Advances in the pathogenesis and ultrasonic diagnosis of senile calcific valvular disease of the heart

Jian-Qiu Gao

Department of Ultrasound, the People’s Hospital of Qianxi County Hebei Province, Tangshan, Hebei Province, 064300

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ABSTRACT

Objective: Senile calcific valvular disease of the heart is an endemic valvular heart disease in the elderly patients. The disease is mainly characterized by degenerative change, thickening, fibrosis and calcification of the valvular connective tissue, which leads to the dysfunction of the valve and its stent. The pathogenesis of calcified valvular heart disease has not been fully elucidated, and it may be related to hemodynamics, atherosclerosis and sex. Echocardiography is the basic method and important basis for clinical diagnosis of calcified valvular heart disease, and it might detect the valvular thickening or calcification. This article aimed to analyze the pathogenesis of senile calcified valvular heart disease. At the same time, this research tried to review the progress on ultrasonic diagnosis of senile calcified valvular heart disease in order to provide references for clinical diagnosis and treatment.

1. Introduction

The senile calcific valvular disease of the heart (SCVDH) is the valvular heart disease specific in the elderly, which is mainly characterized as degenerative change, thickening, fibrosis and calcification of valvular connective tissue, and will result in the dysfunction of valve and its stent[1,2]. However, the pathogenesis of calcific valvular heart disease is not clear, which may be related to cholesterol level, inflammatory cells, alkaline phosphatase, cell death and vasogenic factors. At the same time, the susceptibility factors of senile calcific valvular disease of the heart include hemodynamic factors, advanced age, hypertension, atherosclerosis, bone demineralization, hyperlipidemia and glucose metabolism disorder[3,4]. The purpose of this paper is to analyze the pathogenesis of senile calcific valvular heart disease and review the progress on ultrasonographic diagnosis of senile calcific valvular disease of the heart to provide references for clinical diagnosis and treatment.

2. Pathogenesis of senile calcific valvular disease of the heart

Earlier studies believed that senile calcific valvular disease of the heart was a passive natural aging process, but recent studies have shown that cardiac valve calcification is a process of ectopic calcification, and the pathological process may be the active regulatory process of heart valve of osteopontin, bone matrix protein and other bone-related proteins in the cardiac valve[5,6].

2.1 Osteopontin and calcific valvular disease of the heart

Osteopontin is a phospholipoprotein associated with physiological or pathological mineral precipitation, and it is a protein molecule that regulates bio-calcification function[7]. Osteopontin has the dual physiological functions of inhibiting mineral precipitation and actively promoting mineral decomposition, i.e., osteopontin is a natural inhibitor of heterotopic calcification.
2.2 Vascular endothelial growth factor and calcific valvular disease of the heart

Vascular endothelial growth factor (VEGF), i.e., vascular permeability factor, is the cytokine that is able to increase vascular permeability, and promote vascular endothelial cell proliferation and metastasis as well as angiogenesis. Vascular endothelial growth factor is mainly combined with its receptor to play its pathological and physiological roles. Vascular endothelial growth factor can regulate the physiological processes of fracture repair and perichondral ossification[8,9], and the angiogenesis in calcific valve relies mainly on the vascular endothelial growth factor and transforming growth factor β [10].

2.3 Apoptosis and calcific valvular disease of the heart

Apoptosis is a programmed cell death process, and the apoptosis body removal disorder formed in the process of apoptosis is a key factor in the calcification of the living heart valve. Apoptotic bodies have the effect of altering the vascular endothelial integrity and increasing the visible calcium deposition. The apoptotic body provides the basic part of calcium binding in the pathological process of senile cardiac valve calcification.

2.4 Inflammatory response and calcific valvular disease of the heart

Like atherosclerosis and other diseases, senile calcific valvular disease of the heart is essentially an inflammatory response. Existing evidence has shown that there is the obvious aggregation of lymphocytes and macrophages in cardiac valve calcification site in the process of heterotopic ossification, and the cytokines produced by lymphocytes activate macrophages and are calcified. At the same time, inflammatory response factors promote angiogenesis and cardiac valve calcification by releasing growth factors, chemokines, hydrolytic enzymes and inflammatory mediators[11].

3. Clinical characteristics of senile calcific valvular disease of the heart

Senile calcific valvular disease of the heart usually progresses slowly in clinical practice and has no obvious clinical features within a long time, so it is not easy to be found[12]. The elderly patients with calcific valvular disease of the heart may even be in a subclinical process for life, and once they enter the clinical stage, it indicates that the clinical symptoms are more serious. Senile calcific valvular disease of the heart is clinically manifested as palpitations, shortness of breath, chest distress, exertional dyspnea, angina pectoris and so on, and a few elderly patients with calcific valvular disease of the heart may have headaches, dizziness and other symptoms of cerebral blood supply shortage. Existing evidence has shown that some elderly patients with calcific valvular disease of the heart may be accompanied by colonic vascular lesions and lower gastrointestinal bleeding.

Aortic reflux murmur seldom occurs in clinical practice, and once it occurs, it indicates that the calcification degree of aortic valve is already very serious. Mitral annular calcification can cause significantly adverse effect on the conduction system, and most patients may have atrioventricular block or bundle branch block. In addition, when the calcification is serious and affects valve leaflets, it may induce thrombosis, and thromboembolus detachment can lead to vital organ embolization and be clinically manifested as key visceræ embolism.

4. Predisposing factors of senile calcific valvular disease of the heart

The etiology of senile calcific valvular disease of the heart is not clear and may be related to hemodynamics, age, hypertension, metabolic disorder and other processes[13]. Pathological anatomy has shown that the elderly calcific valvular disease of the heart mainly affects the left heart valve, and the left heart valve is the valve with the largest blood flow impact and pressure. After mitral valve replacement, the buffer effect of valve leaflets disappears, and the left ventricular systolic pressure is mainly born by the valvular annulus, so the patients are prone to mitral annular calcification within three or four years after the operation.

About 1/5-1/2 of the patients with calcific valvular disease of the heart are associated with hypertension[14]. Hypertension can on the one hand, lead to the increase of lysosome in smooth muscle cells and not facilitate the removal of cholesterol in artery walls, and on the other hand, also cause collagen fiber breakage and form gap to cause the adsorption of various calcium salts on tissue surface and cause or aggravate cardiac valve calcification. At the same time, advanced age is also the key factor of the onset of senile calcific valvular disease of the heart: autopsy has shown that the detection rate of valvular calcification is increasing with the growth of the age, and it shows that senile calcific valvular disease of the heart is a degenerative change closely related to age.

Glycolipid metabolism disorder and atherosclerosis are common and frequently-occurring diseases in elderly patients, and senile calcific valvular disease of the heart is also common in elderly patients[6,15]. Evidence has shown that senile calcific valvular disease of the heart has certain correlation with the glycolipid metabolism disorder and atherosclerosis. Esophageal echocardiography has
confirmed that mitral annular calcification and aortic root sclerosis are closely related to the atherosclerosis in aorta and peripheral artery. In addition, echocardiography for aortic valve calcification is a noninvasive, effective and important reference index to identify the coronary artery disease, indicating that atherosclerosis is correlated with senile calcific valvular disease of the heart. Low density lipoprotein levels is closely related to the senile calcific valvular heart disease and coronary artery process, and to reduce lipid levels in the body by drugs or other means could significantly slow down the progress of aortic calcification. For example, the lipid-lowering drug Statin for patients with aortic stenosis can greatly reduce the pathological process of cardiac valve disease, showing that the disorder of lipid level is closely related to the pathological process of senile calcific valvular disease of the heart. At the same time, the elderly patients with calcific valvular disease of the heart are usually accompanied by glucose metabolism disturbance, and to regulate glucose metabolism disturbance can greatly relieve the pathological process of senile calcific valvular disease of the heart, indicating that glucose metabolism is also closely related to the pathological process of senile calcific valvular disease of the heart.

4. Laboratory examination and ultrasound of senile calcific valvular disease of the heart

Senile calcific valvular disease of the heart is usually without significant clinical symptoms in early stage and normally difficult to diagnose, and even the symptoms such as angina pectoris, syncope and heart failure that are manifested in the late stage are not specific typical symptoms of senile calcific valvular disease of the heart. At present, there is no unified diagnostic criteria for senile calcific valvular disease of the heart, but it can be considered in many aspects: over 60 years old; typical valve or valve annulus calcification process in echocardiography, and calcified shadow of valve or valve annulus in the chest CT or X-ray examination; systolic murmurs or/and diastolic murmurs in the aortic valve area, as well as atrioventricular block or intraventricular block in clinical monitoring. The laboratory examination methods of senile calcific valvular disease of the heart mainly include electrocardiogram, echocardiogram as well as chest X-ray and chest CT[16,17]. Ultrasonography can be used in the clinical diagnosis of senile calcific valvular disease of the heart, which reflects the patient’s disease symptoms, and should be widely used and popularized[18,19]. The electrocardiogram of mild senile calcific valvular disease of the heart may show no abnormality, but the electrocardiograms of aortic valve calcification and mitral valve calcification are usually characterized by premature beat, atrial fibrillation, atrial flutter and other atrial arrhythmia symptoms. Echocardiography is the most common method for clinical diagnosis of senile calcific valvular disease of the heart, and it has high sensitivity and specificity. The thickening or calcification of the valve can usually be detected by echocardiography. In addition, the calcification state around the valve can also be detected by echocardiography. At the same time, the mitral valve calcification detection by echocardiography shows obvious strong echo in anterior chamber of atrioventricular junction, and the detection of mitral valve and pulmonary valve calcification and sclerosis as well as tricuspid valve leaflet calcification will show echo enhancement or calcified spots. Senile calcific valvular disease of the heart is usually the degenerative change of heart valve fiber layer and the adsorption sedimentation of calcium salts, early onset is hidden and not easy to find, so it is prone to missed diagnosis, but once it gets worse, it easily leads to the abnormality of hemodynamic parameters in elderly patients with calcific valvular disease of the heart, and will cause congestive heart failure, myocardial infraction, cerebrovascular disease and severe arrhythmia. The lateral chest film of elderly patients with severe calcific valvular heart disease will usually show the expansion in ascending aorta and the calcification symptoms in aortic valve area, and the chest X ray can also detect this type of calcification[20,21]. There is also evidence that shows that the senile calcific valvular disease of the heart that cannot be detected by echocardiography can be detected by CT, indicating that the detection rate, specificity and sensitivity of chest CT are better than those of echocardiography.

5. Treatment, prevention and rehabilitation of senile calcific valvular disease of the heart

There is no effective clinical method to treat and slow down the senile calcific valvular disease of the heart, which is mainly treated by internal medicine or surgical treatment at present. Medical treatment mainly targets possible etiology and conducts corresponding treatment, such as controlling the hypertension, diabetes, hyperlipidemia, coronary heart disease and other susceptible factors in elderly patients with the disease. Generally speaking, for patients without clinical symptoms, their conditions can be dynamically monitored, and no treatment is needed. In addition, once the elderly patients are associated with arrhythmia, heart failure or arterial embolism, the characteristics of elderly patients should be referred to implement corresponding treatment. Although there is no drug for senile calcific valvular disease of the heart at present, the calcitonin and calcium channel blockers have the effect of blocking calcium deposit in the lining of blood vessels, and can be used to treat senile calcific valvular disease of the heart. In addition to medical treatment, valve replacement, balloon valvuloplasty and aortic valve calcification enucleation are the common surgical methods for clinical treatment of senile calcific valvular disease of the heart.
Senile calcific valvular disease of the heart is an age-related degenerative heart disease, and as aging of population increases, senile calcific valvular disease of the heart has become an important cardiovascular disease that affects the life quality and survival of the elderly. Based on the consideration that there is no special drug or therapy for senile calcific valvular disease of the heart, clinical positive response and prevention measures should be taken, for example, the elderly patients should live a regular life and alternate work with rest; timely therapies for hypertension, hyperlipidemia and diabetes mellitus should be done according to the risk factors of senile calcific valvular disease of the heart; to detect and control arrhythmia, heart failure and so on in time to delay the onset of senile calcific valvular disease of the heart. In addition, attention should be paid to matching dietary nutrition, quitting smoking and drinking, minding environmental changes and controlling blood pressure, blood lipids and blood glucose, and taking active measures to facilitate recovery on the basis of disease prevention and relief.

Summary

Senile calcific valvular disease of the heart is insidious, without obvious clinical features, and easy to miss. The aggravation of senile calcific valvular disease of the heart easily causes the change in hemodynamic parameters, arrhythmias and heart failure, and may even cause sudden death. It is believed that the pathogenesis of calcific valvular disease of the heart has not been fully elucidated, which may be associated with the hemodynamics, arteriosclerosis and gender. Electrocardiogram, echocardiogram, X-ray and so on are the important methods for clinical diagnosis of senile calcific valvular disease of the heart. Echocardiography is the basic method and important basis for clinical diagnosis of calcific valvular disease of the heart, and it can detect the thickening or calcification of the valve, so it is worthy of clinical promotion.

References