

Concurrent Extracorporeal Membrane Oxygenation, Plasmapheresis and Continuous Renal Replacement Therapy in a Case of Wegener's Granulomatosis.

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ABSTRACT

Wegener's Granulomatosis is one of the ANCA-associated vasculitis characterized by multifocal vascular necrotizing inflammation and granulomas that commonly present with a pulmonary-renal syndrome. We report a case of 38 year-old female patient who presented with acute respiratory distress syndrome due to diffuse alveolar hemorrhage and multiorgan failure. The patient being in a hemodynamic collapse was aggressively intubated and supported by mechanical ventilation and vasopressor therapy. Despite all effort refractory hypoxemia could not be coped with. Venovenous extracorporeal membrane oxygenation was started through a femoral and jugular vein. Her oxygenation dramatically ameliorated after the beginning of this procedure. 1 gr/day pulse methylprednisolone was administered followed by cyclophosphamide. Concurrent continuous renal replacement therapy and plasmapheresis was begun. Her clinical status improved in days giving rise to weaning of the extracorporeal membrane oxygenation by the day twelve. Extracorporeal membrane oxygenation is reported to be a successful mode of therapy in various cases in the literature including diffuse alveolar hemorrhage due to ANCA-associated vasculitis and concurrent therapy with continuous venovenous hemodialysis is reported to increase survival. Clinicians should be encouraged to use this life saving mode of treatment more often.

Keywords: ANCA, ECMO, granulomatosis with polyangiitis, plasmapheresis, Wegener's granulomatosis.

INTRODUCTION

Wegener's Granulomatosis (WG) is an antineutrophil cytoplasmic autoantibody (c-ANCA) associated vasculitis, characterized by multifocal vascular necrotizing inflammation and granulomas. Alveolar hemorrhage and concomitant glomerulonephritis causing renal insufficiency are associated with high mortality.^[1]

pulmonary hemorrhage to support survival till the effect of medical therapy shows up.^[4]

We report a case of severe diffuse pulmonary hemorrhage and acute renal failure associated with WG successfully treated by the combination of immune suppressive treatment, plasmapheresis, renal replacement therapy and ECMO.

CASE REPORT

A 38 year-old female patient otherwise healthy presented to the emergency service with fever, anuria, shortness of breath and hemoptysis. In the week before presentation, she was treated outpatient with amoxicillin for presumed pharyngitis. Her clinical course deteriorated rapidly with the development of severe acute respiratory failure and hemodynamic collapse requiring endotracheal intubation, aggressive mechanical ventilation, and vasopressor therapy. She was admitted to the medical intensive care unit (ICU) with diagnosis of septic shock, acute respiratory distress syndrome (ARDS) and multiorgan failure. The initial chest radiograph after admission to the ICU revealed

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Initial immune suppressive therapy in WG typically consists of glucocorticoids combined with either cyclophosphamide or rituximab.^[2] Selected patients with severe disease may benefit from the addition of plasma exchange.^[3] Extracorporeal membrane oxygenation (ECMO) can be considered for refractory hypoxemia associated with diffuse

diffuse bilateral alveolar infiltration consistent with ARDS [Figure 1].

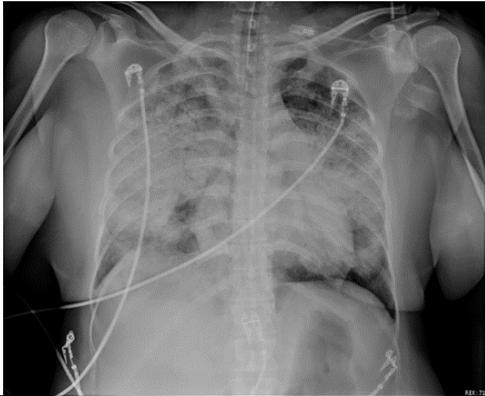


Figure 1: Initial chest radiograph of the patient.

She was in a severe ARDS state ($\text{PaO}_2=50$ mmHg, $\text{FiO}_2=1.0$; $\text{PaO}_2/\text{FiO}_2=50$) and bronchoscopy at bedside revealed diffuse alveolar hemorrhage. She was consulted with Rheumatology and Nephrology departments and because of a life-threatening state; 1gr/day intravenous pulse methylprednisolone treatment was started. Meanwhile, laboratory parameters to highlight the etiology of diffuse alveolar hemorrhage accompanying multi organ failure detected c-ANCA positivity. Despite all challenging efforts on mechanical ventilator refractory hypoxemia ($\text{PaO}_2 < 60$ mmHg) sustained. She was consulted with Cardiovascular Surgery consultants and concluded that ECMO treatment was the only chance for survival. A 22-French inflow cannula was placed percutaneously in the right femoral vein and advanced under transeosophageal echocardiography (TEE) guidance until the cannula tip was at the junction of the inferior vena cava and right atrium. An 18-French outflow cannula was placed percutaneously in the right internal jugular vein and advanced under TEE guidance so that the cannula tip was at the junction of the superior vena cava and right atrium. The ECMO circuit consisted of a centrifugal pump (Delphin; Terumo Cardiovascular Systems, Ann Arbor, Michigan) and a membrane oxygenator (Quadrox; Maquet Medical Systems, Wayne, New Jersey) [Figure 2].



Figure 2: Patient under concurrent ECMO and CVVHDF therapies.

The patient was anticoagulated systemically with a titrated heparin infusion to maintain an activated coagulation time of 180 to 240 seconds. The ECMO flows were maintained between 4.0 and 5.0L/min, representing a normal cardiac index for this patient. After institution of ECMO, arterial blood gas analysis detected a remarkable increase in PaO_2 (108 mmHg). Upon the patient being anuric and suffering of fluid overload and metabolic acidosis due to acute renal failure; continuous venovenous hemodiafiltration (CVVHDF) treatment was decided to be applied through the ECMO circuit because hemodynamic stability could only be maintained by high dose (>0.5 mcg/kg/min) of norepinephrine infusion. According to the recommendations of Hematology consultants plasmapheresis was started with daily 15 units of fresh frozen plasma again through the ECMO circuit [Figure 2] and first dose of cyclophosphamide applied for the treatment of WG. She was closely monitored with daily laboratory investigation and chest x-rays. Multi-disciplinary concurrent treatment gave rise to a significant amelioration in the patient's status. Norepinephrine infusion was declined and ceased on eighth day, CVVHDF was stopped on tenth day of admission due to sufficient urinary flow and decrease in creatinine values. Plasmapheresis was applied daily for 7 days and day after afterwards for a total of 15 days. The ECMO support was weaned on the twelfth day and the patient was decannulated successfully the same day and successfully extubated the day after. A control chest radiograph after extubation was reported to be completely normal [Figure 3].

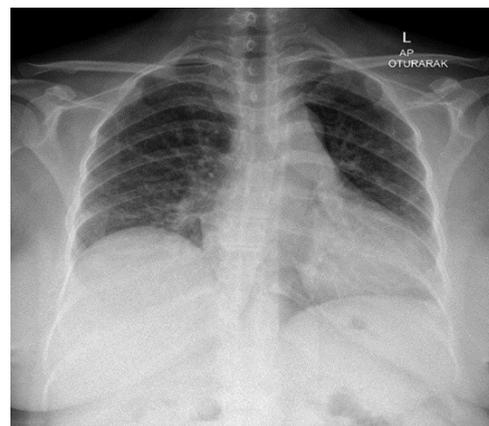


Figure 3: Control chest radiograph after extubation.

DISCUSSION

Granulomatosis with polyangiitis (Wegener's) is a form of systemic vasculitis (polyangiitis) with necrotizing granulomatous inflammation of the upper and lower respiratory tracts, systemic necrotizing vasculitis, and necrotizing glomerulonephritis.^[1]

The severity of symptoms and signs vary

considerably from asymptomatic (one-third of patients) to acute and fulminant alveolar hemorrhage with respiratory failure. The specific clinical manifestations vary depending on whether the patient has tracheobronchial disease, lung parenchymal nodules, interstitial lung disease, or alveolar hemorrhage.

Diffuse alveolar hemorrhage is a prominent and life-threatening pulmonary manifestation of ANCA-associated vasculitis.^[1] It is estimated to occur in 5 to 45 percent of patients with ANCA-associated vasculitis, and may be the initial finding.^[5] When accompanied by evidence of glomerulonephritis, it is considered a form of the pulmonary-renal syndrome.

Immunosuppressive therapy should be considered in all patients with active granulomatosis with polyangiitis. The use of aggressive initial immunosuppression is justified because the mortality rate in untreated generalized granulomatosis with polyangiitis is as high as 90 percent at two years, usually due to respiratory or renal failure.^[6] Mortality has markedly diminished with the introduction of initial therapy with cyclophosphamide and glucocorticoids. Even patients with advanced renal disease, as assessed by serum creatinine concentration or the need for dialysis at presentation, may receive benefit from aggressive treatment.^[7]

Although randomized controlled trials have not been performed, patients with pulmonary hemorrhage should be treated with plasma exchange.^[4] This strategy is based upon the theoretical benefit of removing ANCA by plasma exchange and the observed efficacy of plasma exchange in patients with pulmonary hemorrhage due to anti-GBM antibody disease.^[4]

There are several case reports of ECMO application in adult patients with refractory acute respiratory failure associated with severe pulmonary bleeding secondary to autoimmune vasculitis, including ANCA-associated vasculitis.^[4,8-11] Concurrent continuous renal replacement therapy and ECMO is also reported to increase survival.^[12]

ECMO proved life-saving in our patient. It ameliorated hypoxemia caused by massive pulmonary hemorrhage obstruction and alveolar diffusion problems with less ventilator induced trauma, and it supported the patient until resolution of her respiratory failure, providing time for treatment and control of the underlying disease by plasmapheresis and immunosuppression.

CONCLUSION

Clinicians should not hesitate to use ECMO in the early period of refractory hypoxemia which dramatically improves survival and may also serve

as a circuit for additional therapies like plasmapheresis or hemodiafiltration.

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