Case Report

Persistent cardiac arrest caused by profound hypokalaemia after large-dose insulin injection in a young man with type 1 diabetes mellitus: successful rescue with extracorporeal membrane oxygenation and subsequent ventricular assist device

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Abstract
A 28-year-old man who had a history of type 1 diabetes mellitus with poor medication compliance was referred to the emergency department of our institute with suspected diabetic ketoacidosis. The patient developed sudden cardiac arrest following continuous insulin administration. Laboratory data revealed severe hypokalaemia. Cardiopulmonary resuscitation was performed immediately for 63 minutes. Although his spontaneous circulation resumed, the haemodynamics remained unstable. Peripheral extracorporeal membrane oxygenation was therefore employed for mechanical circulatory support. Echocardiography under these conditions revealed generalised hypokinesia of the bilateral ventricles. The left ventricular ejection fraction was only 10–15%. The chest film revealed bilateral pulmonary congestion. The patient developed multiple organ dysfunction, including acute kidney injury, liver congestion and persistent pulmonary oedema, although the hypokalaemia resolved. A temporary bilateral ventricular assist device (Bi-VAD) was used for superior systemic perfusion and unloading of the bilateral ventricles after 16 hours of extracorporeal membrane oxygenation support. After the start of maintenance using the Bi-VAD, extracorporeal membrane oxygenation was discontinued and the inotropic agents were tapered down immediately. Subsequently, the haemodynamics stabilised. All the visceral organs were well perfused with Bi-VAD support.

Subsequent echocardiography demonstrated recovery from the myocardial stunning, with the left ventricular ejection fraction returning to 50–60%. The Bi-VAD was gradually weaned and successfully removed 12 days after implantation. The patient had an uneventful recovery and was discharged without organ injury. Over one year of follow up in our out-patient clinic, adequate cardiac function and improved diabetes control were found.

Keywords: hypokalaemia, cardiac arrest, cardiogenic shock, ventricular assist device

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Profound hypokalaemia (< 2.5 mmol/l), a severe complication following subcutaneous administration of insulin, is reported in 5–10% of patients with type 1 diabetes mellitus, and can easily be resolved through potassium infusion. Clinical manifestations of hypokalaemia vary in severity, depending on the acuteness and degree of the hypokalaemia. Although mild degrees of hypokalaemia are usually asymptomatic, severe degrees can lead to marked muscle weakness, ileus, and lethal arrhythmia, including cardiac arrest, ventricular tachycardia (VT) and ventricular fibrillation (Vf). The incidence of Vf has been found to be three-to-five-fold higher in patients with low serum potassium compared with patients with high serum potassium concentrations.

Although the mortality rate for hypokalaemia-related VT/Vf has not been reported, the mortality rate for cardiogenic shock following cardiopulmonary resuscitation (CPR) is 50–80%. Herein, we report on a young man who developed refractory hypokalaemia-induced VT/Vf and cardiogenic shock following CPR. We performed emergent veno-arterial (VA)-mode extracorporeal membrane oxygenation (ECMO) in the emergency room; thereafter, a bilateral ventricular assist device (Bi-VAD) was implanted to provide cardiogenic shock after CPR.
Case report

A 28-year-old man with a history of type 1 diabetes mellitus and inadequate compliance with insulin administration was referred to our emergency department due to general weakness with impaired consciousness lasting one day. Laboratory data revealed hyperketonaemia (blood ketone level 7.6 mmol/l), hyperglycaemia [glucose level 1 091 mg/dl (60.55 mmol/l)] and diabetic ketoacidosis (serum bicarbonate level 6.8 mmol/l). Additionally, leukocytosis (white blood cell count 20.90 × 10^3 cells/µl) and hyperkalaemia (K+ 5.3 mmol/l) were noted.

Under suspicion of diabetic ketoacidosis, an insulin pump (insulin actrapid 50 units usage in 500 ml normal saline) was immediately administered at a rate of 60 ml/h. However, cardiac arrest occurred abruptly. An electrocardiogram revealed pulseless VT (Fig. 1) and CPR was immediately performed with sequential defibrillation, which was repeated five times. Laboratory data revealed severe hypokalaemia (K+ 1.6 mmol/l). Large-dose inotropes including dopamine (17.3 mcg/kg/min) and norepinephrine (26.5 mcg/kg/min) were administered. Simultaneously, continuous KCl infusion was performed. However, the haemodynamic status remained inadequate with refractory VT and low cardiac output.

Peripheral VA-ECMO implantation was therefore performed through the right femoral vein and artery at a pump speed of 3 000 rpm and flow rate of 3.3 l/min. A Glasgow coma scale result of E2M2Vt was observed. Blood pressure was approximately 70/60 mmHg irrespective of the high doses of inotropes, and occasional VT was noted despite anti-arrhythmia medication. Moreover, echocardiography revealed generalised hypokinesia of the bilateral ventricles with left ventricular ejection fraction of 10–15%. However, despite the VA-ECMO support, the patient developed multiple organ dysfunction, including acute kidney injury, congestive liver and severe pulmonary oedema.

We therefore changed the VA-ECMO to a temporary continuous-flow Bi-VAD (Levitronix® CentriMag) for better systemic perfusion (Fig. 2). Using a sternotomy and under the guidance of transoesophageal echocardiography, the left ventricular assist device (L-VAD) inflow tube was inserted from the right superior pulmonary vein into the left ventricular apex, whereas the outflow tube was cannulated on the ascending aorta. The right VAD (R-VAD) inflow tube was inserted into the right atrium, and the outflow tube was inserted into the pulmonary artery. The operation time was approximately two hours. The initial L-VAD pump speed was 3 700 rpm and flow rate was 4.74 l/min. The R-VAD pump speed was 3 000 rpm and flow rate was 4.87 l/min (Table 1).

For severe hypoxaemia resulting from pulmonary oedema, an oxygenator was inserted into the L-VAD outflow to optimise systemic oxygenation. Mean arterial pressure (MAP) was maintained at 75–80 mmHg with low-dose norepinephrine (4.3 mcg/kg/min). Potassium level was maintained within the range 4.2–4.7 mmol/l and serum glucose level within 180–220 mg/dl (9.99–12.21 mmol/l).

At the time of maintaining support with Bi-VAD, the ventilator was set at 40% FiO₂ with positive end-expiratory pressure at 8 cmH₂O to prevent alveolar collapse. The support pressure was set at 12–15 cmH₂O to achieve an optimal tidal volume status (6–8 ml/kg), and the plateau pressure was controlled under 24 cmH₂O. During the time of support with VAD, the patient’s MAP was closely monitored and both VAD and inotropic agents were gradually tapered down to prevent vasoconstriction in the vital visceral organs.

Systemic heparinisation was performed to maintain an active clotting time of 140–160 seconds to prevent thromboembolism. Additionally, a broad-spectrum antibiotic was prophylactically prescribed following the Bi-VAD implantation. On day three of Bi-VAD implantation, the pulmonary oedema was completely resolved; subsequently, the oxygenator was taken down from the L-VAD outflow. Although renal function did not recover immediately, it recovered completely after hospitalisation with temporary haemodialysis (post-VAD implantation days one to nine). Following 12-day support with the Bi-VAD, the myocardial stunning was adequately improved; eventually, the Bi-VAD was removed successfully.

Table 1 presents the biochemistry data, inotrope dosages and echocardiography presentation during the VAD course.
The patient was weaned off the ventilator, and extubation was performed three days after VAD removal. The day after extubation, the patient was transferred to an ordinary ward and discharged one week later. Out-patient follow up revealed normal cardiac and renal function and cognition, and adequate control of diabetes.

Discussion

Hypokalaemia is a common electrolyte imbalance present in 20% of hospitalised patients, and some of these patients require immediate pharmacological treatment. Insulin-induced hypokalaemia results in a decrease in serum potassium level due to intracellular potassium shifts and, potentially, the aldosterone-kaliuretic effect of insulin on the renal tubule further increases urinary potassium losses.

The goal of the treatment for insulin-induced hypokalaemia (K+ < 2.5 mmol/l) is to replenish potassium stores through slow intravenous infusion of KCl, with insulin therapy delayed until serum potassium levels are corrected back to > 2.5 mmol/l. The most severe complication of hypokalaemia is lethal arrhythmia, which can be defined as the implantation of VAD-ECMO in a patient who has experienced a sudden and unexpected pulseless condition attributable to cessation of cardiac mechanical activity. Many prospective and retrospective studies have demonstrated the superiority of ECPR over conventional CPR regarding the odds of survival and neurological outcome. ECPR can be viewed as a late intervention in a moribund patient, possibly a candidate for an earlier circulatory support system in case of IHCA.

In our case, the patient experienced in-hospital cardiac arrest (IHCA) resulting from hypokalaemia-induced VT/VF. Extracorporeal CPR (ECPR) restored tissue and organ perfusion to allow stabilisation and recovery of function. ECPR can be defined as the implantation of VA-ECMO in a patient who has experienced a sudden and unexpected pulseless condition attributable to cessation of cardiac mechanical activity. Many prospective and retrospective studies have demonstrated the superiority of ECPR over conventional CPR regarding the odds of survival and neurological outcome. ECPR can be viewed as a late intervention in a moribund patient, possibly a candidate for an earlier circulatory support system in case of IHCA.

Compared with ECMO, which provides both cardiac and pulmonary support, a Bi-VAD usually provides cardiac support only. However, a Bi-VAD can be implemented long term with more cardiac support than ECMO, especially when the ECMO is set up peripherally. Moreover, patients on ECMO support usually require large doses of inotropes, which cause extreme vasoconstriction and lead to malperfusion of the visceral organs. In patients with refractory cardiogenic shock, a VAD has been reported to provide a better survival rate than VA-ECMO.

In the current case, although VA-ECMO was instituted for mechanical circulatory support and the potassium level was corrected back to the normal range, the patient experienced cardiogenic shock with multiple organ dysfunction and exacerbations. Therefore, ECMO was substituted with Bi-VAD implantation for optimal systemic perfusion. More importantly, the Bi-VAD completely unloaded the bilateral ventricle, maximising the likelihood of recovery from myocardial stunning. Based on our experience, the indications for VAD intervention can be defined for these critical patients with ECMO support (Table 2).

In our case, following Bi-VAD implantation, we were able to immediately withdraw the inotropes and all the visceral organs were preserved. Bedside echocardiography showed no distention of the bilateral ventricle. Initially, the pulse pressure was narrowed but returned three days later, which implied that the myocardial stunning was completely resolved.

The CentriMag VAD (Levitronix LLC) was chosen for several reasons. First, it has continuous flow, which is reported to have better outcomes than pulsatile flow, especially for mechanical circulatory support and the potassium removal after 24 hours of implantation. Second, Levitronix CentriMag VAD was used as a temporary short-term VAD as a bridge towards recovery and transplantation, if not the destination. Unlike with long-term VAD, it is easy to implant

### Table 1. Biochemistry data, inotrope dosage and echocardiography presentation during the VAD course

<table>
<thead>
<tr>
<th></th>
<th>Before VAD</th>
<th>POD1</th>
<th>POD2</th>
<th>POD3</th>
<th>POD4</th>
<th>POD5</th>
<th>POD7</th>
<th>POD11</th>
<th>Day 3 after removal</th>
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<tr>
<td>K+ (mmol/l)</td>
<td>1.6</td>
<td>4.2</td>
<td>4.7</td>
<td>3.7</td>
<td>3.5</td>
<td>3.5</td>
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<td>CK (UI/l)</td>
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<td>&gt; 10000</td>
<td>&gt; 10000</td>
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<td>3292</td>
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<td>Tro-1 (ng/ml)</td>
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<td>7.11</td>
<td>5.765</td>
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<td>BUN (mg/dl)</td>
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<td>26</td>
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<td>31</td>
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<td>Cr (mg/dl)</td>
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<td></td>
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<td>3.7</td>
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<td>Urine output (ml/day)</td>
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<td>995</td>
<td>1720</td>
<td>1620</td>
<td>3000</td>
<td>3420</td>
<td>4160</td>
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<td>Urine output (ml/day)</td>
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<td>Ketamine (mcg/kg/min)</td>
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<td>DOPAT (mcg/kg/min)</td>
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<td>9.4</td>
<td>9.35</td>
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<td>Epinephrine (mcg/kg/min)</td>
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<td>L-VAD (rpm/flow)</td>
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<td>3700/5.7</td>
<td>3700/4.86</td>
<td>3600/4.5</td>
<td>3500/4.14</td>
<td>3400/3.81</td>
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<td>R-VAD (rpm/flow)</td>
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<td>3000/5.02</td>
<td>2700/4.4</td>
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<td>MAP (mmHg)</td>
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<td>80-90</td>
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<td>88-100</td>
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<td>30-35</td>
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POD = post-operative day; L-VAD = left ventricular assist device; R-VAD = right ventricular assist device; BUN = blood urea nitrogen; CK = creatinine kinase.

### Table 2. Indications of VAD intervention after ECMO support

1. ECMO flow insufficiency; ECMO complications
2. Any organ dysfunction with ECMO maximal flow
3. Three or more inotropes or large dose
4. Narrow pulse pressure, ≥ 10 mmHg
5. Sustained VT resulted from LV distension
6. Echocardiography: No opening of aortic valve
7. LV thrombus formation
8. Blood stasis in LV, presented as smoke swirl sign
the device without extensively damaging the myocardium. More crucially, repairing the cannulation sites during explanation of the VAD is simple. Third, from the economic perspective, it is much cheaper than a permanent long-term VAD such as the HeartMate and HeartWare devices. Fourth, after CPR, most patients develop pulmonary oedema and poor oxygenation, and an oxygenator is always required for optimal oxygenation. The Levitronix CentriMag VAD, categorised as an extracorporeal VAD, can be easily integrated with an oxygenator, which is not possible with an intracorporeal VAD.

Conclusion

The Levitronix® CentriMag VAD was able to temporarily provide satisfactory mechanical circulatory support in acute decompensated heart failure. It can provide better circulatory support than ECMO. Additionally, it is easy to set up and repair without causing considerable damage to the myocardium if a bridge to recovery is expected. In this case, the Levitronix® CentriMag VAD was successfully implemented to save the life of a young patient who had experienced hypokalaemia-related cardiac arrest resulting from iatrogenic insulin infusion.

References