Fulminant myocarditis in adults and children: bi-ventricular assist device for recovery

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Abstract

Objective: Fulminant myocarditis (FM) is uncommon and may be followed by a rapidly intractable cardiogenic shock. We report five consecutive patients with FM successfully bridged to recovery with a mechanical paracorporeal biventricular assist device (BiVAD).

Methods: Five patients, four adults and one child (mean age 27+/−6 years, range, 5–36 years) underwent implantation from November 1999 to May 2003, for FM. Prior to implantation, all patients required maximal inotropic support, three of them had an intra-aortic balloon pump, the child had an extra-corporeal membrane oxygenation (ECMO) support previously inserted in another institution. Cardiac catheterisation showed a mean CPW of 37+/−1 mmHg, mean CVP 18+/−2 mmHg, and mean CI 1.7+/−0.1 l/min. Echocardiogram showed a severe biventricular hypokinesia, without any ventricular dilatation and a mean LVEF at 12.5%. Two patients were implanted in cardiac arrest under external cardiac resuscitation. All patients underwent BiVAD implantation (MEDOS HIA-VAD). A 72 ml right paracorporeal ventricle (a 23 ml in the child) was instituted between the double stage venous canula used during CPB and a pulmonary artery outflow canula. A 80 ml left paracorporeal ventricle (a 25 ml in the child) was instituted between a left ventricle apical canula and an aorta outflow canula.

Results: There was no death. The mean duration support time was 11+/−6 days (from 7 to 21 days). Two patients experienced transitory deficiency due to a stroke. Four patients showed signs of FM on histological findings. Despite serologic examination and viral genome research on myocardial biopsies, pathogenic agents were not identified. At mean follow-up of 31+/−15 months, all the patients fully recovered with a mean LVEF=60% and no left ventricular dilatation.

Conclusions: In FM with intractable cardiogenic shock, the use of a BiVAD as a bridge to recovery is a life saving approach and should be considered before multi-end organ failure.

Keywords: Heart failure; Shock; Myocarditis; Extracorporeal circulation; Heart assist device

1. Introduction

Several fulminant myocarditis (FM) resulting in early death from intractable cardiogenic shock have been reported. Nevertheless complete recovery can ensue if the patient is successfully supported during the acute phase of the illness [1–11]. Mechanical circulatory support is a life saving approach and must be considered before multi-organ failure, but there are still many questions concerning diagnosis, time of implantation, device selection, peri-operative management and the usefulness of immuno-suppressive therapy.

We report five consecutive patients with acute FM and cardiogenic shock, successfully bridged to recovery with a BiVAD.

2. Materials and methods

2.1. Patients

From November 1999 to May 2003, four adults and a 5-year-old child (three females and two male with a mean age of 23 years; range, 5–36 years) suffering from FM with
Intractable cardiogenic shock were implanted with BiVAD. Pre-operative patient’s characteristics are summarized in Tables 1 and 2. All previously healthy patients had acute onset of symptoms resulting in rapid life threatening cardiogenic shock. Mean delay between onset of symptoms and shock was 3 days. The patients rapidly required increasing inotropic support (dobutamine, dopamine in four patients with epinephrine in three and milrinone in one). EKG showed supra ventricular tachycardia (mean 120 range from 112 to 132/min) with ST modification. Echocardiogram showed severe biventricular hypokinesia, normal valvular anatomy, normal ventricular dimension, but an increase in septal thickness. Additionally a moderate pericardial effusion was found in two patients. Mean ejection fraction (LVEF) was 12.5%, range from 10 to 15. Mean troponine level was 9 ranging from 4.8 to 11.5 UI. Cardiac cathetherization showed cardiogenic shock (CPW 37°C/K 1 mmHg, mean CVP 18°C/K 2 mmHg, mean CI 1.7°C/0.1 l/min). Three patients had coronarography, which showed no coronary arteries disease. No patient had pre-operative endomyocardial biopsy.

### Table 1

**Patient’s pre-implant characteristics**

<table>
<thead>
<tr>
<th>Sex, age (years)</th>
<th>Delay (days)</th>
<th>Symptoms</th>
<th>Heart rate</th>
<th>Systolic blood pressure</th>
<th>Drugs</th>
<th>Device</th>
<th>CA</th>
<th>VA</th>
<th>CI, CVP, CW (l/min per m², mmHg, mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pt1 F, 36</td>
<td>3</td>
<td>Histamine like</td>
<td>116</td>
<td>80</td>
<td>Db, Dp, Ep</td>
<td>IABP</td>
<td>+</td>
<td>+</td>
<td>1.8, 15, 36</td>
</tr>
<tr>
<td>Pt2 F, 26</td>
<td>5</td>
<td>Flu like</td>
<td>120</td>
<td>70</td>
<td>Db, Dp, Ep</td>
<td>IABP</td>
<td>–</td>
<td>+</td>
<td>1.9, 18, 38</td>
</tr>
<tr>
<td>Pt3 F, 25</td>
<td>3</td>
<td>Flu like</td>
<td>132</td>
<td>75</td>
<td>Db, Dp</td>
<td>–</td>
<td>+</td>
<td>+</td>
<td>1.7, 18, 36</td>
</tr>
<tr>
<td>Pt4 M, 21</td>
<td>4</td>
<td>Atypical chest pain</td>
<td>112</td>
<td>85</td>
<td>Db, Dp, Ep</td>
<td>IABP</td>
<td>–</td>
<td>+</td>
<td>1.6, 20, 38</td>
</tr>
<tr>
<td>Pt5 M, 5</td>
<td>3</td>
<td>Flu like abdominal pain</td>
<td>170</td>
<td>65</td>
<td>DP, Db</td>
<td>ECMO</td>
<td>–</td>
<td>+</td>
<td>1.4, 24, 34</td>
</tr>
</tbody>
</table>

Delay, mean delay between onset of symptoms and cardiogenic shock (days); heart rate (beat/min); systolic blood pressure (mmHg). Drugs: Db, dobutamine; Dp, dopamine; Ep, epinephrine; IABP, intra-aortic balloon pump; CA, cardiac arrest; VA, assisted ventilation; CI, cardiac index; CVP, central venous pressure; CW, Capillary wedge pressure.

Due to a rapid aggravation of the patients condition, the required transfers to our department were achieved with maximal inotropic support, IABP in three patient and mechanical respiratory support in two. The child was transferred to our unit with ECMO previously inserted 3 days ago in another institution. At arrival, two patients were immediately supported with a BiVAD. In three other patients, device implantation were performed, respectively, on days 1–3 after arrival.

### 2.3. Implantation

The device used was MEDOS HIA-VAD (MEDOS Medizintechnik GmbH, Stollberg, Germany) which is a pneumatically actuated blood pump. A 72 ml paracorporeal right ventricle was instituted between the right atrium and the pulmonary artery and a 80 ml paracorporeal left ventricle instituted between the apex of the left ventricle and the ascending aorta in adults patients. A 22 ml paracorporeal right ventricle and a 25 ml paracorporeal left ventricle were used in the child. Implantation was performed under CPB after removal of the IABP. Apical canula (Medos, Medizintechnik GmbH, Stollberg, Germany) was inserted to first, under warm blood cardioplegic arrest. The resected left ventricular apex was sent to anatomopathology and microbiology. Arterial canula (Medos, Medizintechnik GmbH, Stollberg, Germany) was anastomosed on a beating heart with lateral aorta and pulmonary cross clamping. We used for the right inflow canula the double stage venous canula (Jostra, Hirrlingen Germany) used during CPB.
2.4. Anticoagulation

Heparinization for CPB and heparine antagonization at the end of CPB was regular. Between post-operative hours, 4–6, intravenous continuous heparine was introduced to achieve an activating clotting time of 140–160 s, and maintain a blood antiXa level between 0.3 and 0.4 UI. Patients received 100 mg/day aspirin from post-operative day 1.

2.5. Device and patient management

Mechanical respiratory support was not discontinued during BiVAD support except for the patient No. 4 who was extubated on post-operative day 8. Inotropic drugs were rapidly decreased so as all patients had no more catecholamine at device removal. No patient had additive immuno-suppressive therapy.

Patients were monitored using swan-ganz catheter including an inline mixed venous saturation catheter. Paracorporeal ventricles were checked twice a day with the help of transillumination technique to detect thrombus formation.

2.6. Recovery evaluation

Left and right ventricular function were daily assessed by TEE in patients under mechanical ventilation. Right and left ventricular contractility and aortic valve opening were studied. Recovery of left ventricular contractility began rapidly on post-implantation day 3, except in patient No. 4 for whom recovery was delayed on post-operative day 16. We considered BiVAD removal when full recovery of ventricular contractility and aortic valve opening were observed despite full flow provided by the device. At this point, after full systemic heparinization, the pulse rate of the BiVAD was decreased to the minimal frequency allowed (40/min) for 1 h and both ventricular contractility and aortic valve opening were assessed.

2.7. Weaning of the device

After CPBP was instituted, BiVAD was stopped and ventricular function assessed by TTE. Warm blood cardioplegic arrest allowed removal of the apex canula and reconstruction of the apex by pericardial lining Dacron patches. Myocardial biopsy was performed through the hole at the apex. Outflow Dacron graft and right atrial canula was removed on beating heart. Patients were weaned from CPB under TEE control.

3. Results

3.1. Mortality

There was no death for these five consecutive patients.

3.2. Time on the device

The mean duration support time was 10+/−6 days (from 7 to 21 days).

3.3. Morbidity

Principal complications are summarized in Table 3. Two patients experienced transient ischaemic cerebral attacks. One day after the BiVAD removal, patient 3 presented with haemoperitonium due to ovarian kyste leaking for which she underwent emergency surgery. Her post-operative course was also complicated by mediastinitis, requiring two redo surgery on days 16 and 24. Including BiVAD removal procedures, 10 reoperations were necessary (reoperation rate 2 per patient). Ventricular support device complications included need for haemodiafiltration for 18 and 5 days in patient Nos 3 and 5, respectively.

3.4. Diagnosis

Four patients had signs of FM on histological findings with foci myocyte necrosis and lymphocytic infiltration

<table>
<thead>
<tr>
<th>Support</th>
<th>Duration (days)</th>
<th>Dialysis</th>
<th>Complication</th>
<th>F U (months)</th>
<th>Condition</th>
<th>LVEF at FU (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pt1</td>
<td>BiVAD</td>
<td>7</td>
<td>--</td>
<td>Bleeding transient ischaemic cerebral attack</td>
<td>47</td>
<td>Alive and well neurological recovery</td>
</tr>
<tr>
<td>Pt2</td>
<td>BiVAD</td>
<td>8</td>
<td>--</td>
<td>Transient ischaemic cerebral attack</td>
<td>41</td>
<td>Alive and well neurological recovery</td>
</tr>
<tr>
<td>Pt3</td>
<td>BiVAD</td>
<td>8</td>
<td>+</td>
<td>Haemoperitonium, mediastinitis after device removal</td>
<td>31</td>
<td>Alive and well</td>
</tr>
<tr>
<td>Pt4</td>
<td>BiVAD</td>
<td>21</td>
<td>--</td>
<td>--</td>
<td>31</td>
<td>Alive and well</td>
</tr>
<tr>
<td>Pt5</td>
<td>BiVAD</td>
<td>7</td>
<td>+</td>
<td>--</td>
<td>6</td>
<td>Alive and well</td>
</tr>
</tbody>
</table>
with interstitial oedema (Figs. 1 and 2). In spite of serologic studies and viral genome research on myocardial biopsies, including in situ hybridization and polymerase chain reaction, pathogenic agents were not identified.

3.5. Clinical and echocardiographic status at follow-up

Mean follow-up for these patients was 31+/−15 months (ranging from 6 to 47 months). No patient had recurrence of myocarditis or congestive heart failure during follow-up. All patients were in class I NYHA. The patients, Nos 1 and 2, had complete neurological recovery. All had TTE, that showed complete ventricular function recovery with mean LVEF: 60% (from 55 to 65%), no left ventricular cavity dilatation, mean LV diameter 46+/−11 mm (from 42 to 54). MVO2max at 12 months follow-up was 24, 28, 31 ml/min per kg in patients Nos 2–4, respectively. These patients were in Weber class A. Isotopic left ventricular ejection fraction at 2 years follow-up was 48 and 46% in patient Nos 2 and 4, respectively.

4. Discussion

Many classification of myocarditis saga described as ‘flaming, smoldering and burned out’ have been proposed [12–15]. The Dallas criteria, as well as the classification proposed by Feneglio (acute, rapidly progressive and chronic) are histological classifications [13], but histological studies have a high incidence of false-negative results [16]. Lieberman et al. [15] have proposed a clinical classification, interesting in diagnosis, prognostic and therapeutic implications. This classification, similar to the viral hepatitis’s one, includes four different entities: fulminant, acute, chronic-active and chronic persistent. The acute form in the Feneglio’s classification has been divided in fulminant and active forms which have different clinical presentation and prognostic. FM are considered to represent 10% of all myocarditis such as the incidence of FM in US should rise 200 cases by year [17,18].

The five patients we present had typical FM. FM are clinically characterized by distinct onset of cardiac symptoms in otherwise young healthy patients after non-specific flu-like symptoms rapidly resulting in severe ventricular dysfunction and cardiogenic shock. These five patients were young healthy patients and the mean delay between onset of symptoms and shock was 3 days. Echocardiographic findings in FM include a dramatic LV dysfunction with a markedly fractional shortening decrease, a normal LV dimension and an increase in septal thickness [19]. On the other hand, patients with acute myocarditis are older, they have indistinct onset of cardiac symptoms and have experienced gradual deterioration of cardiac function before acute deterioration [15]. Echocardiogram in patients with acute myocarditis could show, additionally to the LV dysfunction, some degree of LV dilatation and normal septal thickness [19]. The prognostic of these two clinical forms of myocarditis is different. A better long-term survival has been reported in survivor patients of FM comparatively with patients suffering from acute form of myocarditis who experienced further chronic ventricular dilatation. Patients who survive FM can have for a long time a complete and stable cardiac recovery [20]. We have found such a stable cardiac recovery during a mean 31 month follow-up in our patients.

Benefits of some forms of immunotherapy have not yet been clearly demonstrated. Steroids, immunoglobulin, azathioprine, cyclosporine, monoclonal antibody have failed to prove any benefit [21–23]. In FM, immunotherapy have been experimentally shown to impair viral clearance and thus should not be used [23].

The choice of the device is still debated. In the acute form of myocarditis that requires a long time on device, often as a bridge to transplantation, the implantable LVAD is more
appropriate, expected the right ventricular function is adequate. On the contrary, in FM the device is indicated as a bridge-to-recovery and time on the device is usually short (mean delay of support was 10 days in our patients). So, an extra-corporeal device seems logical. We have used BiVAD in such a diffuse biventricular disease. ECMO has many advantages (rapid peripheral technique of insertion) essentially in children [5,7,8,11]. But as previously reported [24], we observed inadequate unloading of the left ventricle in the child we switched to a BiVAD, and we consider an efficient unloading of the left ventricle as a condition for rapid recovery.

In FM with intractable cardiogenic shock, the use of a BiVAD as a bridge to recovery is a life saving approach and unloading of the left ventricle as a condition for rapid recovery.

References