DILATED CARDIOMYOPATHY ETIOLOGY AND PATHOGENESIS

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Annotation

Causes and conditions for the occurrence of dilated cardiomyopathy, external and internal causative factors, types of conditions, mechanism of disease development, stages of disease development, consequences of the disease

Key words: Dilated cardiomyopathy

Dilated cardiomyopathy (DCM) is a disease of the heart muscle characterized by dilatation and systolic dysfunction of the left ventricle in the absence of filling disorders (hypertension, valvular disease) or coronary artery disease that can cause global worsening of systolic dysfunction. RV dilatation and dysfunction may also be present, but this is not necessary for diagnosis. Link: (https://compendium.com.ua/clinical-guidelines/cardiology/section-12/glava-9-dilatatsionnaya-kardiomiopatiya/)

Dilated cardiomyopathy (DCM) is a disease characterized by dilatation and decreased global contractility of the left ventricle or both ventricles. In the clinical picture of this disease, the main syndrome is progressive chronic heart failure (CHF). Arrhythmias, thromboembolism and sudden death are also typical. Data from histological examination of the myocardium are nonspecific. A feature of the 1995 WHO classification was the identification of new types of DCM: idiopathic, familial/genetic, viral and/or immune, alcoholic/toxic, associated with overt cardiovascular disease, in which the degree of myocardial damage cannot be explained by changes in afterload, preload or severity of ischemia. In addition to this, the term “specific cardiomyopathy” appeared - myocardial damage occurring against the background of specific heart diseases or systemic processes, mainly leading to LV dilatation, a decrease in its ejection fraction (EF) and severe CHF - i.e., in essence, to the development of DCM. In Russia, the term “ischemic cardiomyopathy” has become quite widespread. According to the 1995 WHO classification, this disease is one of the forms of coronary artery disease, in which multiple lesions of the coronary arteries and widespread diffuse fibrosis of the LV myocardium are detected, as well as dilatation of the heart cavities, decreased myocardial contractility, impaired intracardiac hemodynamics and symptoms of CHF, which cannot be explained by the severity of coronary disease and/or myocardial ischemia. In this case, the presence of true LV aneurysms excludes the diagnosis of ischemic cardiomyopathy. However, in our

country, some cardiologists and cardiac surgeons by ischemic cardiomyopathy, on the contrary, mean the presence of one or more post-infarction aneurysms with secondary LV dilatation and severe heart failure, which introduces some confusion.

Epidemiology

It is difficult to judge the true prevalence of DCM, since

the frequency of its detection in different regions is not the same. Idiopathic DCM is observed in 0.4 cases per 1 thousand population, 0.08 new cases per 1 thousand population are detected annually, which is approximately 25% of all cases of cardiomyopathy and is the cause of the annual death of 10 thousand patients. Men get sick on average 3 times more often than women.

Dilated cardiomyopathy is a dysfunction of the myocardium, leading to heart failure, in which ventricular dilatation and systolic dysfunction predominate. Symptoms include shortness of breath, fatigue, and peripheral edema. Diagnosis is based on clinical findings and elevated levels of natriuretic peptides, chest x-ray, echocardiography and MRI. Treatment is focused on eliminating the causes of the disease. If heart failure is severe and progressive, cardiac resynchronization therapy, ICD, relief of severe mitral regurgitation, left ventricular support, or heart transplantation may be indicated.

Etiology

The etiology of DCM has not been definitively established. Many researchers adhere to the polyetiological hypothesis of the origin of the disease - enough cases of the development of DCM, which is the end result of various pathological processes, have been described. There are idiopathic, familial (or genetic), viral (and/or immune) and DCM associated with known cardiovascular diseases.

Idiopathic DCM, which is a primary myocardial disease of unknown cause, develops in 40% of patients. Familial DCM is mainly associated with mutations in cytoskeletal and extracellular matrix genes.

Recently, significant progress has been made in the field of molecular genetics of DCM. In 20% of patients, the disease is inherited or there are indications in the family history. In hereditary forms, the type of inheritance has been established as autosomal dominant, autosomal recessive, and also associated with the X chromosome of the gene or mitochondrial transmission. Mutations were identified in the genes of cardiomyocytes that encode contractile proteins or their regulatory elements, including components of the sarcomere, cytoskeleton, as well as various mechanisms that ensure the coupling of excitation-contraction processes, beta-adrenergic pathways and processes leading to a deficiency of energy mechanisms, including mitochondrial mutations, glycogen metabolism, calcium metabolism, and transcription regulation.

The occurrence of DCM is associated with variants of actin gene mutations; the pathology of the dystrophin protein gene, which is part of the complex that connects

the muscular cytoskeleton of the cardiomyocyte with the extracellular matrix, is also important.

The results of the CARDIGENE study (1999) indicate that in DCM, genetic disorders of the endothelin pathways and polymorphism of the endothelin receptor type A gene are important - the first identified genetic risk factor for the development of the disease.

There is a viral-immunological theory of the occurrence of DCM. In DCM, a number of immune regulation disorders have been identified, including humoral and cellular autoimmune reactivity towards myocytes, a decrease in the content and cellular activity of natural killer cells, and abnormalities in the activity of suppressor cells. The presence of disturbances in immune regulation and a variety of anti-myocardial antibodies in DCM is consistent with this hypothesis: in an immunological study, an increase in titers of antibodies to the Coxsackie B3 virus was detected in 40% of patients with DCM and only in 2% in the group of healthy individuals, while it was not detected in endomyocardial biopsies signs of myocarditis. In 50% of patients with DCM, antibodies to the myocardium are detected, in 49% - anti-interfibrillar antibodies, in 30% - sensitization to cardiac antigen. Activation of autoimmune processes leads to the formation of antibodies to myosin and β1-adrenergic receptors.

The reason for the suppression of the activity of natural killer cells may be a primary violation of their maturation, determined by antigens of the HLA system; in patients with DCM, haplotypes HLA B27, HLA A2, HLA DQ4 and HLA DR4 are most often detected, which indicates a hereditary predisposition to the disease and indicates its possible immune basis. Despite the identification of humoral immunity disorders, in general, the viral-infectious-autoimmune hypothesis remains unproven today. Link: (https://compendium.com.ua/clinical-guidelines/cardiology/section-12/glava-9-dilatatsionnaya-kardiomiopatiya/)

Dilated cardiomyopathy has many known and likely many unknown causes (see table Causes of Dilated Cardiomyopathy [Causes of Dilated Cardiomyopathy]). More than 20 viruses can cause dilated cardiomyopathy. Temperate climate virus V zonax group V is the most common. In Central and South America, the most common cause of infection is Chagas disease, caused by Trypanosoma cruzi.

Other causes include long-term (chronic) tachycardia, HIV infection, toxoplasmosis, thyrotoxicosis and chronic diseases. Many toxic substances, especially alcohol, various organic solvents, iron ions and heavy metal ions, as well as specific chemotherapy drugs (for example, doxorubicin, trastuzumab), cause heart damage. Frequent ectopic ventricular rhythm (>10,000 ventricular extrasystoles per day) associated with left ventricular systolic dysfunction.

Sudden emotional stress and other hyperadrenergic conditions can lead to acute dilated cardiomyopathy, which is usually reversible (eg, prolonged tachycardia). The main cause is acute apical balloon cardiomyopathy (also called takotsubo

cardiomyopathy, stress-induced cardiomyopathy, or broken heart syndrome). This disease affects the apex, and sometimes even the second individual gastric tract, causing regional wall dysfunction and, in some cases, fecal dilatation (ballooning).

Genetic factors are important in 20–35% of cases; >60 known genes and loci associated with disease development.

As a primary myocardial disease, cardiac muscle dysfunction in dilated cardiomyopathy causes other disorders that can cause myocardial dilatation, for example, in the heart in acute coronary heart disease with pathological, occlusive ventricular hypertrophy due to changes in pressure and volume (for example, hypertension, valvular heart disease). It is believed that in some patients dilated cardiomyopathy begins with acute myocarditis (probably viral in most cases), accompanied by variable latency space, spatial diffuse necrosis of cardiomyocytes (as a result of an autoimmune reaction to damage to viral myocytes) and chronic fibrosis. Regardless of the cause, the myocardium dilates, thins, and compensatory hypertrophies (see figure Types of Cardiomyopathy [Forms of Cardiomyopathy]), often leading to functional mitral regurgitation and/or tricuspid regurgitation, as well as atrial enlargement.

Most patients have both stomachs, only the left ventricle (LV) and the right ventricle (RV).

Mural thrombi can occur as a result of blood stasis when the heart chamber is significantly enlarged and nonfunctional. Cardiac tachyarrhythmias often complicate the course of acute myocarditis and the late phase of chronic dilatation, and the development of atrioventricular block is possible. The consequence of dilatation of left atrial fibrillation often leads to atrial fibrillation.

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