MORPHOLOGICAL AND VIROLOGICAL DIAGNOSTICS OF MYOCARDITIS IN PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY.

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A more recent definition and classification of cardiomyopathies was proposed by the American Heart Association (AHA) Scientific Statement Panel, which divides cardiomyopathies as follows: “Cardiomyopathies are a heterogeneous group of diseases of the myocardium associated with mechanical and/or electrical dysfunction, which usually (but not invariably) exhibit inappropriate ventricular hypertrophy or dilatation, due to a variety of etiologies that frequently are genetic. Cardiomyopathies are either confined to the heart or are part of generalized systemic disorders, and often lead to cardiovascular death or progressive heart failure-related disability.”

Cardiomyopathies may be primary (i.e., genetic, mixed, or acquired) or secondary (e.g., infiltrative, toxic, inflammatory). Major types include dilated cardiomyopathy, hypertrophic cardiomyopathy, restrictive cardiomyopathy, and arrhythmogenic right ventricular cardiomyopathy.
Classification of cardiomyopathies

- **Hypertrophic cardiomyopathy** is the most common primary cardiomyopathy and can cause exertional dyspnea, presyncope, atypical chest pain, heart failure, and sudden cardiac death.

- **Dilated cardiomyopathy** can be genetic or acquired and typically presents with classic symptoms of heart failure with reduced ejection fraction.

- **Restrictive cardiomyopathy** is much less common and often associated with systemic disease. Family physicians should be alert for acquired variants of cardiomyopathy,

  - including peripartum and **stress-induced cardiomyopathy**, as well as rare variants, such as **arrhythmogenic right ventricular dysplasia and left ventricular noncompaction**.
Hypertrophic cardiomyopathy (HCM)

- Hypertrophic cardiomyopathy (HCM) is the most common primary cardiomyopathy, with a prevalence of 1:500 persons. It is defined as left ventricular hypertrophy without chamber dilation and is caused by autosomal dominant mutations of genes that code for sarcomere proteins.
- Septal thickening predominates and may cause left ventricular outflow tract obstruction or mitral valve dysfunction.
- Many patients with HCM are asymptomatic and are diagnosed during family screening, by auscultation of a murmur, or incidentally after an abnormal result on electrocardiography. Presenting signs and symptoms most characteristic of HCM include atypical chest pain (which may be associated with meals, dehydration, or exertion) and sudden cardiac death.
- Patients who are diagnosed with HCM may have a family history of unexplained sudden cardiac death. On examination, physicians may hear a systolic murmur. Additionally, electrocardiography findings often show left ventricular hypertrophy and Q waves, and echocardiography results often show hypertrophy of the left ventricle coupled with reduction in ventricular chamber volume.
The etiology of HCM has similarly been sorted and HCM is an autosomal dominant genetic disorder, caused by mutations in at least 10 different genes, which code for sarcomeric proteins[73]. Mutations in the β-myosin heavy chain gene, myosin binding protein C and troponin T account for 70%-80% of all cases. The total number of mutations is > 100 and new mutations are being discovered[74]. These developments in the etiology of HCM resulted in a change of definition and HCM eventually was no longer a heart muscle disease of unknown cause.
THE GOAL OF THE STUDY

- To study the morphological changes and the frequency of viral genome detection in the myocardium in patients with true hypertrophic cardiomyopathy (HCM).
12 women and 4 men,

average age 42.9 ± 13.3 years, 18 to 60 years old

**inclusion criteria:**

- the thickness of the interventricular septum and / or wall of the left ventricle from 14 mm (according to echocardiography)
- genetic verification of primary cardiomyopathy
- myocardial biopsy - endomyocardial (n = 11), intraoperative (n = 4), autopsy (n = 1)

**Clinical and laboratory methods:**

- ECG, echocardiography; MSCT, heart MRI, coronary angiography (as indicated)
- The levels of anticardial antibodies in the blood and the viral genome by PCR in myocardial tissue were determined (herpes viruses 1,2,6 types, zoster, Epstein-Barr, cytomegalovirus, parvovirus B19, entero / adenoviruses) geneticist consultation, DNA diagnostics by direct sequencing method according to Senger

**Morphological methods**

- stained with hematoxylin-eosin, according to Van Gieson, Congo red, PAS, Perls and CD45 (DakoCytomation).
PRIMARY HYPERTROPHIDE CARDIOMYOPATHY CLINICS (n=16)

Obstructive form in 80%, mutations in *MYH7*
Stable heart decompensation -7 patients
Progressive heart failure – 9 patients
Myocarditis – 9 patients
Sudden cardiac death – 1 patient
PRIMARY HYPERTROPHICIDE CARDIOMYOPATHY (n=16)
Viruses in myocardium and blood

16 patients with primary HCM

11 patients with Viruses in myocardium

6 patients with Viruses only in myocardium biopsy
2 patients with Viruses only in blood
3 patients with Viruses in myocardium biopsy and blood

5 patients without Viruses
Detection of viral genome in patients with HCM

- parovirus B19: 14%
- herpes viruses type 6: 14%
- Epstein-Barr: 14%
- and their combinations: 14%
- No viruses: 44%
Coexistence of viruses in blood and myocardium and morphology of myocarditis

16 patients with primary HCM

9 patients biopsy with signs of inflammation in myocardium
- 5 from 6 patients with viruses in myocardium
- 1 from 2 patients with viruses only in the blood
- 3 patients from 6 with viruses in blood and myocardium

7 patients biopsy without signs of myocarditis
- 4 from 4 patients without viruses in the blood and myocardium
- 2 from 6 patients with viruses in the blood and myocardium
- 1 from 2 patients with viruses only in the blood
BIOPSY IN PRIMARY HYPERTROPHIDE CARDIOMYOPATHY (n=16)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency</th>
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<tbody>
<tr>
<td>viral genome, including parvovirus B19, herpes virus type 6, Epstein-Barr virus simultaneously a virus in the blood</td>
<td>73.3%</td>
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<tr>
<td>Dysarray of myocytes</td>
<td>70%</td>
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<tr>
<td>Hypertrophy of myocytes</td>
<td>100%</td>
</tr>
<tr>
<td>Degeneration of myocytes</td>
<td>70%</td>
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<tr>
<td>Inflammatory infiltration in myocardium (&gt;14 lymphocytes)</td>
<td>30%</td>
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<tr>
<td>Inflammatory infiltration in myocardium and endocardium</td>
<td>20%</td>
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<tr>
<td>Fibrosis</td>
<td>90%</td>
</tr>
<tr>
<td>Sclerosis/hyalinosis of vessels/склероз/гиалиноз сосудов</td>
<td>40%</td>
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In the only similar work in 42 patients with HCM and unexplained decompensation, myocarditis during biopsy was detected in 67% (virus-positive in half of the cases) and in none of the 77 patients with stable HCM (A. Frustaci, 2007)
CLINICO-MORPHOLOGICAL RELATIONSHIPS

- Stable heart decompensation - 7 patients with HCM
- Progressive heart failure – 8 patients with HCM and myocarditis
- Sudden cardiac death – 1 patient with HCM and myocarditis and endocarditis
CONCLUSION

1. Myocarditis may develop in patients with HCM and has viral etiology (parvovirus B19, herpes viruses type 6, Epstein-Barr and their combinations)

2. Diagnosis of viral myocarditis in HM is based on myocardial biopsy-morphology together with detection of viruses in the tissue of myocard, while suspicion may based on clinical dates and detection of viruses in the blood.

3. Myocarditis in patients with HCM has poor prognosis and results in progressive heart failure and sudden cardiac death.

4. Myocarditis with a high frequency is detected during myocardial biopsy in patients with HCM, including in the absence of clinical suspicion of it (intact systolic function), which must be considered when prescribing treatment to patients.
Thanks for attention!

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