Extracorporeal Membrane Oxygenator (ECMO) for Life Support in Fulminant Myocarditis

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Fulminant myocarditis refers to acute myocarditis with abrupt onset of severe cardiogenic shock and circulatory collapse. Once regarded as a disease with uniformly high mortality, fulminant myocarditis is now a potentially treatable condition, thanks to advances in intensive care and mechanical circulatory support. We report our first pediatric case of fulminant myocarditis rescued by extracorporeal membrane oxygenator (ECMO) and continuous renal replacement therapy (CRRT).

Case Report

A 3-year-old boy presented to the outpatient department (OPD) at Bangkok Hospital with high fever, malaise and vomiting for 2 days prior to admission. He had no underlying disease except for a history of cow milk allergy. His brother was diagnosed with hand foot and mouth disease 1 week prior to the admission.

Physical examination

A well nourished male patient, febrile, good consciousness but appeared tired:

- Body weight: 14 Kilograms (kg).
- Vital signs: Blood pressure (BP) 118/88 mmHg, Heart rate (HR) 163 beats per minute (bpm), Respiratory rate (RR) 26 breaths per minute, Body temperature 37.7 °C.
- Head, Eyes, Ears, Nose, Throat (HEENT) examination: not pale, no icteric sclera, pharynx not injected.
- Heart: tachycardia, no murmur, no gallop.
- Lungs: no retraction, good air entry.
- Abdomen: soft, no hepatosplenomagaly.
- Skin: small area of blisters at plantar area.
- Other: no cervical lymph nodes detected.
- Neurosigns: stiff neck negative.

Investigations on admission

- Complete blood count (CBC): White blood cell (WBC) 21,120 cells/mm3 (Neutrophils 71.3%, Lymphocytes 24.4%, Monocytes 3.9% Eosinophils 0% Basophils 0.4%), Hemoglobin (Hb) 14.1 g/dL, Platelet 529000/mm3
- Urea Nitrogen (BUN) 17 mg/dL (8-20), Creatinine (Cr) 1.36 mg/dL (0.6-1.5), Electrolytes; Sodium (Na+) 130 mmol/L, Potassium (K+) 4.69 mmol/L, Chlorine (Cl-) 90 mmol/L, Total CO2 15.1 mmol/L, Aspartate Aminotransferase (AST) 153 U/L (0-40), Alanine Aminotransferase (ALT) 72 U/L (0-40), Albumin 3.89 g/dL, Creatine phosphokinase (CPK) 440 U/L (15-220), Creatine Kinase-MB (CK-MB) 18.37 ng/ml (0-3), Troponin-T 2,233 ng/L (0-100), Lactate 14 mmol/L (0.5-2.2)
- Echocardiogram (Echo) showed left ventricular ejection fraction (EF) of 30% in the OPD.

Hospital course

The patient developed cardiac arrest at the OPD after intravenous fluid was given. After cardiopulmonary resuscitation (CPR), he was transferred to the pediatric intensive care unit (PICU) with continuous intravenous inotropic drugs (Adrenaline 2 microgram per kilogram per minute (mcg/kg/min), Dopamine 20 mcg/kg/min and Dobutamine 20 mcg/kg/min). Bedside echocardiogram revealed in the PICU showed further deterioration of left ventricular EF to 12%. Although adrenaline, dopamine and dobutamine were continuously administered, a second episode of cardiac arrest followed admission to the PICU and the patient was resuscitated for another 5 minutes. Physical examination showed marked tachycardia (HR 220 /bpm, sinus tachycardia) and frank pulmonary edema. Electrocardiogram (EKG) revealed sinus tachycardia with no other significant abnormality (Figure 1). Chest x-ray revealed the normal size heart and pulmonary edema (Figure 2A). Elevated troponin-T at 2,233 ng/L (normal 0-100) and CPK at 8.37 ng/ml (normal 0-5) were found and fulminant myocarditis was diagnosed. Because of continuing deterioration, veno-arterial extracorporeal membrane oxygenation (VA-ECMO) was placed 12 hours after admission. Rotaflow centrifugal pump and Quadrox iD oxygenator (Maquet Inc, Rastatt, Germany) were used in this case.

Blood and secretions were sent for viral studies. Blood test for Enterovirus 71 (EV71) IgM was positive. Lumbar puncture was not done due to the unstable clinical status. Intravenous immunoglobulin (2 g/kg) and broad-spectrum antibiotics were given. Supportive treatment was continued. Troponin-T was 4,469 and 3,301 ng/L (0-100) at 48 and 72 hours after admission, respectively. Serum AST and ALT increased to 5,651 and 2,281 U/L at 48 hours after admission. The patient developed acute renal failure with rising blood urea nitrogen (BUN = 88.3 mg/dL) and creatinine (3.6 mg/dL) on the 3rd day of admission. Continuous renal replacement therapy (CRRT) as a continuous venovenous hemofiltration (CVVH) modality with simultaneous pre and post-dilution fluid replacement modes by Prismaflex® machine (GAMBRO company, Sweden) was incorporated into the ECMO circuit by connecting a CRRT inlet line after the centrifugal pump and its outlet line before the oxygenator (Figure 3).

Both machines functioned adequately and there were no significant changes in the pressures of the ECMO circuit after the introduction of the CRRT device, thus achieving the preset negative fluid balances and normalization of the serum BUN and creatinine. We ran both machines for three days and stopped the CRRT one day before weaning the patient off the ECMO. Milrinone and sodium nitroprusside were administrated during the circulatory assisted period. Weaning of ECMO was started after improvement of the EF to 30% and successful decannulation and removal of ECMO was performed on the 7 day of admission with stable hemodynamic status. The echocardiogram demonstrated further improvement of the left ventricular EF to 65% during the next 7 days. Serial chest x-rays showed resolution of pulmonary edema (Figure 2B-D). Serum AST, ALT and creatinine also improved to 46 U/L, 145 U/L and 0.38 mg/dL, respectively on the 10th day of admission. The patient was fully awake and had good cognitive function after the treatment although he developed central apnea and could not be weaned off the ventilator support. Brain stem injury from the EV71 virus was suspected. The patient was transferred to Chulalongkorn hospital for long-term respiratory management. The patient was discharged 3 and half months after the initial admission with tracheostomy (no home ventilator). The left ventricular EF was normal at the time of discharge.

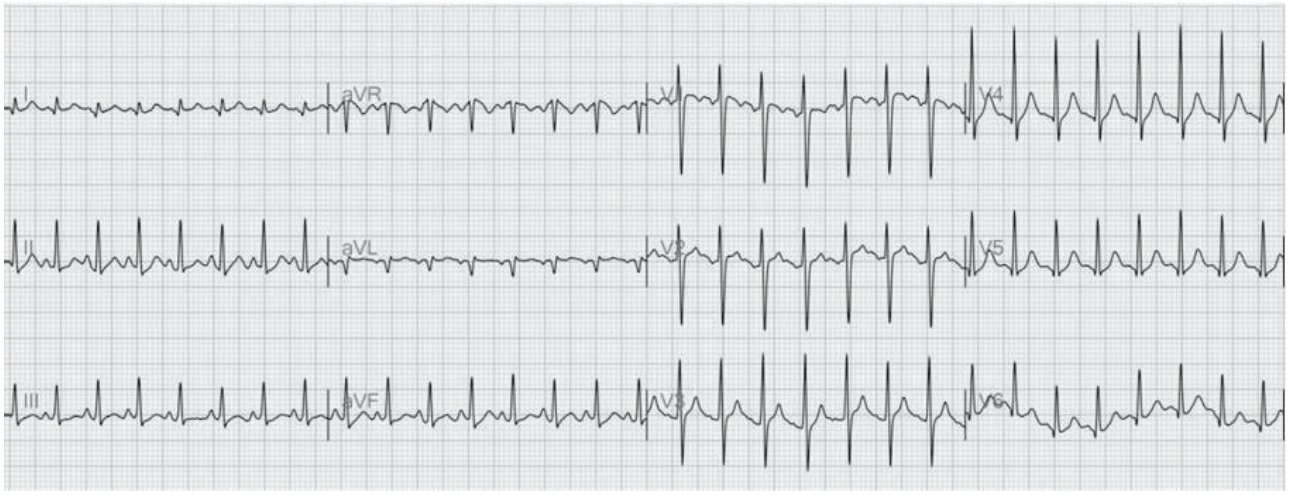

Figure 1: *Electrocardiogram on admission shows sinus tachycardia.*

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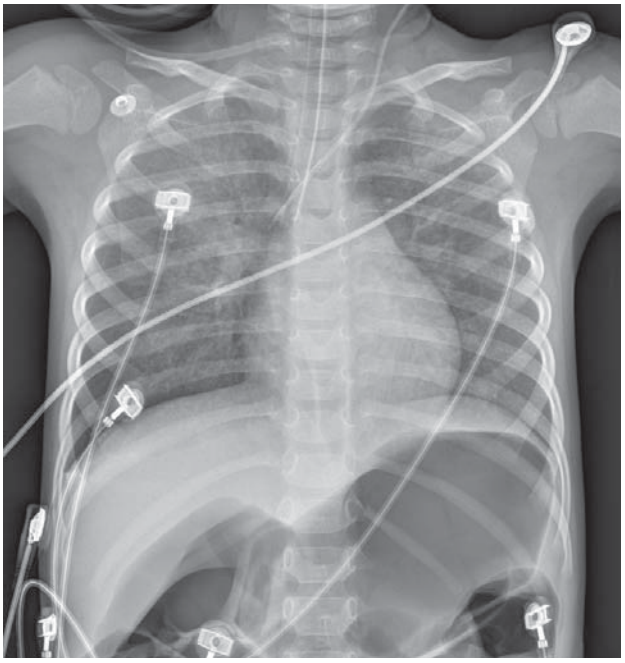

Figure 2A: *On January 20, 2013 at 15:21, a chest x-ray AP supine position reveals early pumonary edema. Heart appeared normal. The tip of the catheter was in SVC, endobroncheal tube is in place.*

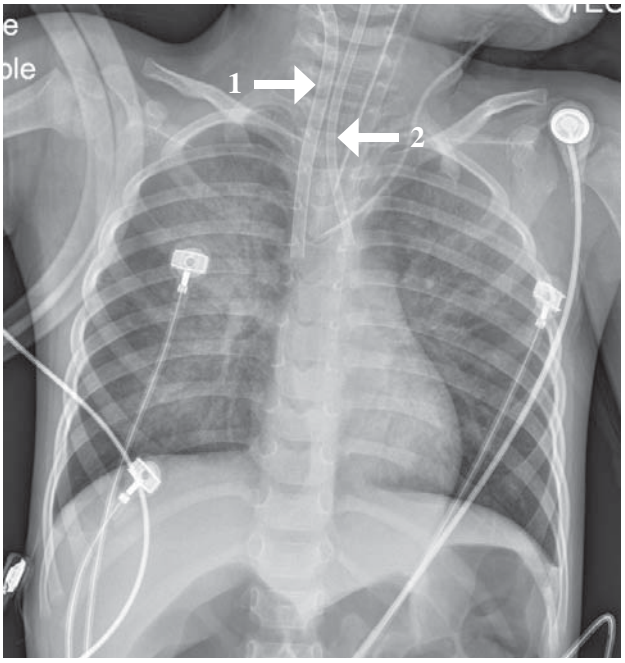

Figure 2B: *On January 23, 2013 at 21:41, a chest x-ray AP supine position and ECMO venous to arterial connection. The tip of catheter 1 is in SVC. The tip of catheter 2 is in the aortic arch. Progressive pulmonary edema developed.*

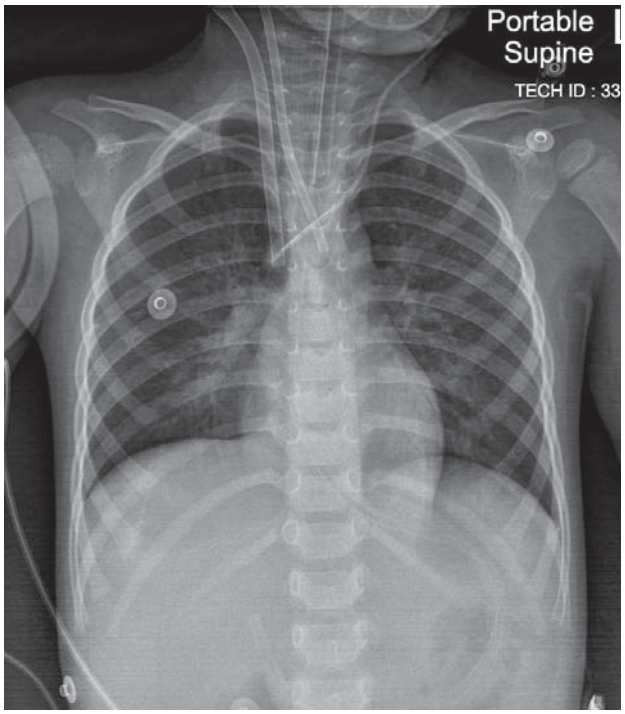

Figure 2C: *On January 24, 2013 at 15:38, a chest x-ray AP supine position reveals improvement of pulmonary edema.*

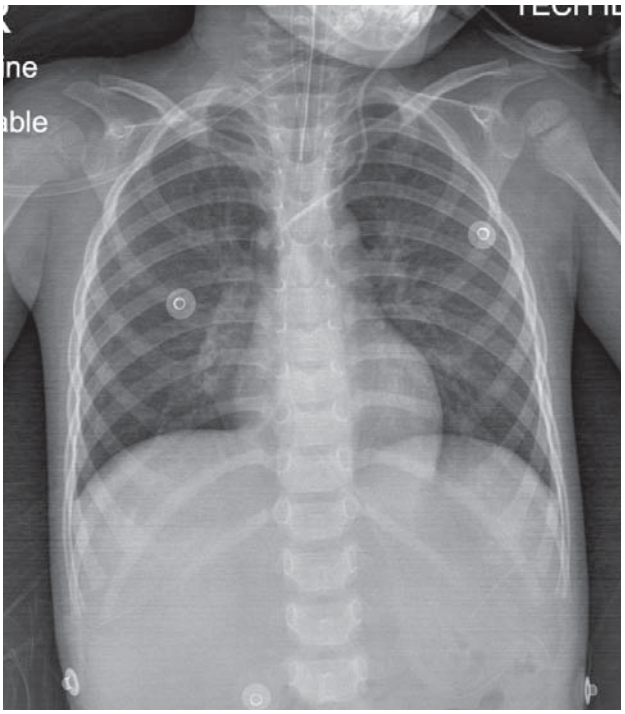

Figure 2D: *On January 27, 2013 at 5:30, a chest x-ray AP supine position and post removal ECMO reveals heart and lung appear normal.*

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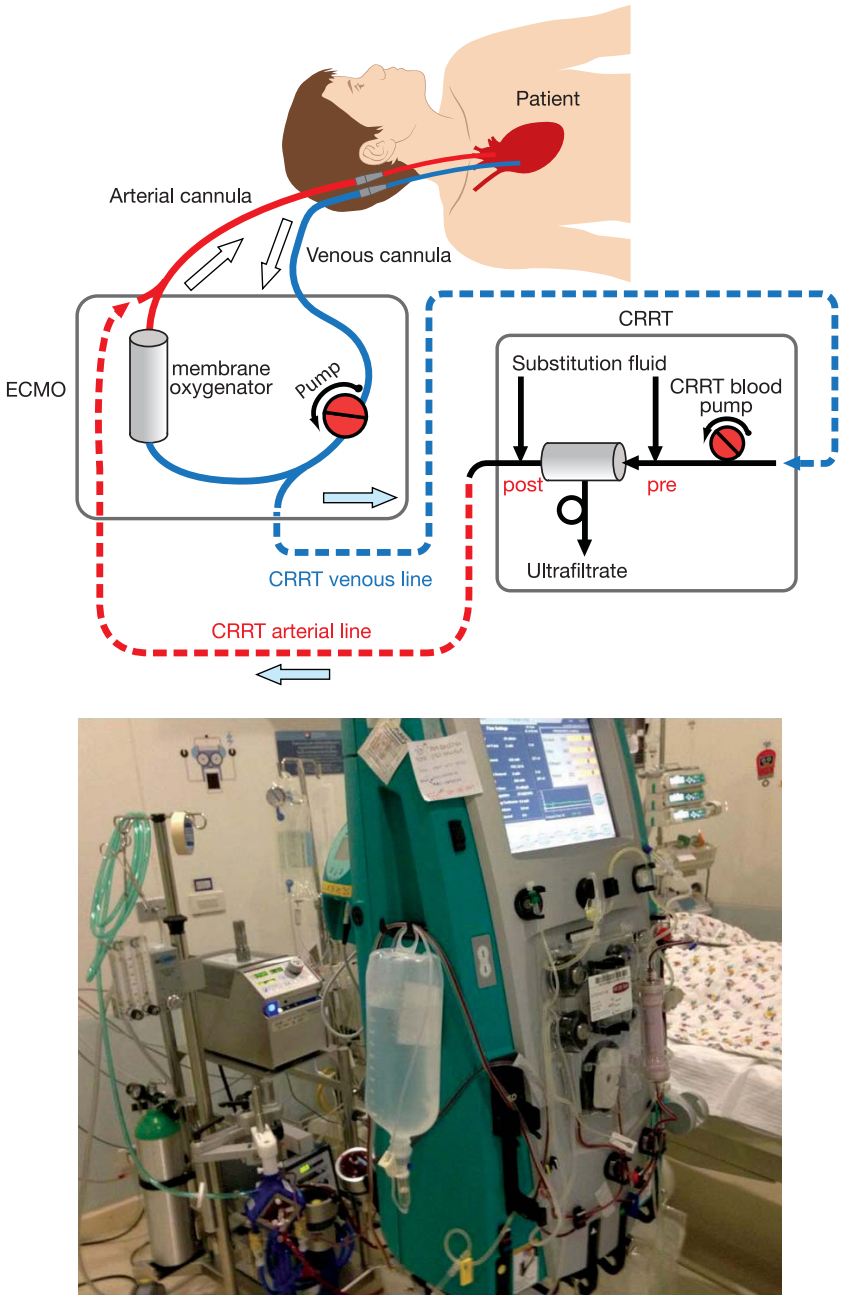

Figure 3: *Diagram of venous-arterial connection with continuous renal replacement therapy (CRRT) incorporated into the circuit.*

Discussion

Hand-foot-and-mouth disease (HFMD) is caused by a group of enteroviruses, most commonly coxsackievirus A 16 (CA16) and enterovirus 71 (EV71). In general, the disease is mild and self-limited except in the case of EV71 infections, which may result in serious complications such as myocarditis and encephalitis.[1] In Thailand, the prevalence of EV71 was high during 2008-2009 and has been increasing since 2011.[2] There are currently no approved vaccines or antiviral therapies for the prevention or treatment of EV71 infection. Acute viral myocarditis is caused by viral induced infiltration of inflammatory cells into the myocardium. Fulminant myocarditis is characterized by rapid onset of pump failure that sometimes leads to death by cardiogenic shock.[3] In our patient, rapid progression of hemodynamic instabilities was observed after admission despite maximal medical therapy necessitating a rescue by ECMO. Laboratory studies confirmed the EV71 infection in addition to history of recent HFMD in his brother.

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The overall survival rate for children with acute myocarditis is about 73% and is lower in patients with fulminant myocarditis.[4] A number of reports suggest that mechanical circulatory support may be used to successfully bridge children with acute fulminant myocarditis to recovery or transplantation.[4-7] The survival rate in patients with fulminant myocarditis undergoing ECMO support are 67-82%.[5-7] In this patient, progressive reduction of EF and hemodynamic instability were observed despite maximal medical treatment. Laboratory investigations also showed severe metabolic acidosis, increased cardiac enzymes levels and decreased renal function. Venoarterial ECMO was then used to successfully salvage the patient despite multiple organ failure. End-organ dysfunction is associated with increased mortality in pediatric cardiac patients requiring extracorporeal support.[6]

Acute renal failure while on ECMO is associated with a decreased risk for survival in pediatric cardiac patients.[6,8] In the absence of primary renal disease, this is usually transient and would not progress to chronic renal failure after concurrent use of CRRT with ECMO.[9] In our patient, the renal function recovered and his serum creatinine was normal before transfer. No complication such as circuit clotting was detected and only one filter was used during CRRT with ECMO. One study reported that the introduction of a CRRT device into the ECMO circuit, similar to what we used in our patient, was safe and effective.[10]

Brainstem encephalitis caused by EV71 in children is a serious complication. Magnetic resonance imaging (MRI) scans can provide important information for clinical evaluation and treatment.[11] In our case, the patient was also affected by central respiratory failure from brainstem encephalitis and required prolonged mechanical ventilation.

Conclusion

Viral myocarditis is an important cause of cardiogenic shock in children outside of the neonatal period and can be fatal if left untreated. No specific treatment is available at this time and supportive treatment is the standard treatment to support the circulation while waiting for a spontaneous recovery. Application of ECMO with or without renal support in selected patients can be life-saving in children who develop refractory shock despite maximal medical treatments.

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Contributors

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