Mechanical Ventricular Assist System Required for Sustained Severe Cardiac Dysfunction Secondary to Peripartum Cardiomyopathy

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A 29-year-old woman developed severe congestive heart failure in the first week after an uneventful full-term delivery. Despite intense medical treatment over the next 6 months, her heart failure symptoms gradually worsened and she eventually developed cardiogenic shock. She successfully underwent the implantation of a left ventricular assist system, but because there was no sign of recovery of ventricular function, she was placed on the waiting list for heart transplantation. After 143 days of support, she suffered from brain hemorrhage, and eventually died after a total of 321 days of left ventricular support. Postmortem examination of the myocardium showed sustained diffuse fibrosis and no inflammatory reaction. This case implies that with severe peripartum cardiomyopathy heart transplantation should be considered without delay even if a mechanical assist system is available. (Circ J 2005; 69: 362–364)

Key Words: Heart transplantation; Left ventricular assist system; Peripartum cardiomyopathy

P eripartum cardiomyopathy (PPCM) is a rare cause of congestive heart failure that has an unclear etiology. PPCM is currently defined by the following 4 criteria adapted from the initial work by Demakis et al.1: (a) development of cardiac failure in the last month of pregnancy or within 5 months of delivery, (b) absence of an identifiable cause for the cardiac failure, (c) absence of recognizable heart disease prior to the last month of pregnancy, and (d) left ventricular systolic dysfunction by echocardiography.2 The incidence of PPCM is roughly estimated as 1 per 3,000–4,000 live births.2 As the natural history of this disease is still unclear, optimal management has not been well established.

We describe a case with PPCM for which a left ventricular assist system (LVAS) was implanted for cardiogenic shock, but there was no significant recovery of cardiac function and histological changes took place during the 1 year of mechanical support.

Case Report

A 29-year-old woman, who had no significant past medical history, underwent an uneventful full-term delivery in early May 1999. Her electrocardiogram at the 33rd week of pregnancy demonstrated no significant abnormalities, but she developed palpitation and dyspnea on exertion at 1 week after the delivery. She had no preceding symptoms suggesting viral infection and a paired anti-viral antibody titer showed no significant elevation. Her symptoms worsened rapidly and orthopnea developed. Her chest X-ray demonstrated marked cardiomegaly and pulmonary congestion (Fig 1). She underwent echocardiography, which showed a severely dilated and poorly contracting left ventricle (LV) (LV enddiastolic dimension/end systolic dimension (Dd/Ds): 58/55 mm) and massive mitral regurgitation (MR). She was placed on continuous dopamine infusion

Fig 1. Chest X-ray on admission shows marked cardiomegaly and pulmonary congestion.
and diuretics, which partly improved her congestive heart failure symptoms. However, she continued to have New York Heart Association (NYHA) class III heart failure symptoms, which were worsened by β-blocker therapy, and eventually, despite intense medical treatment including multiple inotropic supports, she developed cardiogenic shock at the end of November. She was transferred to hospital for emergency percutaneous cardiopulmonary support (PCPS). The next day she underwent implantation of a Toyobo-NCVC LVAS, which is an extracorporeal-type device with drainage from the LV apex. Mitral annuloplasty was performed simultaneously using a 26 mm Cosgrove-Edward ring (Baxter Healthcare Corp, IL, USA) to facilitate possible weaning from the LVAS in the future.

A myocardial specimen taken from the LV apex during the operation demonstrated irregular myocytes with a swollen nucleus and moderate interstitial fibrosis. No obvious infiltration of inflammatory cells can be seen (Hematoxyline–eosin; ×100).

**Discussion**

The etiology of PPCM is still unclear, but there is some evidence that inflammation, possibly related to auto-immunity, may play a role in the early stage of the disease process. However, the incidence of myocarditis in PPCM is reported as variable in the patient population probably because of differences in the timing of the myocardial biopsy. In the present case the wall of the left ventricle was biopsied during the operation at 7 months after the onset of heart failure and no inflammatory cells were found; however, inflammatory cell infiltration might have been observed complete cessation of the LVAS support for 30min after heparin injection. Although her hemodynamic condition did not deteriorate, echocardiography demonstrated generalized hypokinesis of the LV with fractional shortening of 17% (Table 1), but no residual mitral regurgitation. As her cardiac function was not good enough to be weaned from the LVAS she was considered a candidate for heart transplantation (HTX). Approval from the Japanese Circulation Society was obtained and she was placed on the Japan Organ Transplant Network waiting list 62 days after LVAS implantation. The LVAS off-test repeated 1 month later demonstrated almost unchanged LV dysfunction (Table 1).

After 143 days of LVAS support, she suffered from non-infective cerebral embolization that possibly originated from the LVAS followed by post-infarction cerebral hemorrhage. Because the device requires intense anticoagulation to prevent thrombus formation in the pump (prothrombin time-international normalized ratio ranged 3.0–4.0), we had to surgically remove the LVAS and although the operation was successful, she developed severe congestive heart failure in the next few days. An intraaortic balloon pump was inserted and her hemodynamics stabilized, but her cardiac function gradually worsened (Table 1) and she eventually required the implantation of another LVAS 6 weeks after the removal of the first device. She was supported by the LVAS for the next 6 months, but died from a massive brain hemorrhage before a donor heart became available, 18 months after the onset of the heart failure symptoms. Postmortem examination of the myocardium showed sustained diffuse fibrosis and no inflammatory reaction (Fig 3).

**Table 1 Clinical Course of Peripartum Cardiomyopathy**

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<tbody>
<tr>
<td>Admission</td>
<td>Off test</td>
<td>Off test</td>
<td>After LVAS removal</td>
<td></td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>120</td>
<td>105</td>
<td>116</td>
<td>112</td>
</tr>
<tr>
<td>BP (mmHg)</td>
<td>68/46</td>
<td>86/54</td>
<td>103/52</td>
<td>88/56</td>
</tr>
<tr>
<td>mPAP (mmHg)</td>
<td>27</td>
<td>16</td>
<td>NA</td>
<td>21</td>
</tr>
<tr>
<td>PCWP (mmHg)</td>
<td>23</td>
<td>13</td>
<td>NA</td>
<td>16</td>
</tr>
<tr>
<td>CO (L/min)</td>
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<td>4.3</td>
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<tr>
<td>SvO2 (%)</td>
<td>52</td>
<td>60</td>
<td>NA</td>
<td>68</td>
</tr>
<tr>
<td>LVDd (mm)</td>
<td>69</td>
<td>55</td>
<td>54</td>
<td>64</td>
</tr>
<tr>
<td>LVDs (mm)</td>
<td>63</td>
<td>48</td>
<td>47</td>
<td>55</td>
</tr>
<tr>
<td>FS (%)</td>
<td>8</td>
<td>13</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>EF (%)</td>
<td>17</td>
<td>27</td>
<td>27</td>
<td>31</td>
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LVAS, left ventricular assist system; HR, heart rate; BP, blood pressure; mPAP, mean pulmonary arterial pressure; PCWP, pulmonary capillary wedge pressure; CO, cardiac output; LVDd, left ventricular diastolic dimensions; LVDs, left ventricular diastolic systolic; FS, fractional shortening; EF, ejection fraction.
if the biopsy had been taken earlier.

The natural course of PPCM is still unclear, but the initial systolic function or dimension of the LV has been shown to be a significant risk factor for adverse outcomes. The other risk factor relates to the time course of recovery of cardiac function. Demakis et al reported that a cohort of patients who had persistent cardiomegaly after the first 6 months from the onset of symptoms had a dismal prognosis with up to 85% mortality1 Those studies implied that spontaneous recovery will take place in the early stage of the disease process if it occurs.

One treatment option is immunosuppressive therapy. Midei et al described the effectiveness of immunosuppression using steroids in cases having inflammatory cell infiltration in the myocardial biopsy, and also reported a poor prognosis in patients without inflammatory reactions. Therefore, immunosuppressive therapy should be considered in the early stage of the disease process. In the present case, there was no cell infiltration in the myocardial sample taken at the time of the operation. Furthermore, the patient had an extracorporeal type of LVAS, which carries a high risk of infection and for these reasons, we abandoned the immunosuppressive therapy.

The LVAS is currently used mainly as a bridge-to-heart transplantation, but there are increasing reports of bridge-to-recovery use of LVAS not only in patients with fulminating myocarditis but also in those with idiopathic dilated cardiomyopathy and several successful bridge-to-recovery cases with PPCM have been also reported. In the present case, however, cardiac function had only partly recovered during the initial months of LVAS support, but was apparently under the requirement for expected successful removal10. In fact, removal of the LVAS resulted in the recurrence of severe heart failure.

Considering the severely limited number of available heart donors, there are some difficulties in determining the indication and timing of HTX in patients with potentially reversible heart failure. Even if the patients develop heart failure that is severe enough to require mechanical support, there is an option to observe the recovery of cardiac function for a while. However, currently available LVAS have limited safety; thromboembolic events and infectious complications are the main factors restricting long-term use of the LVAS11. Based on previous reports, the patient should be considered a candidate of HTX when recovery has not been observed or function has progressively worsened in the 6 months after onset.12 In the present case the patient developed cardiogenic shock 6 months after the onset of heart failure and functional recovery was not observed during the year. Retrospectively, HTX was the only treatment option and should at least have been considered immediately after stabilization of her condition with LVAS. Obviously, more research is required to clarify the natural history and prognostic factors of the PPCM. The results of HTX in the patients with PPCM have been reported. The largest series reported by Keogh et al showed a significantly increased incidence of acute rejection and infection, but comparable survival with idiopathic dilated cardiomyopathy12.

In conclusion, we present a case of PPCM in which severe cardiac dysfunction was sustained during the year of mechanical circulatory support. It is difficult to determine the indication and timing for HTX because the disease process is potentially reversible; however, it should be considered without delay if the LVAS does not lead to quick functional recovery because of the limited safety of the currently available devices.

References