Case report

Veno-venous extracorporeal membrane oxygenation (VV-ECMO) for life-threatening isolated pulmonary anti-GBM disease

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ABSTRACT

Anti-glomerular basement membrane disease (anti-GBM disease) associated with renal and lung lesions has a poor prognosis. Diffuse alveolar hemorrhage (DAH) is a complication that worsens anti-GBM disease prognosis. We report a rescue case using veno-venous extracorporeal membrane oxygenation (VV-ECMO) for diffuse alveolar hemorrhage due to isolated pulmonary anti-GBM disease; a rare anti-GBM syndrome. A 30-year-old Japanese female with no past medical history. Presented with acute hypoxemic respiratory failure requiring mechanical ventilation. Progressive deterioration and refractory hypoxemia prompted therapy with VV-ECMO. Serum anti-GBM antibody confirmed the diagnosis of anti-GBM disease. Multi-modal systemic therapy with pulse-dosed methylprednisolone, plasma exchange, and rituximab resulted in significant clinical improvement. VV-ECMO for 10 days was uncomplicated. Renal replacement therapy was not required. The patient was extubated on day 18 and discharged from the hospital after 45 days. VV-ECMO supportive therapy for DAH with refractory respiratory failure was demonstrated to be effective pending definitive diagnostic and therapeutic management in this case of isolated pulmonary anti-GBM disease.

Abbreviations

| Abbreviation       | Description                              |
|--------------------|------------------------------------------|
| VV-ECMO            | Veno-venous extracorporeal membrane oxygenation |
| anti-GBM disease   | Anti-glomerular basement membrane disease |
| DAH                | Diffuse alveolar hemorrhage               |
| BAL                | Bronchoalveolar lavage                    |
| ER                 | Emergency room                            |
| HIT                | Heparin-induced thrombocytopenia          |

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1. Introduction

DAH is a clinical syndrome in which alveolar capillaries and pulmonary small arteries and veins are damaged, and alveolar spaces are filled with blood. DAH is a rare condition with multiple etiologies. Supportive care, prompt diagnosis, and specific therapy is required. Mortality rates have been reported as high as 25–50% [1], despite ventilator and supportive ICU care in some cases. A limited number of cases using VV-ECMO for anti-GBM disease are reported [2,3]. Here, we report a rare case of successful VV-ECMO without bleeding complications for hypoxic respiratory failure caused by diffuse alveolar hemorrhage caused by isolated pulmonary anti-GBM disease. VV-ECMO can be used as a supportive treatment until definitive diagnosis and effects of specific curative treatment are effective.

2. Case report

A 34-year-old female developed acute onset of dyspnea over 24 hours. She complained to her husband that “small blood is mixed in her sputum” and that she felt respiratory discomfort beginning the previous day. She presented to a primary care physician with upper respiratory symptoms and began therapy with an inhaled beta agonist and symptomatic treatment for suspected asthma. The following day, progressive symptoms prompted presentation to an emergency room (ER). Percutaneous oxygen saturation (SpO2) was 68% (room air) and chest X-ray showed bilateral diffuse consolidation, and she was transferred to our higher-level acute care hospital.

Physical examination in our ER revealed an alert patent in respiratory distress with blood pressure 140/78 mm Hg, pulse 110 beats/min, respiratory rate was 28 breaths/min, SpO2 90% on 10L/min non-rebreathing mask, with bilateral coarse crackles on auscultation. Chest X-ray demonstrated bilateral diffuse consolidation and CT scan demonstrated bilateral ground glass shadow with consolidation. She was intubated for acute hypoxic respiratory failure and bronchoscopy demonstrated bilateral diffuse airway hemorrhage suggesting DAH (Fig. 1), but bronchoalveolar lavage (BAL) was not performed due to her severe hypoxia.

On admission, initial investigation revealed the following: hemoglobin (Hb): 11.2 g/dL; white cell count: 2.3 × 10⁹/L; neutrophils: 1.0 × 10⁹/L; platelet: 3.0 × 10⁹/L; C reactive protein: 7.2 mg/dL; blood urea nitrogen: 10.8 mg/dL; sCr: 0.53 mg/dL; international normalized ratio of prothrombin time: 0.9; activated partial thromboplastin time: 24 sec; immunoglobulin (Ig) G: 1301 mg/dL; IgA: 202 mg/dL; IgM: 71 mg/dL; C3: 59.4 mg/dL; and C4: 29.5 mg/dL. Test results for ANCA, blood culture, urine culture, sputum culture, T-SPOT, urinary protein, urinary occult blood were all negative; however, anti-GBM antibodies were detected at a level of 6.7 enzyme-linked immunosorbent assay unit (EU).

The patient was diagnosed with isolated pulmonary anti-GBM disease without renal involvement, based on serological and urinary findings. Severe respiratory failure progressed despite administration of pulse-dosed methylprednisolone (1g/day, 3 days). The PaO₂/FiO₂ ratio was 50 with optimized ventilator setting and prone position on 12hrs after hospitalization and veno-venous extracorporeal membrane oxygenation (VV-ECMO) was initiated. VV-ECMO system components and technique utilized the following: Pump (JMS Mix Flow), Oxygenator (Bio Cube 6000), right internal jugular vein drainage cannula (MAQUET HLS cannula 23Fr 38cm), right femoral vein return cannula (MAQUET HLS cannula 19Fr 23cm). Initial ECMO setting with heparin as anticoagulant included; ECMO Flow: 4.5 L/min; ECMO RPM: 4500 rpm; FiO2: 1.0; Sweep gas: 5 L/min, target APTT-R: 1.5–2.5. Anti-GBM antibody positive results were reported on hospital day 4; plasma exchange was initiated for 4 days and methyl prednisolone was decreased to 60mg/day. Rituximab 375mg/m² IV was administered on hospital day 8. The platelet count nadir was 0.24 × 10⁹/L after one week of heparin therapy and the 4T’s score was 5 points concerning for heparin-induced thrombocytopenia (HIT), so heparin was changed to Argatroban hydrate (target APTT 40–60sec). Thereafter, the test revealed that HIT antibodies were positive. On hospital day 12 respiratory failure was improving. The PaO₂/FiO₂ ratio was 350, and VV-ECMO was discontinued, the patient was extubated on hospital day 18 and left the ICU and was discharged on hospital days 20 and 45 respectively. (Fig. 2).

![Fig. 1. Non-contrast CT of the lung shows diffuse ground glass shadow and bronchoscope shows diffuse alveolar hemorrhage.](image-url)
3. Discussion

The causes of DAH are known to be infection, autoimmune disease such as systemic lupus erythematosus (SLE) and antineutrophil cytoplasmic antibody (ANCA) associated vasculitis, prescribed medications, illicit drugs, and others. Our final diagnosis was isolated pulmonary anti-GBM disease based on positive serum anti-GBM antibodies without renal dysfunction during the course of the illness. The characteristics of this disease, which were characterized in this case, include relatively low antibody anti-GBM antibody titers, a strong relationship to smoking, and mild renal damage [4].

The pathogenic anti-GBM antibodies are usually IgG class, but a few cases are caused by IgA or IgG4 alone [5,6]. The sensitivity and specificity of anti-GBM antibodies were 93% and 97%, so they showed low false-negative and high true positive rate [7]. At another point of view, 32% of all anti-GBM positive samples have detectable ANCA, and 5% of all ANCA-positive serum samples also have detectable anti-GBM antibodies, but the mechanism is unclarified [8].

VV-ECMO for DAH patients are very rare cases, especially for anti-GBM disease [9,10]. In this case, VV-ECMO provided successful respiratory support for DAH caused by anti-GBM disease without exacerbation of alveolar hemorrhage or intracranial hemorrhage, despite the risk for potential increased DAH due to ECMO anticoagulation associated HIT induce thrombocytopenia.

We speculate that the anti-GBM disease state was improving with steroid therapy, plasma exchange, and rituximab, limiting hemorrhagic complications. In a previous report, clinical improvement of adults and pediatric ECMO patients with DAH was achieved without exacerbation of pulmonary hemorrhage despite the use of anticoagulants [11]. In our case, ECMO was an effective life-support bridge for DAH combined with HIT, until disease control with fundamental specific therapy became effective.

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Declaration of competing interest

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Both authors conceived the study concept and study design. SG and BB performed complication and synthesis of the data. SG supervised the research project. Both authors participated in interpretation of the results and writing of the report, and approved the final version.

Fig. 2. Clinical course of treatment and oxygenation (PSL: Prednisolone; mPSL: methyl prednisolone).
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