CASE REPORT

A Case of Refractory Hypoxemic Respiratory Failure due to Antineutrophil Cytoplasmic Antibodies-associated Diffuse Alveolar Hemorrhage Rescued by Extracorporeal Membrane Oxygenation

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Abstract

Diffuse alveolar hemorrhage (DAH) is a rare but life-threatening disease. Mortality is very high in those patients who require mechanical ventilation. Traditionally, active bleeding has been considered a contraindication for extracorporeal membrane oxygenation (ECMO) support. There is limited evidence for ECMO in DAH as rescue therapy. Herein, we describe a case of antineutrophil cytoplasmic antibodies-associated DAH with intractable hypoxemic respiratory failure. An appropriate ventilator strategy failed to improve her hypoxemia leading to imminent risk to her life. The patient was rescued with veno-venous ECMO targeting lower than usual range of anticoagulation. ECMO proved to be lifesaving in our patient who was initiated on prompt immunosuppressive therapy and plasmapheresis along with continuous veno-venous hemodiafiltration and hemodynamic support. We feel that ECMO could be considered as adjunctive therapy in severe hypoxemic respiratory failure associated with DAH after careful consideration of the risk of bleeding and a restrictive anticoagulation strategy.

Keywords: Antineutrophil cytoplasmic antibodies-associated vasculitis, Diffuse alveolar hemorrhage, Extracorporeal membrane oxygenation.

Indian Journal of Critical Care Medicine (2020): 10.5005/jp-journals-10071-23585

Introduction

Diffuse alveolar hemorrhage (DAH) is a feature of several immune and nonimmune disorders characterized by generalized bleeding into the acini of the lung parenchyma presenting with the cardinal clinical syndrome of hemoptysis, anemia, diffuse radiographic pulmonary infiltrates, and hypoxemic respiratory failure. Antineutrophil cytoplasmic antibodies (ANCA)-associated vasculitis (AAV) is the most common cause of DAH. Immunosuppressive therapy is the first-line treatment for AAV-related DAH, but the management of catastrophic respiratory failure may become a priority in severe cases that are refractory to conventional mechanical ventilation. The Extracorporeal Life Support Organization (ELSO) general guidelines recommend that extracorporeal membrane oxygenation (ECMO) should be considered when the expected mortality is higher than 50% despite optimized ventilatory care.[1] There is limited evidence for ECMO in DAH as a rescue therapy that can support gas exchange, providing the time necessary for definitive treatment, especially the immunosuppressive medications to take control of the underlying disease.[2,3] Herein, we present a case of DAH due to AAV with life-threatening respiratory failure managed by ECMO. The literature search revealed that only one such case has been reported earlier from India.[2]

Case Description

A 34-year-old non-smoker, nonalcoholic female presented with complaints of cough and hemoptysis for 2 days and breathing difficulty for 1 day. There was no history of any comorbid illness. On general physical examination she had rapid shallow breathing with a respiratory rate of 40/minute, pulse rate 146 beats/minute, and blood pressure 80/60 mm Hg. On room air, her oxygen saturation (SpO_2) was 37%. The examination of the respiratory system demonstrated bilateral fine crepts. The arterial blood gas (ABG) findings showed pH 7.04, pO_2 41.5 mm Hg, pCO_2 77.9 mm Hg, and bicarbonate 16 mmol/L, indicating severe respiratory acidosis, hypoxia, and hypercapnia. The patient was immediately intubated and mechanically ventilated. The initial ventilator settings were controlled mechanical ventilation (CMV) mode with tidal volume (TV) of 300 mL, respiratory rate (RR) 32/minute, positive end-expiratory pressure (PEEP) titrated up to 10 cm H_2O, and fraction of inhaled oxygen (FiO_2) 100%. She was hemodynamically supported with intravenous fluid resuscitation and noradrenaline infusion. Her diagnostic workup showed Hb 6.2 g%, ESR 85 mm/hour, serum urea 78 mg/dL, serum creatinine 4 mg/dL, and C-reactive protein

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How to cite this article: Goel MK, Chauhan M, Kumar A, Wadwa P, Maitra G, Talegaonkkar M, *et al.* A Case of Refractory Hypoxemic Respiratory Failure due to Antineutrophil Cytoplasmic Antibodies-associated Diffuse Alveolar Hemorrhage Rescued by Extracorporeal Membrane Oxygenation. Indian J Crit Care Med 2020;24(9): 879–881.

Source of support: Nil

Conflict of interest: None

230.5 mg/L. Coagulation profile revealed PT (INR) 1.49 and PTTK 32.6 seconds (control: 29.6 seconds). Routine urine examination detected red cell count of 2,142/µL. The chest X-ray showed bilateral airspace consolidation with relative apical sparing (Fig. 1).

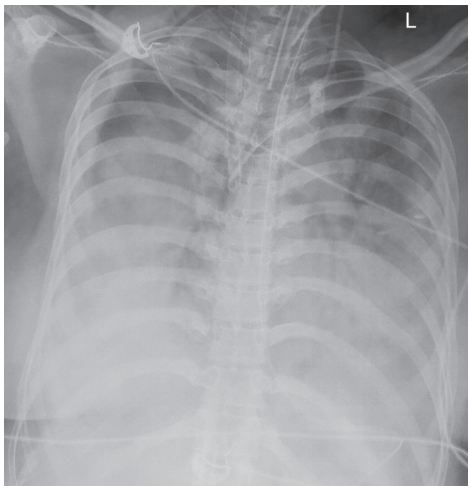
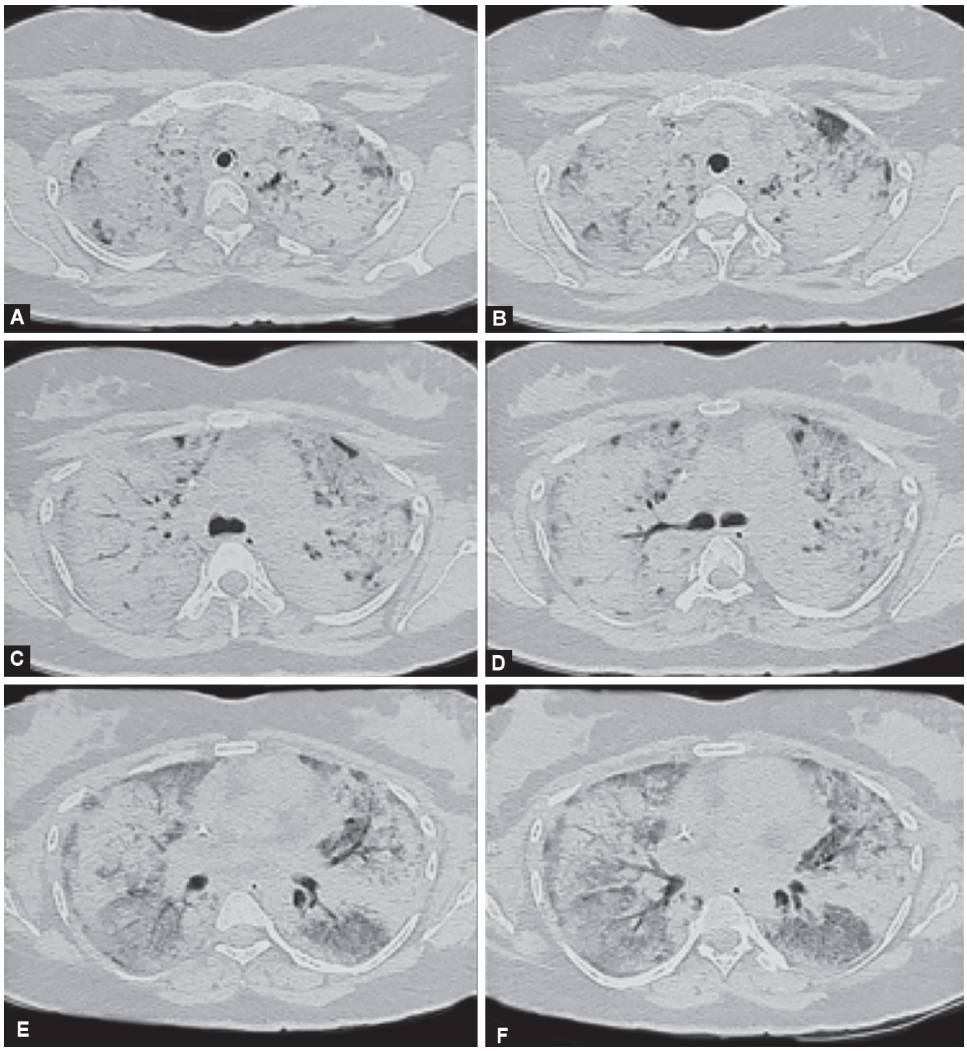


Fig. 1: Chest X-ray on day 1 showing bilateral airspace consolidation sparing the apices of lung parenchyma

Two-dimensional ECHO findings indicated normal left ventricular ejection fraction 55% with no regional wall motion abnormalities. High-resolution computed tomography (HRCT) of the chest revealed bilateral consolidation with diffuse alveolar filling pattern and ground-glass haze (Fig. 2). Based on the clinical history of hemoptysis, acute hypoxemic respiratory failure, coupled with low hemoglobin in routine blood tests and typical HRCT chest findings, a possibility of diffuse alveolar hemorrhage was considered. A quick flexible bronchoscopy was performed through the endotracheal tube. Cytology examination of bronchoalveolar lavage fluid showed the presence of hemosiderin laden macrophages. Pulse methylprednisolone therapy was initiated immediately with a dose of 1 g administered intravenously. A recruitment maneuver was applied on CMV mode, but the patient continued to remain hypoxic. The mode was changed to pressure-control inverse-ratio ventilation (PCIRV) with Pmax 30 cm H_2O, RR 32/minute, I:E ratio 1.5:1, FiO_2 100%, and PEEP 12 cm H_2O. ABG taken after 2 hours showed pH 7.119, pCO_2 67.6 mm Hg, pO_2 54.4 mm Hg, HCO_3 17.6 mmol/L, SpO_2 77%, and lactate 11.4 mmol/L. Lung compliance was 18 mL/cm H_2O. After 4 hours of mechanical ventilation, due to persistence of intractable hypoxia with the PaO_2–FiO_2 ratio of 54.4 and Murray Score of 3.8 points, we decided to rescue her with veno-venous extracorporeal membrane oxygenation (V-V ECMO).



Figs 2A to F: High-resolution computed tomography of the chest showing bilateral consolidation with diffuse alveolar filling pattern and ground glass haze

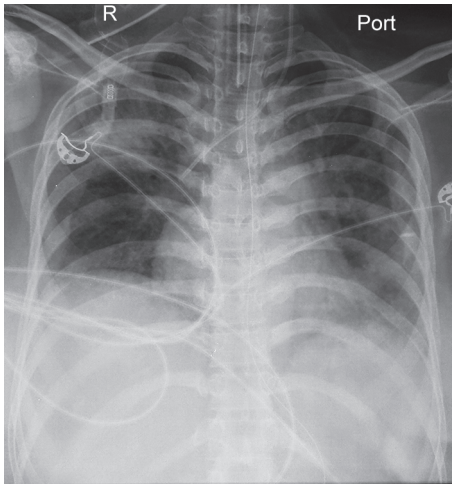


Fig. 3: Chest X-ray on day 7 showing significant resolution of the airspace opacities

Percutaneous insertion of an outflow 22F venous cannula (Edwards® Lifesciences Corporation, Irvine, USA) in the right femoral vein and 20F arterial cannula (Edwards® Lifesciences Corporation) for return in the right internal jugular vein was done under ultrasound guidance. V-V ECMO was initiated on a Deltastream® DP3 with HILITE 7000 LT oxygenator (Medos Cardiopulmonary Solutions, Stolberg, Germany). The initial ECMO flow rate was set at 4 L/min and sweep gas at 3 L/minute with FiO_2 of 1.0. The SpO_2 rose quickly to over 97% after initiating ECMO. For anticoagulation, the activated clotting time (ACT) was maintained within a range of 140–160 seconds using unfractionated heparin infusion. Renal support was also initiated with continuous veno-venous hemodiafiltration (CVVHDF) due to deranged renal function and anuria. Her immunological profile results showed elevated titers of ANA 1:320, cytoplasmic ANCAs 1:160, and serine proteinase 3 antibodies (anti-PR3) 31.2 U (negative <3.5). Hence, a final diagnosis of AAV with diffuse alveolar hemorrhage with pulmonary and renal involvement was established. The patient was treated with methylprednisolone 1 g daily for 3 days followed by a pulse dose of cyclophosphamide 1 g intravenously. Five cycles of plasmapheresis were also given. The patient responded favorably with gradual improvement in clinical, radiological (Fig. 3), and ventilator parameters in the subsequent days. The CVVHDF could be stopped on day 4, ECMO was weaned off on day 7, and the patient was successfully extubated from the ventilator on day 9.

Discussion

Diffuse alveolar hemorrhage is often a life-threating syndrome that may present with acute respiratory failure. The mortality is reported as 77% when mechanical ventilation is required in these cases.[4,5] ECMO was initiated in this patient, as she had life-threatening refractory hypoxemia with a calculated mortality risk of 80% according to the ESLO criteria.[1] Prone position ventilation, although considered, could not be attempted before initiating ECMO due to hemodynamic instability. Successful use of ECMO has been described in patients with DAH due to vasculitis and other autoimmune disorders mainly in the form of case reports.[2,3,6–10] In the largest series of 19 cases enrolled over a period of 10 years, Seelinger et al.[11] described that VV-ECMO in refractory respiratory failure due to DAH was feasible, did not lead to aggravation of pulmonary bleeding, and was associated with a hospital survival rate of 53%. However, they reported fatal intracranial hemorrhage in 16% of the cases which was possibly due to global endothelial injury and inflammation as part of the underlying pathophysiology of vasculitis and was not related to ECMO.

In this patient, lower than the usual range of ACT was targeted for achieving anticoagulation. Earlier reports[2,3] observed that the use of anticoagulation during ECMO in patients with DAH may not be associated with increased bleeding risks. Cases with use of heparin-free ECMO with favorable outcome have also been reported.[6–8] However, avoidance of anticoagulation can lead to circuit thrombosis and systemic thromboembolism. Novel surface material and coating in the modern ECMO oxygenators and circuits are likely to render anticoagulation unnecessary, but this approach is far from being routinely implemented. ECMO proved to be lifesaving in our patient who was initiated on prompt immunosuppressive therapy and plasmapheresis along with other supportive care involving hemodynamic management and CVVHD. We feel that ECMO could be considered as adjunctive therapy in severe hypoxemic respiratory failure associated with DAH after careful consideration of the risk of bleeding and a restrictive anticoagulation strategy.

References

1. ELSO Adult Respiratory Failure Supplement to the ELSO General Guidelines. Version 1.4 August 2017.
2. Rawal G, Kumar R, Yadav S. ECMO rescue therapy in diffuse alveolar haemorrhage: a case report with review of literature. J Clin Diagn Res 2016;10(6):OD10–OD11. DOI: 10.7860/JCDR/2016/20649.7969.
3. Delvino P, Monti S, Balduzzi S, Belliato M, Montecucco C, Caporali R. The role of extra-corporeal membrane oxygenation (ECMO) in the treatment of diffuse alveolar haemorrhage secondary to ANCA-associated vasculitis: report of two cases and review of the literature. Rheumatol Int 2019;39(2):367–375. DOI: 10.1007/s00296-018-4116-z.
4. West S, Arulkumaran N, Ind PW, Pusey CD. Diffuse alveolar haemorrhage in ANCA-associated vasculitis. Intern Med 2013;52(1):5–13. DOI: 10.2169/internalmedicine.52.8863.
5. Quadrelli S, Dubinsky D, Solis M, Yucra D, Hernández M, Karlen H, et al. Immune diffuse alveolar hemorrhage. Clinical presentation and outcome. Respir Med 2017;129:59–62.
6. Patel JJ, Lipchik RJ. Systemic lupus-induced diffuse alveolar haemorrhage treated with extracorporeal membrane oxygenation: a case report and review of the literature. J Intensive Care Med 2014;29(2):104–109. DOI: 10.1177/0885066612464335.
7. Hohenforst-Schmidt W, Petermann A, Visouli A, Zarogoulidis P, Darwiche K, Kougioumtzi I, et al. Successful application of extracorporeal membrane oxygenation due to pulmonary haemorrhage secondary to granulomatosis with polyangiitis. Drug Des Devel Ther 2013;7:627–633. DOI: 10.2147/DDDT.S47156.
8. Claudio CP, Charbonney E, Durand M, Kolan C, Laskine M. Extracorporeal membrane oxygenation in diffuse alveolar haemorrhage secondary to systemic lupus erythematosus. J Clin Med Res 2014;6:145–148.
9. Zhen G, Xin L, Li-ya J, Ling-feng X. Extracorporeal membrane oxygenation for the management of respiratory failure caused by diffuse alveolar haemorrhage. J Extra Corpor Technol 2009;41:37–40.
10. Barnes SL, Naughton M, Douglass J, Murphy D. Extracorporeal membrane oxygenation with plasma exchange in a patient with alveolar haemorrhage secondary to Wegener's granulomatosis. Intern Med J 2012;42(3):341–342. DOI: 10.1111/j.1445-5994.2012.02720.x.
11. Seeliger B, Stahl K, Schenk H, Schmidt JJ, Wiesner O, Welte T, et al. Extracorporeal membrane oxygenation for severe ARDS due to immune diffuse alveolar hemorrhage. A retrospective observational study. Chest 2020;157(3):744–777. DOI: 10.1016/j.chest.2019.10.021.