

CASE REPORT

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Clinical Course and Treatment of Dilated Cardiomyopathy During Twenty Years of Follow-up

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ABSTRACT

Objective: Demonstration of idiopathic dilated cardiomyopathy with unusual flow, unpredictable clinical picture and complex therapy. **Case report:** Patient A.P., female, 38 years old, had symptoms of dilated cardiomyopathy (with possible infectious myocarditis in the background) at age 17. After hospitalization for ten months and ten days, while waiting for heart transplantation (with threatening death outcome), without a clearly pronounced threatening arrhythmia, but with a low ejection fraction and a poor general condition, remission occurred. The therapy focused primarily on the treatment of heart failure, prevention of arrhythmia and thromboembolism. Normalization of the disease by improving the function of the left ventricle (expected in 16% of patients) occurred and lasted for 4 years, followed by an exacerbation of the disease that lasted for two years. In the next few years the patient was stable, had a first child with normal pregnancy. During the second trimester of the second pregnancy, there was an exacerbation (postpartum dilatation cardiomyopathy) lasting for couple of months. At the time of case report (May 2017), the patient is stable on therapy (ACE inhibitor, beta blocker, diuretics, If channel blocker), without limitation of physical capacity, mother of two children, unemployed. **Conclusion:** The clinical course of dilated cardiomyopathy is extremely unpredictable and therapy is very complex and demanding.

Keywords: dilated cardiomyopathy, clinical course, therapy.

1. INTRODUCTION

Cardiomyopathies are very heterogeneous group of heart muscle disorders, which cause heart dysfunction, and are characterized by progressive flow and often have long and unrecognized asymptomatic phase (1). In particular, primary cardiomyopathy, especially dilated, has increasing prevalence (1/2500 population aged from 30 to 40 years, and possibly more). Dilated cardiomyopathy (term established by W. Brigden 1957, and clinical characteristics first described by J.F. Goodwin in 1961), is chronic, mostly irreversible myocardial disease. It is primarily characterized by dilatation and systolic dysfunction of the left ventricle (remodeling with normal thickness of the walls). It can be genetic or acquired, inherited (25 to 50%) or non inherited, and is clinically divided into primary and secondary (Table 1). The diagnostic protocol of dilated cardiomyopathy includes anamnesis, physical examination, electrocardiography (ECG), ergospirometry, continuous 24-hour ECG Holter monitoring, radiological examination, echocardiography, CT angiography, MRI of the heart,

radionuclide ventriculography, and invasive diagnostics (catheterization, endomyocardial biopsy) with genetic analysis. Endomyocardial biopsy with cardiac catheterization may contribute to the clarification of the etiology, and in 25-30% of patients with a clinical picture of dilated cardiomyopathy, the cause of the disease is the mutation of a number of genes that encode different proteins in the heart muscle (e.g. troponin, myosin, desmin, etc.). The broad etiologic spectrum includes, apart from postmyocardial and ischemic dilatations, drug-induced dilatation (alpha-interferon, cytostatic drugs), drug addiction (cocaine), severe malnutrition, selenium deficiency (Keshan disease), carnitine deficiency, beriberi, and hereditary muscle diseases (Duchenne and Becker muscular dystrophies, Emery-Dreifuss muscular dystrophy), mitochondriopathy, delayed diseases, and some endocrinological and autoimmune diseases (2). Dilated cardiomyopathy is the most common cause of heart failure and the most common indication for heart transplantation.

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Therapy is demanding, highly sophisticated, extremely complex and multidisciplinary.

2. AIM

Demonstration of idiopathic cardiomyopathy with unusual flow, unpredictable clinical picture and complex therapy, with stages of improvement of stabilization, i.e. remission and exacerbation.

3. CASE REPORT

Patient A.P., female, born in 1979, has been diagnosed with dilatation cardiomyopathy in 1996. Anamnestically, disease started with tonsillitis, possible myocarditis (which was never proven), with pronounced symptoms of heart failure and general symptoms. She was hospitalized and after one month, the left ventricular ejection fraction was 10% with the aforementioned signs of congestive heart failure. She was hospitalized for 10 months and 9 days, with standard therapy for vitally endangered patient, oxygen support, numerous adjuvant therapy, and intensive monitoring. Therapy was administered (ACE inhibitor - ramipril, cardiotonic - digoxin, beta-blockers - metoprolol and combination of diuretics - furosemide and spironolactone), with the indication of heart transplantation. Clinical improvement occurred with an ejection fraction that was gradually increasing and at the age of 21 she entered in remission or stabilization phase, with the ejection fraction value of 48-57% (regular echocardiography was performed every three months). For the following four years therapy remained the same, but in Jun 2004 (after an episode of low immunity), ejection fraction fell to 25%, with a clinical deterioration of the disease. The patient was hospitalized for a period of two months, and the condition stabilized, and she was discharged with therapy that was the same but without cardiotonic. Ejection fraction was stabilized, and in year 2006 it was 50%. At the age of 27, the patient decided on the first pregnancy that was successful with beta blocker (metoprolol) in therapy. After the first pregnancy, the ejection fraction was 40% and she was treated with the same therapy with eplerenone (25 mg) instead of spironolactone. The ejection fraction was controlled and did not fall below 45%. At the end of 2015 the patient became pregnant for the second time, and the pregnancy went neatly until eighth month (35 weeks), when she was urgently admitted to hospital, due to sense of suffocation and inability to walk. Ejection fraction decreased to 18% (brain natriuretic peptide (BNP) was 2600 pg/ mL (reference values are 100-400 pg/ mL)). During pregnancy she received only metoprolol in therapy. Physicians decide to continue with her pregnancy, in the 39th week they performed c-section, and the condition stabilized again after twenty days. In October 2016 new mode of therapy was

administered, ramipril (2.5 mg, in the morning), metoprolol (47.5 mg, in the morning), spironolactone (50 mg, once a day) and ivabradine (5 mg, twice a day) with torasemide (5 mg, once a day). LifeVest Defibrillator was carried from 06 December 2016 until 27 February 2017 when it was removed. When removed and after examination (ejection fraction was 44%) she continued with ramipril therapy (1.25 mg) metoprolol (23.75 mg), torasemide (5 mg), spironolactone (25 mg) and ivabradine (7.5 mg, twice a day) with potassium supplements, and compliance with non-pharmacological measures (fluid intake restricted to 1.5 L/ day). The echocardiographic finding in March 2017 showed left ventricular dilatation with moderately reduced left ventricular function and left ventricular wall hypokinesia with ejection fraction of 44% (insignificant pericardial effusion was present, inferior vena cava with physiological flow, preserved valves function - Doppler sonography showed slight insufficiency of mitral valve with dilatation of anulus). Evaluation of a patient with ejection fraction 44% showed no indication for an implantable cardioverter defibrillator (ICD), and conservative procedure and medication therapy were recommended. Regular check-ups and body mass reduction, regular control of renal function parameters and electrolytes were recommended. She is led under the diagnosis of dilated cardiomyopathy and heart failure NYHA stage II without any indication for the ICD prophylactic implantation.

4. DISCUSSION

Regardless of the type and the etiology of initial myocardial damage in dilated cardiomyopathy, the end result is a dilated and slightly contracted left ventricle. In adults, the usual causes of cardiomegaly with impaired systolic function (hypertensive, ischemic or valvular disease) can easily be excluded. Clinically, dilated cardiomyopathy requires in at least 20 to 35% of cases genetic testing, especially if there are indications of idiopathic, family cardiomyopathy with suspected syndrome disease or peripartum cardiomyopathy. About 50 genes are directly associated with the emergence of dilated cardiomyopathy (titin (TTN), lamin (LMNA), desmin (DES) and gene for sodium voltage-gated channels (SCN5A)) (4,5). LMNA, SCN5A and DES gene testing is indicat-

Hereditary	Combination (hereditary and non-hereditary)	Acquired
Hypertrophic	Dilated	Inflammatory (myocarditis)
Arrhythmogenic right ventricular dysplasia	Restrictive (non hypertrophic and non-dilated)	Peripartum
«sponge» like left ventricle		Alcoholic
Glycogen accumulation (PRKAG2, Danon)		Induced by tahycardia
Conduction disorder		Takotsubo cardiomyopathy (acute left ventricular apical ballooning syndrome)
Mitochondrial myopathy		
Ion channels disorders (short and long QT syndromes, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia)		

Table 1. Classification of cardiomyopathies (1, 2)

ed in patients with conduction disturbances or sudden death syndrome (mutations in the lamina A / C and desmin were common in patients with conduction disorders) (1). Laboratory findings (hyponatremia, continuously elevated BNP and atrial natriuretic peptide, elevated levels of norepinephrine and renin) indicate the existence of the disease (6, 7, 8). The plasma concentration of BNP and NT - proBNP (N terminal pro BNP - inactive form) can be greatly increased and is a good indicator of stage and prognosis, and also serves to evaluate the success of medication treatment (1).

BNP sensitivity in diagnostics is 93%, while specificity is 90% (9). Twenty years of patient monitoring in conditions, highly specialized institutions, in developed western countries, were likely to indicate genetic testing but also endomyocardial biopsy. Treatment doubts remain associated with possible inflammatory cardiomyopathy in the first hospitalization (worth discussing non use of anti-inflammatory drugs, antiviral and / or immunomodulatory drugs). Standard therapy is the use of ACE inhibitors, angiotensin II receptor blockers, diuretics and mineralocorticoid-receptor antagonists (eplerenone), with the I-f channel blocker (ivabradine). The use of digitalis as well as phosphodiesterase inhibitors is a two-edged sword (1.4). Alternative treatment options are likely to make more sense in specific cardiomyopathies (thiamine, selenium, carnitine, magnesium). Use of antiarrhythmics must be done very careful, and anticoagulant therapy has not been proven to be useful. Intermediate intravenous infusion of dobutamine alone or in combination with milrinone and levosimendan infusions are administered in patients suspected of entering in the terminal stage of the disease (1, 2, 7). Potassium-sparing diuretics (spironolactone, eplerenone) are recommended in all patients with symptoms, and ejection fraction $\leq 35\%$, and affect mortality and reduce hospitalization (1). Ivabradine slows the rate of heart rate through the inhibition of the channel I-f in the sinus node and therefore should be used only for patients with sinus rhythm (European Medicines Agency approved ivabradine for use in Europe in patients with heart failure and ejection fraction $\leq 35\%$ with frequency ≥ 75 bpm) (1, 7). Recently, the combination of angiotensin II receptor blockers (valsartan) and neprilysin (NEP) inhibitors (sacubitril) proved to be superior to ACE inhibitors (enalapril), with reduced risk of death and hospitalization (1). Temporary mechanical support for circulation is indicated in patients with acute cardiac weakness that are resistant to conventional therapy, with potential for myocardial recovery. Pregnancy is contraindicated in most women with dilated cardiomyopathy and asymptomatic pregnancies with family history of idiopathic dilated cardiomyopathy may have an increased risk of developing peripartum or pregnancy-related cardiomyopathy, which is now considered part of the spectrum of dilated cardiomyopathy and should be carefully controlled.

Prolactin blockade based therapy is recommended (1, 9). Regarding the clinical course, it could be said that the disease is unpredictable and that any disturbance or provocation of the body's response to external and inter-

nal factors, and some physiological conditions, may be a trigger for exacerbation. Therapeutic guidance is often on the test, a doctor is in dilemma, and the patient can sometimes be hard to motivate on unsafe daily risk on an insecure field.

Newer drugs, regardless of the potential, and also toxicity, are always limited in possible interactions. In a bad field, other technical solutions and procedures are often questionable. Younger doctors in these patients remain helpless and need clinical assistance and selflessness and a lot of understanding by the cardiologist to jointly continue the struggle for the patient. Essentially the aim of the treatment remains to improve the clinical picture, reduce the symptoms and improve the quality of life (10, 11).

5. CONCLUSION

Dilatation cardiomyopathy has a poor prognosis and the stabilization is expected in 1/4 patients. Out of the total number, 1/3 of the patients have progression of the disease even irrespective of the good initial response to the therapy. It seems that the most effective way of the treatment is heart transplantation. The clinical course of dilated cardiomyopathy is extremely unpredictable and therapy is extremely complex and demanding.

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- **Conflict of interest:** none declared.

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