Sarcomeric and non-sarcomeric forms of hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy is one of the most common types of cardiomyopathy with a frequency of **1:500** and also one of **the most frequent causes of sudden death in young individuals and athletes**. It is characterized by the thickening (hypertrophy) of the myocardium without the presence of left ventricular dilatation. Other pathologies that could explain the myocardial hypertrophy have to be excluded (e.g. arterial hypertension, aortic valve stenosis, ischemic heart disease, etc.).

The most common cause of hypertrophic cardiomyopathy is **mutation of genes encoding the sarcomeric components of cardiomyocytes**. However, the situation is complicated by the fact that **a specific mutation is identified in only about 50% of patients.** The condition is also complicated by the occurrence of mutations in which their association with hypertrophic cardiomyopathy is still unclear (variations of unclear significance). In some cases, hypertrophic cardiomyopathy also occurs in metabolic and neuromuscular disorders (**Fabry's disease** , Friedreich's ataxia).

The article on sarcomeric and non-sarcomeric forms of hypertrophic cardiomyopathy is a more detailed addition to the etiopathogenesis subsection in the article on hypertrophic cardiomyopathy. More information about this disease can be found in the relevant article.

Sarcomeric forms

Mutations most frequently affect the genes coding for the contractile myofilaments of the sarcolemma of cardiomyocytes. Mutations **in the beta myosin heavy chain** (*MYH7*) and **myosin binding protein C** (*MYBPC3*) genes predominate, present in up to 30% of screened hypertrophic cardiomyopathy patients. In about 5-7% the mutation affects the genes for troponin T (*TNNT2*) or alpha-tropomyosin (*TPM1*).

Non-sarcomeric forms

These forms of hypertrophic cardiomyopathy account for roughly 10% of all forms of this cardiomyopathy and include various metabolic and storage diseases. The development of cardiomyopathy is an important prognostic factor in them.

Fabry disease

Fabry disease is a genetically determined **X-linked** disease belonging to the group of lysosomal storage diseases. The pathophysiological basis is the **activity of the enzyme alpha-galactosidase A**. This leads to the **intracellular accumulation of glycosphingolipids**, which are deposited, among other things, in cardiomyocytes and in the walls of small vessels, which leads to their insufficiency. The disease most often manifests itself in men, however, women are also affected. Early clinical manifestations include anhidrosis, acroparesthesia, and specific skin lesions. Other manifestations are cerebrovascular, renal and cardiovascular involvement, dominated by more or less pronounced left ventricular hypertrophy.

Danon's disease

This disease also belongs to the lysosomal genetically conditioned diseases linked to the X chromosome. Pathophysiologically the involvement of the **lysosomal membrane protein 2 (*LAMP-2*) gene** is essential. The clinical picture of the disease is dominated by **cardiomyopathy, mental retardation and skeletal myopathy**. The prognosis of patients, especially men, is very unfavorable. In women, the disease usually has a less progressive course. There is occasionally extreme thickening of the walls of the left ventricle and the gradual development of ventricular dilatation, severe systolic heart failure and malignant arrhythmias.

Friedreich's ataxia

The disease is genetic and has an autosomal recessive type of inheritance. The basis of the disease in the vast majority of cases is **the amplification of genetic information** on chromosome 9 in the area encoding the protein **frataxin** , which plays a role in the assembly of Fe/S proteins of the respiratory chain. The main manifestation is a **neurodegenerative disease** with the development of ataxia, hearing impairment and eye problems. **Cardiovascular involvement** with the development of milder left ventricular hypertrophy is also typical, as well as heart failure, which is the dominant cause of patient mortality.

Others

There are a number of other etiologies of the so-called non-sarcomeric forms of hypertrophic cardiomyopathy, including, for example, Pompe disease, **PRKAG2 syndrome** (a defect in the gene for adenosine-monophosphate-activated protein kinase active during the energy processes of the cell, the clinical picture is dominated by conduction disorders), mitochondrial cardiomyopathy (defective oxidative phosphorylation, multiorgan impairment,

in the case of myocardial impairment with a very poor prognosis), **mucopolysaccharidosis**, **glycogenosis**, etc. In general, the diagnosis of these forms is based on **genetic**, laboratory or biopsy examinations of patients. Treatment is mostly supportive and symptomatic.

Links

Related Articles

- Hypertrophic cardiomyopathy

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