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Case Reports

A case series of the successful use of ECMO, continuous renal replacement therapy, and plasma exchange for thrombocytopenia-associated multiple organ failure

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Abstract We present three cases of pediatric patients with thrombocytopenia-associated multiple organ failure and the evidence for providing extracorporeal organ support. All three patients had severe cardiac dysfunction, respiratory failure, and acute kidney injury treated with venoarterial extracorporeal membrane oxygenation, continuous renal replacement therapy, and plasma exchange. Despite the presence of multiple organ failure and high risk of mortality, all three patients survived with minimal long-term sequelae.

In recent years, extracorporeal membrane oxygenation (ECMO) for multiple organ failure and sepsis has become more commonplace. Even though the diagnosis of sepsis was previously a contraindication to ECMO, VA ECMO is being used to support through multiple organ failure secondary to a reversible underlying etiology [1]. Current recommendations from the American College of Critical Care Medicine include ECMO as an option in refractory septic shock for neonatal and pediatric patients [2]. Venoarterial (VA) ECMO provides cardiac output in addition to oxygenation and ventilation. The ECMO circuit serves as a heparinized platform into which other organ support modalities such as renal replacement therapy and therapeutic plasma exchange can be easily added.

Fluid overload has repeatedly been shown to be associated with mortality in critically ill children, and there are 7 pediatric studies that demonstrate the initiation of continuous renal replacement therapy (CRRT) before the accrual of greater than 10 to 20% fluid overload is associated with greater survival [3–9]. In each of these studies, percent fluid overload was defined by the formula described in the 2001 article by Goldstein et al., ([Fluid in − fluid out]/PICU admission weight) * 100 [3]. These 7 studies have a combined total of more than 800 patients and suggest that early initiation of CRRT in critically ill children with AKI and fluid overload may improve outcomes [10]. The pediatric section of the 2012 Surviving Sepsis Campaign guidelines recommend the use of diuretics to reverse fluid overload once shock has resolved, and if fluid overload is refractory to diuretics, starting continuous venovenous hemofiltration or intermittent hemodialysis to prevent greater than 10% total body weight fluid overload [11]. In critically

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ill pediatric patients, in whom adequate vascular access can be difficult to attain, connecting a CRRT device or an in-line hemofilter to the ECMO circuit is a considerable advantage [12]. The use of CRRT with ECMO allows for adequate nutrition, blood product transfusion, and medication administration, while avoiding worsening of fluid overload. Despite these advantages, a recent international survey revealed that 23% of responding centers use no form of renal replacement therapy for patients on ECMO [13].

Nguyen et al. described a two-part study of children with thrombocytopenia associated multiple organ failure (TAMOF). The first part of the study demonstrated that children with TAMOF had decreased activity of the von Willebrand-cleaving metalloprotease known as a disintegrin and metalloprotease with thrombospondin motifs (ADAMTS)-13, compared to children with multiple organ failure without thrombocytopenia. The second part of the study demonstrated an increase in ADAMTS-13 activity, a reduction in organ failure, and an increase in 28-day survival in those treated with intensive plasma exchange therapy versus standard therapy [14]. Adult studies of plasma exchange for thrombotic microangiopathies have shown a similar reduction in organ failure and improved outcomes [15–18]. It is thought that TAMOF represents a microangiopathy similar to thrombotic thrombocytopenic purpura (TTP). Patients with TTP have systemic microvascular aggregation of platelets and microthrombi mediated by ultra-large von Willebrand factor (ULVWF) multimers and a deficiency of the von Willebrand-cleaving ADAMTS-13, resulting in severe thrombocytopenia, microangiopathic hemolytic anemia, and neurologic abnormalities. With TTP, ischemia of the brain and gastrointestinal tract is common, and renal dysfunction can occur. The basis of therapeutic plasma exchange for TTP is the repletion of ADAMTS-13, removal of ADAMTS-13 inhibitors, and removal of thrombogenic ULVWF multimers [19].

In this case series, we will present the successful use of VA ECMO, CRRT, and plasma exchange for recovery from thrombocytopenia-associated multiple organ failure.

1. Case 1

A 14 year-old male presented to our intensive care unit with respiratory failure and severe hypotension. He was diagnosed with influenza three days before admission, and his primary care physician gave him a prescription for oseltamivir. On admission to the pediatric intensive care unit, the patient's chest x-ray revealed almost complete opacification of the lung fields. He was switched from conventional mechanical ventilation to a high frequency oscillatory ventilator with inhaled nitric oxide for refractory hypoxia. Despite support with infusions of epinephrine, dopamine, vasopressin, and aggressive fluid resuscitation, an age appropriate blood pressure could not be maintained. An echocardiogram revealed severely depressed biventricular function. The patient also developed a coagulopathy, acute kidney injury, and fluid overload. His initial blood urea nitrogen (BUN) was 42 mg/dL, and his initial creatinine was 4.94 mg/dL. The patient's calculated percent fluid overload was 40.7% in the first 24 h of his ICU admission. Within the first 24 h of admission, his international normalized ratio (INR) reached 2.2. He was started on broad-spectrum antibiotics and oseltamivir was continued. In addition to being positive for influenza A, methicillin sensitive staphylococcus aureus grew from his initial endotracheal tube culture.

As the patient had refractory septic shock with multiple organ failure, the decision was made to cannulate the patient for VA ECMO. A 21 French cannula was placed in the right carotid artery and a 23 French cannula was placed in the right internal jugular vein. An ECMO flow of 4.7 l/min (100 ml/kg/min) was achieved soon after cannulation. The patient's acute kidney injury and fluid overload were treated with continuous venovenous hemofiltration (CVVH). A commercially available CRRT device was connected directly into the ECMO circuit. As the patient met the criteria for TAMOF, daily plasma exchange was provided for 8 days. On hospital day 2, the patient's ADAMTS-13 level was depressed at 38% and his platelet level was as low as 35 thousand/μl. After completing his course of plasma exchange, the patient's ADAMTS-13 level was improved at 52%, and his platelet count had improved to 102 thousand/μl.

After 10 days of VA ECMO and CRRT, he was successfully decannulated from ECMO. He continued on CVVH for an additional 4 days. As per our standard of care in the pediatric intensive care unit, we used regional anticoagulation with citrate for this patient who required CRRT, but was no longer anticoagulation with heparin. On day 22 of his hospitalization, he received a tracheostomy. He was discharged from the hospital 43 days after admission. An MRI of the brain revealed a right middle cerebral territory infarction with gyriform enhancement. He required admission to inpatient rehabilitation for critical illness myopathy and left-sided hemiparesis. During his inpatient rehabilitation stay, he was able to have his tracheostomy removed. An outpatient echocardiogram revealed completely normal cardiac function. He does have mild, residual left hand weakness, but this has improved over time. He is otherwise healthy and very active. Currently, he is a sophomore in high school.

2. Case 2

A 14 year-old male was admitted to our intensive care unit with respiratory failure and profound hypotension. An echocardiogram revealed severely depressed biventricular function. He required over 10 l of fluid resuscitation and a high dose epinephrine and dopamine infusion for refractory