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EC CARDIOLOGY
Case Report

Salvage Extra-Corporeal Membrane Oxygenation (ECMO) in Systemic Vasculitis with Severe Active Hemoptysis: A Port for Treatment and Bridge to Recovery

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Abstract

Severe acute respiratory distress syndrome (ARDS) can be caused by diffuse alveolar haemorrhage (DAH) which is a rare and potentially fatal complication of the systemic vasculitis. The use of ECMO in DAH may be considered to be relatively contraindicated due to the requirement for systemic anticoagulation. The increased risk of infection and sepsis with ECMO insertion for relatively long unexpected duration while the patient is on immune-suppressive drugs needed for treatment is another major concern in these cases. In this report we present such a case of DAH in active hemoptysis with drop in Hemoglobin to 5gm%. The patient was crashed and despite been ventilated on emergency basis and high setting, the O2 saturation as well as the pO2 was not picking up. A recent history of discharge from the Nephrology Department after been admitted as a case of rapidly progressive glomerulonephritis was taken after which she was considered for regular hemodialysis as an out-patient case. The case was referred on emergency basis to us as an ECMO team, for salvage ECMO insertion. The ECMO circuit was used successfully as a port for Hemodialysis, alternating with plasma-pheresis as well as a bridge to recovery. The patient could be weaned and separated from the ECMO after 11 days with recovery of the lung gas exchange parameters as well as the marked improvement in the Chest X-Rays and from the ventilator after 2 more days. She passed increasing amounts of urine and pelvi-abdominal ultrasonography showed preserved cortico-medullary differentiation. She was discharged home after 36 days as a case of chronic kidney disease (CKD) with tapering of the corticosteroids and the immune-suppressant drugs doses and change to the oral form.

Keywords: *ECMO; ARDS; DAH; Vasculitis; Extra-Corporeal Membrane Oxygenation*

Introduction

The term pulmonary-renal syndrome is used to describe a great number of diseases in which pulmonary hemorrhage and glomerulonephritis coexist together. Veno-Venous (VV) ECMO and concomitant aggressive immune-suppressive therapy has been used successfully in reported cases with refractory hypoxemia and impending respiratory failure due to Diffuse Alveolar Hemorrhage (DAH) secondary to various causes including auto-immune vasculitis [1,2]. These few cases provided evidence that the anticoagulation used with VV-ECMO does not worsen the pulmonary hemorrhage. Nevertheless, the use of ECMO in these patients is still widely considered to increase the bleeding risk due to the need of anticoagulation for circuit patency and platelet dysfunction [3]. The successful case reports are not considered to the level of evidence so-far.

Case Presentation

A 39-year-old Female, Presented to the Emergency Room, with Mild Hemoptysis that was increased within 24h to severe degree and drop of her hemoglobin to 5 gm%, Severe Shortness of Breath (SOB). She was hypoxic with O_2 Saturation 70(s)%. She was crashed and ventilated on emergency basis and kept on high ventilator settings. Despite of being on FiO_2 of 100% for 3 hours and PEEP of 12 mmHg, the PO_2 of her Arterial Blood Gases (ABG) was 50(s). The ECMO team was called for salvage insertion. ARDS (P/F Ratio < 100), Chest X-Ray was highly suggestive (total opacity of the right lung and the lower-mid zone of the left lung).

The past history revealed recurrent polyarthritis, mouth ulcer, conjunctivitis, upper respiratory tract infection with chronic sinusitis.

Prior to the recent presentation with 10 days, she had been admitted under Nephrology Department, because of hematuria followed by oliguria. Urine analysis revealed urinary sediment, as well as red blood cell casts and creatinine jumped to 7.9 mg/dl. Rapid progressive glomerulonephritis was posted up-on these findings.

Kidney Biopsy and Immunological assay studies was taken for the proper diagnosis. Hemodialysis (HD) was done and patient discharged home with HD Catheter in the right internal jugular vein and in a stable condition after 1 weak.

Urgent pulmonology consultation for bronchoscopy was requested but was not done because of the critical situation and being on high ventilator settings. The ventilator settings had to be elevated while on Pressure Controlled Ventilation (PCV) (biphasic positive airway pressure to 35/15 cm H_2O, Positive End Expiratory Pressure (PEEP) of 10 cm H_20, inspiratory to expiratory ratio of about 1:1). Fractional inspired oxygen (FiO_2) was 100% but hypoxemia persisted (PaO_2 of 56.3 mmHg). Continued haemoptysis resulted in repeated airway obstruction and reduced alveolar diffusion capacity as well.

The patient started to show brady-arrest on the monitor despite the known fact of having normal echo-cardiography. On emergency basis while resuscitation, the V-V ECMO was inserted in conjunction with transfusion of 4 Units packed red blood cells. Cardio-help System of Maquet (MAQUET Cardiopulmonary AG, Hirrlingen, Germany) and (Right multistage medtronics cannula in femoral vein - Right internal jugular return cannula) (21fr. - 19fr. cannula). Systemic heparinization as usual with target ACT around (160 - 180) and activated partial thromboplastin time (aPTT) between 41 - 66 seconds keeping in mind that the patient was in active bleeding. Arrangement with the Nephrology and Rheumatology departments for HD and Plasma-pheresis, alternatively every other day, through the ECMO Circuit (Input and Out-put access Lines). Both canulae were inserted percutaneously after assessment of the caliber of both target veins with bedside ultra-sonography. The ECMO flow was initially set to 4 L/minute. Gradual decreasing of the high settings of the ventilator (biphasic positive airway pressure and fractional inspired oxygen levels) over the first 24h guided with the blood gases.

Hemoptysis dramatically decreased in the 1st day after insertion of the ECMO and stopped completely after the 3rd day of ECMO initiation. Clinical, radiological, and laboratory findings showed progressive improvement that allowed ECMO weaning and discontinuation.

The platelet count during the period of ECMO insertion was always above 50,000 so, she did not receive any transfusion.

The double antibiotic (Vancomycin-Meropenem) -antifungal regimen was started as usual with all ECMO cases and as per our policy.

IV Corticosteroids as usual with vasculitis cases in pulsed dose and maintained there-after, therefore, the first prednisolone pulse of 500 mg intravenous (IV) was given. Immunosuppressive therapy was held initially to minimize the high risk of infection and then resumed after exclusion of sepsis (no fever -normal WBCs Count) and relatives consents. Cyclophosphamide 750 mg monthly for 6m was started+ Mycophenolate (Cellcet). The initial dose was given after the third HD set being washable during filtration.

The kidney biopsy was with high percentage crescent changes (> 50%) with granulomatous inflammatory changes.

Anti-double-stranded DNA antibodies, rheumatoid factor and RNP were negative. ANCA profile (Anti-Neutrophil Cytoplasmic Autoantibody) was also negative but Anti-glomerular-basement membrane (Anti GBM) antibodies were positive and Good-Pasture's Syndrome (GPS) appeared to be the most likely diagnosis.

After the 11th day of ECMO initiation and stability of the arterial blood gases on low settings of the ventilator and the ECMO as well, the ECMO was explanted and there were no exacerbations of pulmonary hemorrhage, no new events of extra-pulmonary hemorrhage or clotting complications during the follow up thereafter. After 2 days more, 13th day of ECMO initiation, the patient was stable and could be extubated safely.

In-hospital Continuous VV hemofiltration was continued according to the fluid balance status and the radiological findings of both lungs through the previously inserted HD catheter in the right internal jugular vein daily and replaced by HD three times a week. Plasmapharesis was performed for 6 sets more after removal of the ECMO with marked reduction of the Anti GBM 3 titers. The patient was discharged home in 36th day.

Pulse cyclophosphamide was prescribed for a total of 6 months, up to a total dose of 4.73 gm, followed by azathioprine (100 mg orally, daily) and prednisolone (tapered to 5 mg orally daily).

Discussion

The majority of Extra-corporeal Life Support Organization (ELSO) database cases of pulmonary vasculitis who received ECMO had a diagnosis of Wegener's (granulomatosis with polyangiitis), and the remaining diagnoses included hypersensitivity-angiitis, Good-Pasture's Syndrome (GPS) and thrombotic micro-angiopathy. The first successful use of ECMO to support an adult patient with ANCA-associated systemic vasculitis complicated by severe respiratory failure caused by diffuse alveolar hemorrhage was reported in 1994. It was presented also with severe form of Pulmonary-Renal failure Syndrome and required massive doses of immune-modulating drugs [4].

The diagnosis in such cases is usually neither easy nor definitive if only based on the clinical picture but in our opinion should go step by step according to the immunological assay. The initial clinical picture, the presence of red blood cell casts, together with acute renal failure and diffuse hemorrhagic alveolar infiltrates, takes us immediately to see the Anti-double-stranded DNA antibodies as well as the kidney biopsy to diagnose SLE (Systemic Lupus Erythematosis). If negative, the ANCA profile is the second step which is positive in most of the cases.

In ANCA positive cases which is usually due to the high PR3-ANCA levels (proteinase 3-Anti-Neutrophil Cytoplasmic Autoantibody) (Cytoplasmic or c-ANKA), the diagnosis of GPA presenting as pulmonary-renal syndrome is usually the primary provisional diagnosis. In few cases, the anti MPO-ANCA subtype (peri-nuclear or p-ANCA) (anti-myeloperoxidase-Anti-Neutrophil Cytoplasmic Autoantibody) is high and Charge Strauss come as a less common diagnosis.

In ANCA negative cases, the Anti gbm is diagnostic to GPS although Anti MPO can be positive in few cases. The RNP is usually diagnostic for the Raynaud and the mixed connective tissue disease. The rheumatoid factor should be included also in the assay [5-7].

The tissue biopsies specially the renal one is of great importance especially it is technically easy to attain with almost no complications rather than the pulmonary biopsy which is rarely indicated. The deposition of the antibodies on the glomerular basement membrane seen by immune-fluorescent (IF) staining together with the high titer of the circulating Anti-GBM antibodies is diagnostic for GPS. It has also been taken as a prognostic factor in the outcome and usually the presence of crescents affecting > 50% of glomeruli as in our case is a serious prognostic sign [8].

In our opinion, the prognosis can be improved dramatically as in our case by the early aggressive therapy which is usually based on corticosteroids; immunosuppressive drugs as well as plasma-pharesis and this can be documented in the falling down of the Anti GBM titre. When the patient decompensate due to respiratory insufficiency, VV-ECMO should emerge as a rescue mode of management as in many case reports [9-13].

The inclusion of plasma-pharesis is supported by observational studies that suggest improved renal and patient survival compared with historical cohorts treated with immune-suppression alone [14]. In addition, a large contemporaneous Chinese study of 221 patients suggested better outcomes in patients who received plasma-pharesis in addition to cytotoxic and corticosteroid therapy [15].

ECMO insertion is usually associated with an inflammatory response that results in a hyper-coagulable state, thus requiring anticoagulation with heparin to maintain an ACT of 1.5 times the normal (around a cutoff value of about 180) to prevent thromboembolic events in the non-biological surfaced circuit. This issue is of a great challenge in cases with active bleeding or even high risk to bleed. Only few case reports available suggest avoiding anticoagulation during ECMO in cases with DAH [4,6,13,16]. However, these patients remain at a very high risk of circuit thrombosis and systemic thromboembolism, which can increase morbidity and mortality.

We used anticoagulation during ECMO run to maintain the circuit patency without any adverse effect. This may be due to the usage of fresh frozen plasma and cryoprecipitate and platelets according to the assay of the Thrombo-Elasto-Gram (TEG) Results. Also, it can be attributed to the fact that the modern ECMO technology requires lower levels of anticoagulation for to maintain patency which minimizes the risk of bleeding. In this particular case we accepted ACT levels between 160 - 180 and heparin was titrated accordingly.

Insertion of central lines in an immune-compromised patient usually carries a higher risk of inducing bacteremia and fatal sepsis. This was another challenge in our case as we had to start the pulse corticosteroids with the immunosuppressive drugs as well and on urgent basis to control the progression of the autoimmune syndrome.

To our mind, it was of great importance to canulate the patient percutaneously under complete aseptic technique and with the least handling under guidance of the bed side Sonography to determine the exact caliber for the proper sizing of the canula and site prick of the jugular and femoral veins with no any extravasation or complications.

In our current case, ECMO proved to be life-saving by maintaining oxygenation for the vital organs with decreased ventilator induced injury to the lungs. The ECMO circuit could be used as a port for Renal Replacement Therapy and plasma-pharesis as well. It could also offer the pulmonary diseased vasculature the time needed to respond to the immune-suppressive drugs and the plasma-pharesis. ELSO data supports our opinion and suggests that DAH related to vasculitis should not be considered as a contraindication.

To our knowledge, this maybe the first adult case of GPS to be managed with HD and Plasma-pharesis Sets alternatively through the ECMO Circuit after the only reported child case in 2012 [17]. This case can add to the questionnaire raised by others [5,18].

Conclusion

VV-ECMO offers an excellent rescue as well as salvage mode of management in Severe Respiratory Failure (ARDS) in case of Pulmonary-Renal Syndromes associated DAH. ECMO should be considered as a platform for management and bridge to recovery in such cases.

Disclosure

The authors have declared no conflicts of interest.

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