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Left ventricular non-compaction associated with genetic disturbance of folic acid metabolism

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Short title: Left ventricular non-compaction and folic acid metabolism abnormality

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32-years old woman visited clinic for pre-operative clinical examination. Breast surgery was planned but during the pre-operative examination patient underwent ECG and it showed frequent polymorphic premature ventricular beats. Patient has never had any symptoms. No history of cardiovascular or rheumatic diseases was present.

Patient was examined by cardiologist. 24-hours ambulatory ECG monitoring showed sinus rhythm and 8500 polymorphic premature ventricular beats evenly distributed during the time of examination, included 432 coupled extrasystoles.
Cardiac Echo showed non-dilated heart chambers, non-affected valvular structures, high trabecularity of left ventricle and reduced ejection fraction (36%). Left ventricular non-compaction was considered.

Cardiac MRI with contrast enhancement was performed and confirmed left ventricular non-compaction with reduced systolic function.

Left ventricle end-diastolic volume – 200 ml., end-systolic volume – 131 ml., end-diastolic volume index – 122 ml/m², end-systolic volume index – 80 ml/m², stroke volume – 68 ml., cardiac output – 3.78 l/min., left ventricle ejection fraction – 34%. Diffusely reduced myocardial contractility was detected, but it was more pronounced in lateral-inferial-septal region. Interventricular septum – 11.8 mm., inferior wall – 13.7 mm. High trabecularity of sub-endocardial region was found. End-diastolic ratio of layers – 2.3 in segments 7,12, 15-17.

According to the presence of interventricular septum edema with the signs of inflammation located in lateral-inferior region of left ventricle associated with mild elevated levels of C-reactive protein (2.68 mg/l) and hs-troponin T (22.0 ng/l) sub-acute myocarditis was suspected (Fig. 1). Myocardial biopsy was not performed for technical reasons.

Patient was referred to genetic center for further examination. 2 mutations were found: MTFHR 1298 homozygote CC and MTFHR 677 heterozygote CT. Patient's relatives not underwent genetic testing. No hereditary cardiovascular diseases in close relatives were documented.

Left ventricular non-compaction is a cardiomyopathy caused by impaired evolution of prenatal myocardial compaction process. During embryogenesis the intertrabecular recesses interact with the left ventricle endocardium. It leads to the formation of myocardial capillaries [1]. Left ventricular non-compaction can be presented as solid abnormality as in combination with other hereditary structural defects [2].
MTHFR gene codes MTHFR-protein (methylene-tetra-folic-reductase enzyme) that is responsible for intracellular biochemical reaction of homocysteine transformation to methionine. This enzyme requires pyridoxine, cyanocobalamin and folic acid to perform its biological role. Detected gene mutations are known to be associated with structural conformation changes of MTHFR-protein binding sites responsible for linking with folic acid. Alterations of the folic acid intracellular metabolism during the period of embryogenesis results in neural tube malformations [3,4]. One of them is left ventricular non-compaction.

Also, we need to take into account the possible role of comorbid sub-acute myocarditis on left ventricular non-compaction as the additional factor for myocardial heterogeneity. Interestingly, the association of myocarditis with left ventricular non-compaction was previously been described [5].

Patient received recommendations to delay surgical procedure and start medical treatment with amiodarone.

On the next visits to the clinic patient had no complaints, no clinical signs of heart failure and no thromboembolic events.

Summing up, we would like to underline that sporadic genetic mutation of genes responsible for folic acid metabolism can lead to the formation of left ventricular non-compaction. This cardiomyopathy may have prolonged asymptomatic course (for decades of years). Comorbid subacute myocarditis, probably, can significantly increase the risk of clinically significant arrhythmic events.
References:


Fig. 1. Cardiac MRI (A, B) and Echo (C) showing a left ventricular non-compaction (details on text, own observation).