Progress in Atherosclerosis and treatments

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Abstract. Atherosclerosis is a lethal disease due to the fact that it is basically asymptomatic and acute. It is characterized by the formation of foam cells inside the patients' arteries. The formation of foam cells is highly related to the high blood concentration of LDL which is mainly caused by the high volume of cholesterol intake. The people who are smoking, with high blood pressure, diabetes, old age or sedative lifestyle are very much vulnerable to atherosclerosis. Patients with contracted atherosclerosis often do not feel any discomfort until the condition is serious, therefore, regular examinations are vital to reduce the casualty rate of the patient, particularly for those people among the high-risk group. The most effective therapy for atherosclerosis is through a surgeon, while some medicines can improve the symptoms of the disease. However, atherosclerosis can rarely be reversed by drug treatment. Therefore, a healthy lifestyle is very important for the people who contract or are vulnerable to atherosclerosis. This includes low calories, low cholesterol diets and doing plenty of exercise.

Keywords: Atherosclerosis, Intima, Cholesterol, Inflammation, Foam cells.

1. Introduction

Atherosclerosis is a notorious disease which occurs at inner layers at some major arteries [1]. It is not a contemporary disease accompanied with modern civilization, instead, it was frequently reported in paleopathology. The earliest evidence of atherosclerosis was made in 2003 by William A. Murphy et al with the help of CT scan of a 5300-year-old mummy named Ötzi, the Iceman. It reports that the atherosclerotic lesions were spotted in the mummy's aorta, and in the coronary, carotid as well as iliac arteries, which proves that macrophage build up existed even in human early civilization [2]. Even though with a very long history, atherosclerosis is still one of the most causes of death, disability and hospitalization in contemporary society [3]. The high casualty rate of atherosclerotic diseases can be mainly blamed on the hidden symptom of atherosclerosis; therefore, the patients are often not alarmed until a significant blockage is formed inside the main conduit arteries [4]. Regarding this, an early diagnosis and regular examination is crucial for the survival of the patients. And atherosclerosis is able to be slow down or even stop atherosclerosis by the activities which are beneficial to get rid of the risk factors, such as stopping smoking, healthy diets and maintaining an energetic lifestyle [5]. In general, atherosclerosis is hardly reversed but certain medication and healthy lifestyle, including stopping smoking, good diet and enough exercising are beneficial to stop atherosclerosis getting worse.

2. Mechanism

The process of formation of artery blockage can be concluded to three stages, refer as lipid invasion, oxidation, and modification, which follows with the inflammation at the damaged intima of the walls of the arteries [6]. Our artery is made up of three major layers, named as the intima, media and the adventitia from inside to outside. The innermost layer of the artery is the intima and it is made of endothelial cells. This endothelial cell layer is semi porous. Under certain conditions, for instance, with the influence of risk factors, this barrier becomes permeable to LDL and then some immune cells. This early risk development can be found even in childhood and adolescence [7-9]. After some very small low density lipoprotein LDL forces its way into the intima, it will immediately be oxidized due to the oxide abundance environment inside our arteries as their main mission is transporting oxygen inside our body. LDL. Early fibroatheroma occurs among the group of people in their teens and 20s [10,11], the macrophage circulating inside the artery is attracted by the oxidised LDL and also enter the intima at the location of the oxidised LDL, the macrophage will phagocytose the oxidised LDL and as it engulfs more and more oxidised LDL, the macrophage is now full of lipids and they are known as foam cells. HDL can usually keep the progression of foam cells under control in normal conditions, finally macrophage plaque formation occurs in age groups over 55 years. During the stage of plaque development, a yellow streak inside the arterial walls is built up and sometimes rupture [12,13], In a condition where the HDL level is low, the form cell will keep getting bigger and bigger by keep engulfing more oxidised LDL, eventually the oxidised LDL will poison and kill the foam cells. apoptosis. The apoptosis of foam cells will trigger the recruitment of other white blood cells and the release of inflammatory cytokines. Cytokines start to recruit and activate other inflammatory cells and promote their retention inside the blockage, in consequence a vicious circle is created to push forward the development of lesions inside the arterial walls.

3. Symptom

Atherosclerostic blockage is characterized as a yellow streak and foam cell debris on the artery wall. It is visible by CT scan but the atherosclerosis is basically asymptomatic. Many people with atherosclerosis don't experience any symptoms, especially if their disease is mild. But when the buildup inside the arteries reduces the enough blood flow reaching some organs, symptoms would arise and could produce serious damage [14]. According to the clinic statistics, the macrophage plaque begins to produce some obvious symptom when the artery is blocked by 70% or more [15]. And the symptoms might be varied depending on the location of the blockage. It can be at the heart, brain, digestive system, kidney, limb and so on, which depends on the restriction of blood flow on the specific pathway. The symptom of chest pain, also named as Angina, is a very alarming signal that the flow to the heart is restricted. The people with Angina symptoms should be hospitalized for medical or surgical treatment because the reduction of blood supplies to the heart may cause permanent damage to cardiac muscles. Though the symptoms of atherosclerosis are not obvious and painful, it is necessary to have a full examination and receive proper treatments when people feel relevant symptoms or over certain age, because macrophage blockage can be very lethal, particularly at the situation of plaque rupture which refers to that the plaques can split open (rupture), exposing the material within to the bloodstream. This material triggers blood clot formation. These blood clots can suddenly block all blood flow through the artery, which is the main cause of a heart attack or stroke. Therefore, for those people with risk factors, even though they do have any symptoms. should take regular examinations annually.

4. Trend of contraction of atherosclerosis

The peak of coronary heart disease mortality was seen in 1960s and then went downhill quickly afterward. 3 According to a recent study, there appears to be a significant drop of mortality of atherosclerosis in most high-income countries since the middle 20 century. It is likely because of advances in medical diagnosis and treatment as well as awareness of healthy lifestyle in those developed regions. On the basis of gender respect, compared with men, young women are less vulnerable to atherosclerosis [16]. It might be contributed to the fact that more men are smoking and with higher blood

pressure than women. Other than the sex, race differences also play a role on the risk of atherosclerosis. It is reported that male blacks, Hispanics, and Asian-Pacific islanders have the higher stroke mortality rates (adjusted for age) than Whites. It is noticeable that White and Black women often experience a second stroke during the following 5 years after the first event [17].

5. Treatment

5.1. Surgical treatment

There are both surgical and medical treatments for atherosclerosis. Surgeon is a very important treatment for atherosclerosis, particularly when the patients are in a very emergent condition, and the drugs cannot help the release of symptoms of atherosclerosis. The surgical procedure can be the following ways: arterial reconstruction to reconnect the pathways of blood flow back to or nearly back normal; an operation to improve the efficiency the cardiac circulation; Symptom improvement, mainly refers to the chest pain by limiting or removing the function of damage to cardiac tissues [18]. Among those treatments, arterial reconstruction is the most important and effective way to cure atherosclerosis. This surgical process aims to increase the blood supplies to the heart by physically dilating the narrowed blood vessel. Sometimes a small mesh tube called a stent is placed in the artery to open up the blood transporting channels. A stent is a mesh coil that is capable of holding its structure. During this treatment, A guide wire is used with a flat balloon at the tip of the guide wire, the balloon is coated with a stent on its surface. The guide wire will help the balloon with the stent to reach the destination which is the part of the artery with lipid plaque formed. The balloon is then inflated to give structure to the stent to widen narrow artery walls. And the guide wire will remove the balloon and the stent is left inside. Another way to improve the blood circulation is to bypass the artery bypass surgeon, instead of opening up the blood vessel, this means of treatment is to make a detour for the narrowed arteries. The blood therefore is able to find the ways to supply to the main organs like heart, kidney. Finally, the most direct way is to remove plaque buildup from the carotid arteries to restore the blocked or narrowed pathway inside the blood vessel. In general, physical surgeons are very much effective and suitable in emergency situations.

5.2. Medication

Generally speaking, atherosclerostic blocks cannot be reversed through drug treatment, however, the risks of getting atherosclerosis can be reduced by some main therapies. First of all, prevention is always better than medication. This means a healthy lifestyle is vital for the treatment of atherosclerosis. To remove the risk of the buildto -up in the arteries, patients should keep away from smoking and alcohol, and reduce sugar and saturated fat intake. Apart from those risk control, doing proper regular exercise is also very beneficial to prevent even reverse the disease. On the basis of minimizing the risks, there are some medical treatments that are universally used in the clinic. For example, Antiplatelet drugs like aspirin are widely used to reduce the risk of stroke and heart attack. But the use of antiplatelet drugs always comes with another risk of hemorrhage [19], therefore, it can only be used with caution. Apart from antiplatelets medication, some blood pressure mediators are also popular in the clinic, like Beta blockers. On the one hand, Beta Blockers are able to lower the blood pressure which is the main cause of atherosclerosis, on the other hand, it can also dilate the blood vessels. The expansion of arteries, particularly for the Coronary Artery, are very much effective to prevent the symptom of Angina while the Angina is the top killer caused by the atherosclerostic blockage. Nevertheless, the side effects of blood pressure mediators are rather heavy and it has to be taken consistently. I tend to believe that the most recommended treatment is by cholesterol lowering drug, for example, Statins. This therapy produces the lowest side effects and focuses on removing the initial risk of atherosclerosis, cholesterol, therefore, it becomes more and more popular in the therapy of atherosclerosis. Of course, there are still some other drugs for the treatment of atherosclerosis, such as anti-oxidation agent, anti-inflammatory drugs. In the clinic, more than one kind of treatment should be combined for the therapy. For instance, the patient with diabetes at the same time must be treated with anti-diabetes medication.

6. Conclusion

In conclusion, atherosclerosis is a very dangerous disease and without perfect medical treatment at present. A very good and healthy lifestyle and efficient exercise is very crucial for the treatment. Besides, some traditional herbs which are used in the heart-relative disease might give us direction on finding the new medicines for Atherosclerosis.

References

- [1] Insull, W., Jr. (2009). The Pathology of Atherosclerosis: Plaque Development and Plaque Response to Medical Treatment. The American Journal of Medicine, 122(1A), 1-8.
- [2] Murphy, W. A., Jr., Zur Nedden, D., Gostner, P., Knapp, R., Recheis, W., & Seidler, H. (2003). The Iceman: Discovery and Imaging. Radiology, 226(3), 614-629.
- [3] Benjamin, E. J., Muntner, P., Alonso, A., et al. (2019). Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association. Circulation, 139(10), e56-e528. https: //doi.org/10.1161/CIR.00000000000659
- [4] Martel, J. (2024, April 11). What is atherosclerosis? Healthline. https://www.healthline.com/ health/atherosclerosis
- [5] WebMD Editorial Contributors. (n.d.). Atherosclerosis, Symptoms, Causes, and Prevention. WebMD. https://www.webmd.com/heart-disease/what-is-atherosclerosis
- [6] Insull, W., Jr. (n.d.). The Pathology of Atherosclerosis: Plaque Development and Plaque Responses to Medical Treatment. The American Journal of Medicine. https://www.amjmed. com/article/S0002-9343(08)01017-6/pdf
- [7] Stary, H. C. (2003). Atlas of Atherosclerosis: Progression and Regression (2nd ed.). New York: Parthenon Publishing Group.
- [8] Strong, J. P., Malcom, G. T., McMahan, C. A., et al. (1999). Prevalence and extent of atherosclerosis in adolescents and young adults: Implications for prevention from the Pathobiological Determinants of Atherosclerosis in Youth Study. JAMA, 281, 727-735.
- [9] Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Research Group. (1993). Natural history of aortic and coronary atherosclerotic lesions in youth: Findings from the PDAY study. Arteriosclerosis, Thrombosis, and Vascular Biology, 13, 1291-1298.
- [10] Virmani, R., Kolodgie, F. D., Burke, A. P., et al. (2000). Lessons from sudden coronary death: A comprehensive morphological classification scheme for atherosclerotic lesions. Arteriosclerosis, Thrombosis, and Vascular Biology, 20, 1262-1275.
- [11] Eggen, D. A., & Solberg, L. A. (1968). Variation of atherosclerosis with age. Laboratory Investigation, 18, 571-579.
- [12] Cheruvu, P. K., Finn, A. V., Gardner, C., et al. (2007). Frequency and distribution of thin-cap fibroatheroma and ruptured plaques in human coronary arteries: A pathologic study. Journal of the American College of Cardiology, 50, 940-949.
- [13] Moreno, P. R., Purushothaman, K. R., Zias, E., et al. (2006). Neovascularization in human atherosclerosis. Current Molecular Medicine, 6, 457-477.
- [14] Dunleavy, B. P., & Yoon, C. (2022, December 30). What is Atherosclerosis? Symptoms, Causes, Diagnosis, Treatment, and Prevention. Medically reviewed by Chun Yoon, MD.
- [15] Parker, H. (2023, April 27). Clogged Arteries (Arterial Plaque). Medically reviewed by Jabeen Begum, MD. https://www.webmd.com/heart-disease/clogged-arteries-arterial-plaque
- [16] Poznyak, A. V., Sukhorukov, V. N., Guo, S., Postnov, A. N., & Orekhov, A. N. (2023). Sex Differences Define the Vulnerability of Atherosclerosis. Clinical Medicine Insights. Cardiology, 17, 11795468231189044. https://doi.org/10.1177/11795468231189044
- [17] Howard, V. J. (2013). Reasons underlying racial differences in stroke incidence and mortality. Stroke, 44, S126-S128.
- [18] Riccioni, G., & Sblendorio, V. (2012). Atherosclerosis: from biology to pharmacological treatment. Journal of geriatric cardiology: JGC, 9(3), 305–317. https://doi.org/10.3724/SP.J. 1263.2012.02132

Proceedings of ICBioMed 2024 Workshop: Computational Proteomics in Drug Discovery and Development from Medicinal Plants DOI: 10.54254/2753-8818/71/2024.LA18222

[19] Capodanno, D., & Angiolillo, D. J. (2023). Personalised antiplatelet therapies for coronary artery disease: What the future holds. European Heart Journal, 44(32), 3059–3072. https://doi.org/ 10.1093/eurheartj/ehad362