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CLINICAL VIGNETTE

Acute Respiratory Failure from Goodpasture's Syndrome Treated with ECMO

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Case Presentation

A 23-year-old man with no significant past medical history presented to the emergency department with one week of cough productive of yellow sputum, shortness of breath and several episodes of hemoptysis and chest pain. The SpO2 was 96% on room air and he was afebrile. WBC was 10.0 with a normal differential. The chest x-ray showed patchy, mild, infiltrates bilaterally (Figure 1). He did not use drugs and quit smoking one month prior to presentation though had been using an electronic cigarette. He was diagnosed with community-acquired pneumonia and was discharged from the emergency department with azithromycin, ibuprofen and hydrocodone/acetaminophen.

He returned 3 days later with worsening dyspnea and severe hypoxemia (SpO2 61% on room air). He was again afebrile. WBC had increased to 18.2 with 83% neutrophils and 9% lymphocytes. His chest x-ray showed diffuse, bilateral infiltrates, significantly worse than his prior x-ray (Figure 2). Initial ABG on a nonrebreather face mask was: PaO2 53 mmHg, PaCO2 34 mmHg, and pH 7.43. He was admitted to the ICU with a diagnosis of pneumonia with acute respiratory failure and given broad spectrum antibiotics. Although he was initially placed on BiPAP, he required intubation within a few hours of admission.

Evaluation for an infectious etiology was negative including blood and sputum cultures, urine Legionella and pneumococcal antigen, influenza PCR and viral respiratory DFA panel. Bronchoscopy on the day of admission showed mucosal erythema and friability with blood in the trachea and all lower airways. BAL could not be performed due to worsening hypoxemia during the procedure. Because alveolar hemorrhage was suspected, ANCA and anti-glomerular basement membrane antibody levels were sent. Urinalysis was remarkable for 3+ blood. Methylprednisolone, 125 mg q 6 hours was started on day 2 and increased to 250 mg q6 hours on day 3. Anti-GBM AB returned > 8 units and ANCA was negative. He was thought to have Goodpasture's syndrome but was too unstable for lung or renal biopsy. Cyclophosphamide, 100 mg IV daily and plasmapheresis were started.

Despite high PEEP and a lung protective ventilator strategy, his respiratory status continued to worsen with severe hypoxemia and hypercapnia. He required paralysis and heavy sedation. Although renal function was normal on admission, the creatinine increased from 0.9 to 2.1 by hospital day 3 and dialysis was started on day 4. He also developed shock and norepinephrine was started on day 7. Due to severe subcutaneous emphysema, bilateral chest tubes were placed on day 7 (Figure 3). The ABG on day 8 was as follows: PaO2 41, PaCO2 53, pH 7.25 on pressure control 20/rate 30/I:E 2:1/PEEP 16. He was transferred to Ronald Reagan Medical Center on day 8 for extracorporeal membrane oxygenation (ECMO).

The initial intent was to perform veno-venous (VV) ECMO via bilateral femoral veins. However, there was difficulty in cannulating the left femoral vein so veno-arterial (VA) ECMO was started via the right femoral vein and artery. Just prior to starting ECMO he had a brief cardiac arrest lasting 1 minute so therapeutic hypothermia was provided for 24 hours.

The following day he was noted to have diminished perfusion to the lower extremities and bilateral compartment syndrome was suspected. In the operating room he was found to have thrombosis of his left superficial femoral artery. He underwent thrombectomy, bilateral fasciotomies, and conversion of the right femoral VA ECMO to VV ECMO via a dual lumen catheter in the right internal jugular vein. VV ECMO was continued for 8 days. He had a total of 15 days of plasmapheresis and remained on cyclophosphamide and methylprednisolone. He eventually required tracheostomy and bilateral leg skin grafts.

During this time he had gradual improvement in his respiratory status. However, he had severe peripheral muscle and diaphragmatic weakness. He progressed to the point where he tolerated a tracheostomy collar during the day but remained on nocturnal mechanical ventilation with pressure support. Seven weeks after his initial presentation, he was transferred back to the community hospital. By week 10, his renal function had improved and he no longer required dialysis. His oxygenation also improved and he only required 28% O2 though still required nocturnal mechanical ventilation by week 11 (Figure 4).

Discussion

ECMO was first developed in 1968[1] and has been used as a rescue therapy for patients with respiratory failure since the 1970s[2]. It provides a mechanism for directly oxygenating and removing CO2 from the blood. There are several modalities of ECMO. In veno-venous (VV) ECMO, blood is removed from and returned to the venous system. Venous access can be obtained from either a single peripheral vein with a dual lumen catheter or two separate venous access points. In veno-arterial (VA) ECMO, blood is removed from the venous system and returned to the arterial system. Extracorporeal removal of CO2 (ECCO2R) refers to the removal of CO2 alone, which can be achieved with a smaller catheter and lower flow rates, though is less effective in oxygenating blood[3-6].

VV ECMO is used for patients with respiratory failure while VA ECMO is used for patients with both respiratory and cardiac failure or cardiac failure alone. In both modalities, oxygenation is determined by the fraction of delivered oxygen and the blood flow through the circuit. Removal of CO2 is controlled by adjusting the flow rate of the sweep gas. By removing CO2 and improving oxygenation, ECMO facilitates "lung rest" by allowing lower tidal volumes and plateau pressures and reduces ventilator-induced lung injury[3-6].

Although previous randomized trials did not show improvement in survival, these studies have been criticized for several reasons. The first randomized trial for ECMO was conducted in the United States by the National Institutes of Health in the 1970s for patients with severe ARDS[2]. Patient survival was extremely low (<10%) and only VA ECMO was provided. ECMO was also removed if no benefit was observed after 5 days. In addition, because a lung protective strategy was not applied, patients suffered the effects of barotrauma and volutrauma. Because the circuits were not heparin coated at the time, high levels of anticoagulation were required and many patients had bleeding complications. A second study in 1990s, was a single-center randomized, controlled trial using ECCO2R[7]. This study was stopped after only 40 patients were enrolled due to futility.

Recently, there has been a resurgence of interest in ECMO due to the results of a randomized trial[8], observational studies[9], experience with the recent influenza A (H1N1) pandemic[10,11] and advances in technology[12]. The only recent randomized trial, CESAR (Conventional Ventilation or ECMO for Severe Adult Respiratory Failure), was conducted in the United Kingdom between 2001 and 2006[8]. The patients randomized to the control group were given conventional treatment at their designated hospitals while the patients randomized to the ECMO arm were transferred to single center. Ninety patients were randomized to each arm. Although a standardized protocol for ventilator management was implemented in the patients randomized to the ECMO arm, no protocols for mechanical ventilation were mandated in the control arm. Mortality and severe disability at 6 months was significantly lower in the ECMO group (37 vs. 53%). However, the trial was criticized for several reasons, including the lack of a standardized protocol in the control arm[13]. Also, 22 of the patients in the ECMO arm improved with conventional treatment and never received ECMO or died prior to receiving ECMO. Lastly, a higher percentage of patients in the ECMO arm received corticosteroids.

Several technologic advances have improved the safety and feasibility of ECMO[12]. First, membrane oxygenators are more efficient, durable and biocompatible and are less likely to cause thrombocytopenia and coagulation. Therefore, lower levels of anticoagulation can be permitted. Centrifugal pumps are also superior to previous roller pumps. Lastly, advances in vascular catheter design, such as dual-lumen catheters, allow a single point of venous access in VV ECMO and can reduce vascular complications.

Indications for ECMO in respiratory failure are evolving and there is considerable debate regarding its true efficacy given the paucity of controlled clinical trials. In general, however, VV ECMO is

usually used as a rescue therapy in severe but potentially reversible causes of respiratory failure such as ARDS, severe pneumonia, and graft failure in lung transplantation[3,6]. Although ECMO has been used much less commonly in respiratory failure from pulmonary hemorrhage, there have been several reports of its use in systemic lupus induced diffuse alveolar hemorrhage[14], Goodpasture's syndrome[15] and granulomatosis with polyangiitis[16]. Contraindications are not clearly defined but include any irreversible and life-threatening condition such as advanced malignancy and prolonged or unwitnessed arrest[3-6]. Because anticoagulation is required, any condition that precludes anticoagulation is also a contraindication to ECMO. In addition, because earlier application of ECMO may be associated with better outcomes, some centers do not recommend its use for patients who have been mechanically ventilated for more than 7 days.

This case illustrates the successful use of ECMO as a means of respiratory support in a young, previously healthy patient with a reversible condition. He had clearly failed to improve with conventional mechanical ventilation during the first few days of treatment for Goodpasture's syndrome and we believe that the likelihood of death was extremely high without ECMO. By instituting ECMO, he was given time to allow the therapies for Goodpasture's syndrome to take effect. The arterial thrombosis and limb ischemia also illustrate one of the major potential complications of ECMO[17]. While there is significant controversy regarding the widespread application of ECMO in respiratory failure, it should be considered in similar situations when conventional treatment has failed.

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