Medical Expertise

"Development of the European Network in Orphan Cardiovascular Diseases"
„Rozszerzenie Europejskiej Sieci Współpracy ds Sierocych Chorób Kardiologicznych"

Title: 49-year old female with cardiac failure and mitochondrial myopathy.

RCD code: III-2B.5

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CASE SUMMARY

The authors presented a case of a 49 year-old female with congestive heart failure (CHF) due to dilated cardiomyopathy (DCM) most likely in the course of mitochondrial myopathy (MM). She has suffered from progressive muscle weakness and oculomotor dysfunction since she was 13. In the age of 28 (1992) she was diagnosed with myasthenia gravis and a thymectomy was performed. No symptoms relief was however observed and in 2002 she underwent peripheral muscle biopsy, which revealed presence of ragged red fibers. Suspicion of MM was raised.
Since 2007 she has been recurrently hospitalized due to signs of CHF. In 2013 she was admitted to hospital due to a cardiopulmonary decompensation. Coronary angiography revealed no abnormalities of coronary arteries. Severe impairment of ejection fraction (EF) was diagnosed (EF=20%).
Currently she complains of progressive loss of exercise capacity. She is in class III by New York Heart Association (NYHA). Concomitant conditions include diabetes mellitus 2 and arterial hypertension. She gave birth to 2 children – 1st by natural vaginal delivery and the second by C-section, either without major complication. On physical examination she has no signs of pulmonary congestion or peripheral edema. Biochemical evaluation reveals mild anemia, elevated NT-proBNP (1410pg/mL), elevated transaminases, cholesterol and triglycerides. ECG shows regular, sinus rhythm 80bpm, left axis deviation, negative T in I, aVL. Echocardiography shows dilated left atrium, EF of 25%, mild mitral and tricuspid regurgitation. Right heart catheterization (RHC) discloses significant impairment of left

ventricular systolic function (cardiac index of 2,2l/min/m2), with no signs of pulmonary hypertension (mean pulmonary artery pressure of 17 and pulmonary vascular resistance of 1,8 Wood units). Cardiopulmonary exercise test reveals severe impairment of exercise capacity with VO2max of 7,4 ml/kg/min. The test is terminated after 3 minutes and 2,5 METs workload due to lower limbs weakness. Holter ECG shows sinus tachycardia with mean HR of 83 bpm. Abdominal USG does not reveal any significant abnormalities. Neurological consultation discloses signs of myopathy, likely with genetic background. No contraindications for heart transplantation are expressed.
The authors are in doubt whether this patient is a good candidate for heart transplantation (HTx).

DISCUSSION

Mitochondrial diseases (MD) are heterogeneous group of disorders, that result from a dysfunction of the mitochondrial respiratory chain – a key component of cell energy metabolism. Primary dysfunction of mitochondrial function is caused by mitochondrial or nuclear DNA mutation(s). In around 70% of cases the disease is caused by mutations of the mitochondrial DNA (mtDNA). True prevalence of MDs remains unknown. It is estimated to affect 1 of 10 000 adults [1]. Clinical spectrum of MDs is vast and variable. Tissues with higher energy demand like brain, eyes, skeletal muscles or the heart are often affected earlier and more pronouncedly. Both, single organ (e.g., the eye in Leber hereditary optic neuropathy [LHON], the ear in nonsyndromic hearing loss with or without aminoglycoside sensitivity or muscles in isolated proximal myopathy etc.) or multisystemic presentations with prominent neurologic and myopathic feature may be seen. Clinical syndromes include the Kearns-Sayre syndrome (KSS), chronic progressive external ophthalmoplegia (CPEO), mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS), myoclonic epilepsy with ragged-red fibers (MERRF), neurogenic weakness with ataxia and retinitis pigmentosa (NARP), or Leigh syndrome (LS).

Common neurological signs of MDs are fluctuating encephalopathy, seizures, dementia, migraine, stroke-like episodes, ataxia, and spasticity. Non-neurological findings include ptosis, external ophthalmoplegia, proximal myopathy and exercise intolerance, cardiomyopathy, sensorineural deafness, optic atrophy, pigmentary retinopathy or diabetes mellitus.

Most patients with mitochondrial disease are prone to develop cardiac complications. Cardiovascular disorders most often observed include cardiomyopathies (hypertrophic, dilated, or left ventricular (LV) non-compaction) and arrhythmias including conduction disease or ventricular pre-excitation. The severity can range from non-symptomatic to devastating multisystemic disease with heart failure and ventricular tachyarrhythmias. Observational studies show, that cardiac involvement is present in as many as 78% of patients with MD [2]. 75% of these patients have muscle weakness, 37% dyspnea, 28% syncope, 25% palpitations and 22% chest pain [3]. Cardiomyopathy is diagnosed in around 25% of patients, with HCM most frequent (19%). Electrocardiographic findings include pre-excitation patterns (22%), atrio-ventricular blocks (9%) or intra-ventricular conduction abnormalities in 22%. Cardiovascular involvement is bound to 33% five – year death rate. Cardiac involvement in MD is progressive and carries a burden of significant morbidity and early mortality.

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EXPERT'S OPINION

Treatment of patients with MD and concomitant systemic complications require multidisciplinary approach. No specific disease-modifying therapies yet exist. There seem no evidence based standards for the treatment of MD patients with CHF. Therefore, current European Society Guidelines for the treatment of heart failure should be applied. Systematic up-titration of beta-blockers, ACE inhibitors and spironolactone is advised. Indications of CRT-D implantation should also be reviewed.

Qualification for the heart transplantation (HTx) requires careful evaluation. Poor exercise tolerance observed in this patient is in an important part caused by muscle weakness. Presence of irreversible nuero-muscular disorder as well as diabetes mellitus are considered relative contraindications for HTx. Additionally, it has to be remembered, that post-operative immunosuppression may have a negative effect on muscles.

On the other hand a few publications are available, presenting successful outcome of HTx in this group of patients [4,5]. For this reason detailed neurological, transplantological, anesthesiological, cardio-surgical and cardiological evaluation is required prior final qualification.

CONCLUSION

1. Heart failure pharmacological treatment optimalization following ESC Guidelines is advised.
2. Consideration of the CRT/CRT-D implantation should be done.
3. HTx should be considered in case of non-surgical treatment failure.
4. Prior final HTx qualification careful neurological, transplantological, anesthesiological, cardio-surgical and cardiological evaluation is required.
5. Family screening should be advised.

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