Case report

Successful treatment of fulminant myocarditis with biventricular mechanical circulatory support: A two-year follow-up

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Article history:
Received 23 December 2013
Received in revised form 4 February 2014
Accepted 6 February 2014
Available online 29 March 2014

Keywords:
Biventricular mechanical circulatory support
Fulminant myocarditis

Abstract

Fulminant myocarditis (FM) is an inflammation of the myocardium characterized by progressive acute heart failure leading to cardiogenic shock that develops over several hours. In this article, we present a case of a female patient with acute fulminant lymphocytic myocarditis who was successfully treated with biventricular MCS.

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1. Introduction

Fulminant myocarditis (FM) is an inflammation of the myocardium characterized by progressive acute heart failure that develops over several hours or days [1–3]. Compared with acute myocarditis, following differences are identified in FM, in addition to the rapid progression of the heart failure: common signs of viral infection preceding the manifestation of the disease by 2–4 weeks, more frequent disorders of the ventricular conduction, atrioventricular (AV) blocks and ventricular arrhythmias; laboratory results showing higher levels of cardiac-specific enzymes; and more frequent hepatorenal dysfunction. Echocardiography reveals the characteristic non-dilated left ventricle with thicker walls and reduced ejection fraction [4]. Diagnosis of FM by means of coronary angiogram excludes acute coronary syndrome, and the use of an endomyocardial biopsy (EMB) identifies and differentiates forms that are poorer in terms of prognosis, such as giant cell or necrotizing eosinophilic myocarditis, from benign forms such as acute lymphocytic or hypersensitivity myocarditis [3,5].

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http://dx.doi.org/10.1016/j.crvasa.2014.02.003
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The prognosis of fulminant lymphocytic and hypersensitivity myocarditis has been significantly improved by the new developments in the drug treatment of acute heart failure and/or the implantation of a mechanical circulatory support (MCS) device, since, after the initial critical phase had been managed, these FMs have a benign prognosis, leading most commonly to complete recovery. In this report, we present a case of a female patient with acute fulminant lymphocytic myocarditis who required biventricular MCS in the initial phase of cardiogenic shock, accompanied by unstable ventricular tachycardia.

2. Case report

A 53-year-old, non-smoking female patient with a body mass index (BMI) of 27 kg/m², a history of thyroid disease, and no other significant medical history was referred to our clinic with cardiogenic shock accompanied by persistent ventricular tachycardia episodes. The patient was admitted to the respective cardiac clinic on February 17, 2011, at 3:00 p.m. in a precollapse state following 2 days of viral infection, with overall malaise, difficult breathing, and chest pain. The initial electrocardiogram (ECG) showed sinus rhythm with heart rate of 84 beats/min, left anterior hemiblock, right bundle branch block, and a higher-degree intermittent AV block; laboratory results detected positive troponin I levels (>40 μg/L). Coronary angiography, performed to exclude a coronary event, showed regular findings. However, the transthoracic echocardiogram (TTE) showed dysfunction of the non-dilated left ventricle (LV): LV end-diastolic diameter (LVEDD) = 52 mm; wall thickness of interventricular septum (IVS) = 10 mm; posterior wall thickness = 11 mm; ejection fraction (LVEF) = 35% and signs of dyssynchrony. The patient was transferred to our facility on February 18, 2011, at 2:00 p.m. because of cardiogenic shock, requiring a combination of inotropic support (norepinephrine 0.1 μg/kg/min, dobutamine 5 μg/kg/min), ongoing slow ventricular tachycardia of 130/min (Fig. 1), and incipient alteration of organ function. The patient was conscious, short of breath at rest, hypotensive (85/40 mmHg) and displayed signs of peripheral vasoconstriction. Chest fluoroscopy demonstrated signs of interstitial lung edema and non-dilated heart shadow. Echocardiography revealed reduced systolic LV function (LVEF = 20%, LVEDD = 56 mm, IVS = 9 mm), moderate functional mitral regurgitation, slightly reduced right ventricle (RV) function, and increased filling pressures in both ventricles. Laboratory results revealed significantly increased levels of B-natriuretic peptide (BNP) (1595 ng/L) and troponin I (45.9 μg/L), aspartate aminotransferase (AST) = 4.72 μkat/L, alanine transaminase (ALT) = 1.95 μkat/L, creatinine = 80.4 μmol/L, urea = 10.0 mmol/L, C-reactive protein (CRP) = 30.2 mg/L, glycemia = 7.9 mmol/L; hemoglobin (Hgb) = 117 g/L, and lactate = 2.2 mmol/L. The condition was diagnosed as FM with a rapid progressive syndrome of low cardiac output, and the urgent implantation of short-term mechanical cardiac support (MCS) was indicated. The CentriMag ventricular assist system (Levitronix LLC, Waltham, Mass) was used.

The patient was transferred to the operating room at 4:00 p.m. in critical condition. Paroxysmal supraventricular tachycardia (SVT) (150/min.) resistant to repeated defibrillation occurred following anesthesia. Critical systemic hypotension required indirect and, following longitudinal sternotomy, direct heart massage through the anterior mediastinum. Bolus injections of norepinephrine were administered to maintain at least a minimum perfusion pressure. After heparin administration, extracorporeal circulation was introduced in a standard way. Vascular prostheses (Vasçutek 8) were applied first to ascending aorta and then to the pulmonary artery; two tobacco-pouch sutures with pericardial pads were applied to free walls of both atria. Cannulas of the CentriMag left and right ventricular assist device (LVAD and RVAD, respectively) were introduced and the systems were voided of air. Gradually, the activities of both CentriMag devices were initiated (LVAD, 3700 rpm with cardiac output (CO) = 5.5 L/min; RVAD, 3600 rpm with CO = 4.0–4.5 L/min). Extracorporeal circulation was used for 115 min, and protamine was administered; possible bleeding sources were reviewed; hemostasis was achieved; 3 drains were introduced; definite suture was postponed; vasopressor support by means of norepinephrine oscillated at approximately 0.3 μg/kg/min; and maximum lactate level was 6.3 mmol/L. Bleeding revision was performed on postoperative day (POD) 1, definite suture on POD 2, and extubation on POD 3 after discontinuation of inotropic support.

Myocardial RV biopsy confirmed acute lymphocytic myocarditis (20 lymphocytes/mm²) accompanied with plaques of myonecroses and minimum interstitial necrosis (Fig. 2).

Fig. 1 – ECG at admission showing ventricular tachycardia 130/min.

Fig. 2 – Biopsy showing interstitial inflammatory infiltrate.
Immunohistochemical examination detected massive presence of T-lymphocytes (anti-CD3 positive cells) and the presence of macrophages (Fig. 3). A frozen cardiac sample was also sent for virology examination; the polymerase chain reaction (PCR) test failed to detect the etiologic agent. A slight Epstein-Barr positivity did not explain the ongoing acute myocarditis. Other cardiotropic viruses were negative (herpes simplex virus, human herpesvirus 6, cytomegalovirus, and enteroviruses). It was not possible to establish disease etiology using a panel of serologic examinations for cardiotropic agents. A basic immunologic examination was performed, which excluded systemic autoimmune disease or vasculitis; only antibodies against thyroglobulin and thyroid peroxidases were detected as positive, with a regular thyroid-stimulating hormone (TSH) value that was compatible with the diagnosis of autoimmune thyroiditis at the euthyrosis stage.

Further postoperative course displayed no complications. Echocardiography performed on POD 7 detected a slight increase in LVEF to the value of 25–30%; systolic RV function was slightly reduced. A further improvement of the non-dilated LVEF (LVEDD = 44 mm) to the value of 45–50% was detected on POD 12, as well as minor AV regurgitation and insignificant pericardial effusion. After the reduction of MCS rounds with the flow rate of 2.0 L/min, LV remained undilated, EF = 45% with accentuated paradoxical IVS movement and hypokinetic anteroseptal wall. The total duration of biventricular CentriMag support was 20 days. Satisfactory clinical features, improvement of laboratory results, and satisfactory systolic function of both ventricles according to TTE examination enabled us to perform CentriMag explantation on March 11, 2011. The hemodynamic situation in early phases after explantation was stable; only 5 μg/kg/min dobutamine was administered after explantation. Follow-up RV biopsy performed during explantation detected hemorrhagia in the epicardial area as well as regression of round-cell inflammatory cellulization, mild interstitial fibrosis, and isolated granulocytes in the fibrous tissue, with no signs of myocyte damage. The overall conclusion was regressive myocarditis with a minor degree of fibrosis (Figs. 4 and 5).

The course of post-MCS-explantation treatment was free from complications – an ECG detected sinus tachycardia of 104/min and incomplete RBBB. Chronic heart failure medication was provided to the patient due to the threshold LV systolic function (Table 1); maximum beta-blocker and angiotensin-converting enzyme (ACE-) inhibitor dosages were limited due to the threshold systemic blood pressure. Table 1 shows the development of cardiac markers and some echocardiographic and biochemical indicators before MCS implantation, during unloading of both ventricles, in the period close to MCS explantation, and during long-term patient follow-up in the outpatient setting. At present, the patient has been followed for 24 months in the outpatient department without any significant breathlessness during regular exercise. However, the patient reported decreased performance compared to the period before the disease and decreased tolerance of medication used to treat chronic heart failure due to inclination to hypotension with blood pressure of 100–110/70 mmHg as a response to a minor maintenance.
dose of beta-blocker (bisoprolol 2.5 mg daily), ACE-inhibitor (ramipril 1.25 mg daily), and spironolactone. Three months following MCS explantation, the BNP levels returned to normal; there is also evidence of normal levels of cardiace-specific troponin I enzyme after 6 months. Echocardiography follow-up examinations revealed long-term threshold nondilated LV systolic function, with EF of 50–55% and hypokinetic anteroseptal wall, and threshold RV systolic function, with no signs of pulmonary hypertension at rest. Good LV function was confirmed also by follow-up MRI scan 6 months after explantation. The patient underwent repeated spiroergometry testing, which detected a slightly improving but decreased exercise tolerance (maximum O$_2$ consumption was 20.4 ml/kg/min, i.e., 73% of the normal value 20 months after explantation), with an adequate ventilation response to exercise without hyperventilation, as well as a 6-min walk test in which she repeatedly walked more than 500 m, slightly exceeding the standard for her age and gender. After a one-year incapacity for work, the patient returned to work where she exercises in her profession.

3. Discussion

We report on a case of a successful treatment of pharmacologically resistant cardiogenic shock accompanied by paroxysmal ventricular tachycardia in a female patient with lymphocytic FM. Treatment during the acute phase by means of biventricular Levitronix CentriMag MCS resulted in recovery of the LV systolic function and arrhythmogenic substrate stabilization.

The FM course is characterized by a rapid progression of acute bilateral heart failure toward the phase of cardiogenic shock. It can also be complicated by serious rhythm disturbances of the heart such as AV blocks and ventricular arrhythmias. Thorough monitoring of patients with FM in a comprehensive cardiac clinic disposing of MCS is a prerequisite for the successful treatment of its initial phase to bridge the episodes of pharmacologically resistant cardiogenic shock. Extracorporeal membrane oxygenation (ECMO) and paracorporeal biventricular MCS are the most common types of MCS used in these conditions [3].

Endomyocardial biopsy has a decisive effect on the treatment of these patients. The detection of giant cell or necrotizing eosinophilic myocarditis is an indication for immunosuppressive treatment [1-3,6-9], as well as a secondary indication for biventricular MCS implant. Cooper et al. described successful immunosuppressive treatment administered in a female patient with necrotizing eosinophilic myocarditis treated by paracorporeal MCS, which led to the restoration of LV systolic function [8].

However, the restoration of LV systolic function in patients with fulminant forms of lymphocytic myocarditis is to be expected at approx. 2 weeks; therefore, circulatory instability in these cases may be bridged by means of a short-term MCS such as ECMO.

Initial clinical state prior to MCS is another factor. In particular, the use of ECMO is favorable in patients with cardiogenic shock and insufficient oxygenation with artificial ventilation [3], as well as in patients with unclear neurological status following cardiopulmonary resuscitation as bridge-to-decision. Biventricular paracorporeal MCS is recommended in patients with critically reduced cardiac index (≤1.5 L/min m$^2$) and possibly in patients with hemodynamically significant ventricular arrhythmias and signs of advanced LV remodeling, indicating the need of long-term MCS [10]. Past published results showed that paracorporeal MCS procedure outnumbered the ECMO technique (n = 155, 46% vs. 24%) [11]; however, Mirabel et al. [12] recently published evidence of a significantly increased use of ECMO as opposed to paracorporeal MCS (n = 41, 15% vs. 85%). However, ECMO is the predominantly used procedure in children with FM [13,14]. Survival of 68–73% of adult patients after MCS discontinuation has been reported [11,12,15,16], with the restoration of LV function as opposed to the necessity to perform heart transplant. In children, previous publications have reported 46% survival after MCS discontinuation [13]. Recently published results report successful bridging of the acute phase in as many as 75% of cases [14], with the restoration of LV function in 43% of the patients, whereas only 32% of these patients needed heart transplant [14]. The short period between symptom manifestation and MCS implantation seems to be the most significant indicator of successful restoration of LV function in FM patients after MCS implant. Atluri et al. [17] report a significantly shorter interval in patients with restored LV function compared to the rest of the patient group (median of 7 days vs. 21 days). These results support the use of MCS in FM patients with pharmacologically resistant acute cardiac failure.

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<tr>
<th>Date</th>
<th>Before MCS implantation</th>
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Table 1 - Biochemical and echocardiographic markers development before and after MCS implantation.
4. Conclusion

In patients with rapidly progressing heart failure refractory to drug treatment, implantation of short-term mechanical cardiac support may help to bridge the period of hemodynamic instability. This is particularly true for FM patients in whom the threshold for MCS use is lower than that in cases of acute heart failure caused by other reasons. This procedure, together with the immediate transfer of the patient into a respective cardiac clinic, should be the chosen method.

Funding body

This study was supported by project of the Ministry of Health of the Czech Republic within the project for the development of research organization 00023001 (IKEM) – institutional support. The Center for Experimental Medicine (IKEM) received financial support from the European Commission within the Operational Program Prague – Competitiveness; project “CEVKOOK” (#CZ.2.16/3.1.00/22126).

Ethical statement

The authors whose names are listed immediately below declare that all procedures performed at the Institute for Clinical and Experimental Medicine Prague are carried out with the approval of the ethics committee.

Conflict of interest

No conflict of interest.

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