Atherosclerosis is hardening, losing of stiffness of arteries because of athermanous plaque this formation can be seen in the artery wall. Atherosclerosis is silent without any symptoms for years as it takes time to cause narrowing or closing of the artery due to clots and symptoms that occur only after severe narrowing and closing that ceases blood to different body organs that instead lead to many other complications. Plaque is formed of different types of fatty deposits which also include cholesterol, cellular waste products, calcium, and fibrin. Plaque can be seen in the heart, legs, brain, arms, and kidneys. This can give rise to various conditions like coronary heart disease, angina pectoris, carotid artery disease, chronic kidney disease. The likelihood is determined by a combination of acquired and inherited risk factors. There is an increased prevalence of mortality in the United States, Africa, India, and Southeast Asia. The countries of the former Soviet Union hold a dubious distinction of having the highest ischemic heart disease mortality rate. The article gives detailed description on pathogenesis of athermanous and plaque along with its complications.

INTRODUCTIION

Atherosclerosis is a slow disease that takes several years to show its symptoms and it may begin in childhood or early 30s. This is idiopathic but there are many causes like hypertension, high cholesterol, and triglycerides. Lie habits is a huge part of causes but there are also other factors. Atherosclerosis starts in arterial walls which consist of three layers lined by smooth tissue. Three layers include

- Intima, the inner single-layered endothelium
- Media, smooth muscle layer to bear high flow pressure of blood
- Adventia, the connective tissue.

Basics of atherosclerosis

Atherosclerosis is an inflammatory disease and is the primary cause of heart diseases, occurred due to accumulation of inflammatory cells in middle layer that causes to blockage of the flow of blood. Pathogenesis is a complex process and involves high levels of serum low-density lipoprotein cholesterol. Due to high levels of LDLs present in blood flow, the endothelial cells undergo changes leading to activation/dysfunction and cause LDL particles to undergo infiltration and accumulation of fluid which in turn attracts other inflammatory cells and leads to plaque formation.

Plaque progression occurs when the vascular secretion of chemotactic and growth factors segregate and lead to generation of vascular smooth muscle cells (VSMC).[1] When the intima layer is invaded by VSMC, LDLs present in extracellular matrix (ECM) undergo oxidation mainly proteoglycans. Oxidized LDLs become the direction for the accumulation of pro-inflammatory mediators like interleukins, tumor necrosis factor, etc. causing the development of plaque. The oxidized LDLs attracts macrophages and convert into foam cells then into fatty streaks.

Steps of atherosclerotic plaque

Atherosclerosis has several stages of information and progression of plaque which are briefly described in the following:

1. **Fatty streak development**: This may start in early life like in the 20s itself. This is an initial step of plaque formation where LDLs enter middle layer and undergo accumulation when their amount increases in blood then oxidize to pro-inflammatory cells. Due to this accumulation, the inflammatory mediators activated and secrete VSMC that attracts monocytes, lymphocytes, mast cells, neutrophils, proteoglycans, collagen, elastic fibers.

Monocytes in intima get develops into foam cells via macrophage formation. This lipid deposition is considered as the first stage and can be treated based on the amount of accumulation of lipids.[2]

2. **Fibroatheroma formation**: It is observed in late teens. In this step the foam cells and inflammatory cells play a key role in the progression of atheroma. Proteoglycans that are secreted from extracellular matrix increases the lipid-binding capacity. In this process, few cells may die and these dead cells progress the inflammation.[3]

All the dead cells are accumulated and covered by a lipid-rich core which occupies about 50% of arteries diameter leading to obstruction.

3. **Thin-cap fibroatheroma and rupture**: This is seen in persons above 50 yrs. A thin cap develops over the plaque. In some areas the cap becomes thin and may rupture leading to thrombogenesis which is a life-threatening risk. This occurs mainly in the cardiovascular system leading to many diseases. The ruptured caps sometimes heal and involve again the accumulation of collage leading progression of atheromatous plaque.[4]

Localization of plaque

After the atherosclerotic plaque formation the stability of plaque is also an important factor for complicating the condition. Atherosclerotic plaque mainly occurs at coronary arteries, major branches of aortic arch, abdominal aorta.[5] Hemodynamic factors like blood flow velocity and alteration in shear stress are factors that effects the growth of paque. While large necrotic core, high macrophage content, reduced collagen levels, thin fibrous cap leads to rupture of plaque making it more complicated.

Complications of atherosclerosis

The complications vary depending on plaque formed in vessel. Most common locations of plaque formation include:

- Dorsal area of the abdominal aorta
- The femoral artery at adductor hiatus
- Proximal coronary arteries
- Descending thoracic aorta
- Internal carotid arteries
- Renal arteries.

There are two types of plaque formation depending upon the stability of plaque. They are:

a) **Vulnerable plaques**: This type of plaque forms thrombi (75%) due to plaque rupture. Thin cap fibro atheroma formation is an underlying mechanism in formation of vulnerable plaques. Other features include remodeling, hemorrhage, Inflammation and calcification, angiogenesis. Vulnerable plaques contain high amounts of inflammatory mediators that makes the plaque to rupture very easily.[6]

b) **Stable plaques**: These are mostly silent and doesn't undergo further proliferation and doesn't cause that harm when compared with vulnerable plaques. So, these don't undergo rupture and are stable in their place of formation.

The complications of atherosclerosis can be understood with the following consequences:

- ✓ **Narrowing of vessel wall**: The rupture causes the release of pro-coagulator mediators into the bloodstream at plaque and leads to erosion and fissuring of the fibrous cap surface. This cap is dissolved with the help of pro-fibrinolytic enzymes called streptokinase and tissue plasminogen activator. This leads to thrombus formation seen in stroke, myocardial infarction, intestine gangrene.
- ✓ **Chronic occlusion**: when the plaque becomes incompletely ruptured this leads to the accumulation of more and more collagen into plaque this leads to increase in clot and obstruction of blood flow. This is clinically seen in angina or intermittent calcification.
- ✓ **Embolization:** This is seen when the disrupted atheroma is migrated to distal vessels causes occlusion in those sites. These are mainly seen in the popliteal artery resulting in gangrene of leg.
- ✓ **Aneurism:** After plaque rupture, the lesion extends to the middle layer of blood vessel leading to atrophy i.e. change of shape and appears bulge like structures o blood vessels called aneurism.
- ✓ **Chronic kidney disease:** Atherosclerosis leads to narrowing, preventing oxygenated blood to kidneys. This effects kidney functioning leads to chronic kidney disease.[6]
- ✓ **Stroke or TIA in the brain:** When the large vessel in the brain is occluded due to plaque formation it results in the insufficient flow of blood and nutrients to the brain leading to an ischemic condition that leads to Intracranial atherosclerotic disease (ICAD).[7]

- ✓ **Erectile dysfunction in male:** In a way it is not directly related to heart but the penis requires free blood flow for proper erection. When the plaque forms in arteries that allow blood flow to the penis it results in erectile dysfunction.
- ✓ **Peripheral artery disease:** This is normally seen when the arteries of legs are blocked due to plaque formation or it may also occur due to embolization of atheroma that leads to pain and numbness of feet, decreased nail growth on toes, non-healing sores.

DISCUSSION

Atherosclerosis is a major risk factor for many diseases. Hypercholesterolemia, an increase of LDL, a decrease of high-density lipoprotein (HDL), lipid oxidation, and hypertension are factors that lead to atherosclerosis. Lipid oxidation is the first step of the process, Malondialdehyde (MDA) shows lipid peroxidation levels, C - reactive protein (CRP) indicative marker of inflammation, fibrinogen accumulation is atherogenic. People with Diabetes, family history of cardiovascular disease (CVD), age, obesity, sleep apnea is at higher risk (risk factors) for atherogenesis.

The summary of the atherogenesis is described in the following order:

- Endothelial injury and dysfunction: Increased vascular permeability, leukocyte adhesion, thrombosis.
- Accumulation of lipoproteins: Mainly LDLs are accumulated at injury and undergo oxidation.[8]
- Monocyte adhesion to endothelium: Here foam cells formation occurs and also migration of monocytes into intima occur.
- Platelet adhesion: Now in intima the monocytes and macrophages attract platelets nearby that area.[9]
- Release of mediators: These adhesion molecules activates other factors that release VSMCs, pro-inflammatory mediators for further growth of plaque.[10]
- Smooth muscle cell proliferation: This leads to the activation of the immune system mainly T-Cells.
- Accumulation of lipids: The plaque increases in size by attracting more amounts of lipids.[11]

CONCLUSION

Atherosclerosis can cause chest pain, dizziness, weakness. The process takes lots of years and is asymptomatic in starting and symptoms appear at a late stage and few times it cannot show any symptoms but leads to more complications. But when mild symptoms appear the stage can be seen. By looking at the plaque phenotype at different stages, the prevention on early treatment could prevent complications.

ABBREVIATIONS

LDL: low-density lipoprotein; VSMC: vascular smooth muscle cells; ECM: extracellular matrix, TIA: transient ischemic attack, ICAD: Intracranial atherosclerotic disease, MDA: Malondialdehyde, HDL: high-density lipoprotein, CRP: C - reactive protein, CVD: cardiovascular disease.

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