Chin Med Sci J
September 2019

Vol. 34, No. 3 P. 226-229
doi:10.24920/003478

CASE REPORT

Management of an Adult with Goodpasture's Syndrome Following Brain Trauma with Extracorporeal Membrane Oxygenation: A Case Report

Shan Wang[1†], Haiyan Yin[1†], Youfeng Zhu[1], Pei Tao[1], Rui Zhang[1], Yonghui Ma[1], Jianrui Wei[2*]

[1]Department of Intensive Care Unit,
[2]Institute of Clinical Nutrition, Guangzhou Red Cross Hospital, Medical College, Jinan University, Guangzhou 510220, China

Key words: extracorporeal membrane oxygenation; pulmonary hemorrhage; Goodpasture's Syndrome; anti-glomerular basement membrane antibody

Abstract A 22-year-old man suffered from acute pulmonary hemorrhage and deteriorated renal function occurred within 3 days after traumatic brain injury. Mechanical ventilation cannot correct his severe hypoxemia, therefore, venoarterial extracorporeal membrane oxygenation (VA-ECMO) support was initiated and finally resolved his hypoxemia. Concomitantly, continuous renal replacement therapy was performed to improve his kidney function. Although no anti-glomerular basement membrane (anti-GBM) antibody was detected in serum, Goodpasture's syndrome was considered. After treated with methylprednisolone pulse therapy and plasmapheresis, his renal function was significantly improved. ECMO was eventually discontinued after 60 hours of treatment and extubated on day 10. He was discharged home with normal pulmonary and renal functions.

GOODPASTURE'S syndrome is a rare autoimmune kidney disease mediated by anti-glomerular basement membrane (anti-GBM) antibodies. Its pathological characteristic is crescentic glomerulonephritis with linear deposits of IgG on the GBM.[1] The patients usually present with an acute renal failure as a result of a rapidly progressive glomerulonephritis, accompanied by pulmonary hemorrhage.[2] Here, we report a young man with Goodpasture's Syndrome presenting with an acute kidney injury, pulmonary alveolar hemorrhage and negative anti-GBM antibody in serum. Venoarterial extracorporeal membrane oxygenation (VA-ECMO) was used to improve a rapid decline in his oxygen saturation.

Received November 13, 2018. Published online June 18, 2019.
*Corresponding author Tel: 86-18928900398, E-mail: jianrui_wei@sina.com
†These authors contributed equally to this work.
Supported by the Natural Science Foundation of Guangdong Province of China (No. 2015A030313735) and the Science and Technology Planning Project of Guangdong Province of China (No. 2014A020212651).

CASE DESCRIPTION

A 22-year-old man, complaining of a headache, nausea, and vomiting, was admitted to our emergency

department on September 2, 2017. Three days ago, he fell down with his head forward. Computed tomography (CT) revealed the following injuries: a subarachnoid hemorrhage in the right brain, bilateral frontal lobe contusion, and occipital fracture. During the first two days in neurosurgery department, his symptoms became better, his initial blood pressure was 100-110/60-70 mm Hg, and oxygen saturation was greater than 92% (on room air). White blood cell count was 11.87×10^9/L ↑ (RI, 4.00×10^9-10.00×10^9/L). Biochemical examination revealed hemoglobin 141 g/L (RI, 120-160 g/L), C-reactive protein 286.8 mg/L ↑ (RI, 0-3.0 mg/L), lactic acid 1.22 mmol/L (RI, 0.70-2.10 mmol/L), creatinine 76 μmol/L (RI, 60-120 μmol/L), urea 4.4 mmol/L (RI, 3.0-8.5 mmol/L) and hypokalemia. Urine volume was approximately 1000 ml/d, and urinalysis showed numerous erythrocytes. The chest X-ray imaging showed no abnormal changes (**Figure 1A**). Blood, sputum and urine cultures were negative.

On the third night, tachypnea, hypoxia and hypotension suddenly appeared and progressively worsened. His oxygen saturation declined from 60% to 40% within minutes, blood pressure was 112/43 mm Hg, and respiratory rate was 28 times per minute. An emergent bronchoscopy showed a mass of hemorrhagic secretions with active bleeding. Due to severe hypoxia, he was intubated and placed on a mechanical ventilation with a positive end-expiratory pressure of 18 cm H_2O, a plateau pressure of 32 cm H_2O, and a P/F ratio of 56. Shortly after the procedure, the oxygen saturation rose to 75%. Then he was transferred to the ICU.

However, after 9 hours of intubation, hypoxemia was more severe with a $PaCO_2$ of 53 mm Hg, a PaO_2 of 34 mm Hg, as well as an oxygen saturation of 71% on a fraction of inspired oxygen of 2.0 L. Meanwhile, metabolic acidosis occurred with lactic acid rising to 8.89 mmol/L and a pH of 7.345. Renal function test showed urea nitrogen 18.5 mmol/L ↑ and creatinine 597 μmol/L ↑ in blood. Continuous renal replacement therapy was started. Moreover, his breathing difficulty was not resolved, and bleeding in airway still continued. His B-type natriuretic peptide (BNP) raised to 28 457 pg/ml, myoglobin to 1483 μg/L, hs-cTnT was 0.02 μg/L, and D-dimer was 580 μg/L. The echocardiogram revealed ejection fraction was 64%, stroke volume 54 ml, left ventricular end-diastolic volume 138 ml, left ventricular end-diastolic dimension 42.90 mm, and inferior vena cave diameter 16.27 mm, which indicated that his left ventricular function was preserved. A chest X-ray revealed extensive alveolar infiltrates in the lower lobe of both lungs (**Figure 1B**).

Based on the above examination results and clinical symptoms, cardiogenic pulmonary edema as well as acute pulmonary embolism were excluded. Considering that his BNP and myoglobin increased remarkably, a diagnosis of acute pulmonary heart disease was made, which had progressed to acute respiratory distress syndrome. VA-ECMO was initiated *via* cannulation of the right femoral artery and vein (13 Fr/15 cm arterial and 21 Fr/55 cm venous HLS Cannula, Maquet GmbH, Germany). Blood test showed a prothrombin time of 19.10 s ↑, hemoglobin 75 g/L ↓, and platelet 22×10^9/L ↓, so 12 U of cryoprecipitate, 400 ml of fresh frozen plasma and 25 U of platelet were given *via* intravenous drip. In the meantime, intravenous heparin at 1.5 ml/h was administrated to achieve an activating clotting time (ACT) of 180-220 seconds. ECMO centrifugal pump run at 1006.2 ×*g*, maintaining 3.75-3.85 L/min blood flows with fresh gas flows of 7 L/min.

With the support of VA-ECMO and continuous renal replacement therapy, his pulmonary hemorrhage and refractory hypoxemic respiratory failure were ameliorated. After 26 hours of ECMO, arterial blood gas showed a pH of 7.389, a $PaCO_2$ of 56 mm Hg, a PaO_2 of 59 mm Hg, and lactic acid 2.04 mmol/L. The arterial oxygen saturation maintained over 94%. BNP decreased to 1857 pg/ml, myoglobin to 469 μg/L, and hs-cTnT to 0.016 μg/L. However, renal function examination showed creatinine (502 μmol/L) and urea nitrogen (17.7 mmol/L) remained over the normal values. Serum auto-antibody detection showed that anti-SSB, anti-SSA, anti-RPS and anti-nuclear antibod-

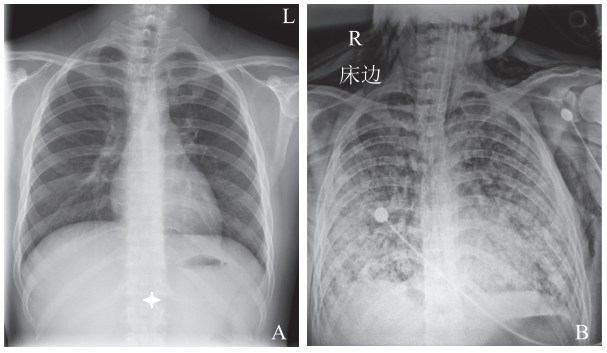

Figure 1. A. On the 1st day in the neurosurgery department, chest X-ray showed no abnormal changes. B. Before venoarterial extracorporeal membrane oxygenation was inserted, chest X-ray revealed extensive alveolar infiltrate in the lower lobe of bilateral lungs.

ies (ANA) were positive, the titer of ANA was 1:640, but anti-neutrophilic cytoplasmic antibodies (ANCA) and anti-GBM antibody were not found.

After a multidisciplinary team consultation, we reached the following conclusions: (1) CT imaging of the brain performed on the day before the onset of acute pulmonary hemorrhage and hypoxemia, showed no further disease progression, making us rule out the possibility of nervous system disease; (2) Taking the rapid development of the disease as well as serum auto-antibody results into consideration, autoimmune disease was proposed to be the etiological factor; 3. Despite the fact that these findings did not meet the diagnostic criteria, a preliminary diagnosis of Goodpasture's Syndrome was made. Therefore, methylprednisolone pulse therapy (1000 mg/d × 3 days) and plasma exchange (3500 ml) were initiated. Three days later, the pulmonary infiltrate and oxygen saturation improved remarkably (**Figure 2A**). Circuit flows were gradually lessened.

After 60 hours of treatment, ECMO was discontinued and extubated on day 10. When renal function normalized, plasma exchange was ceased, continuous renal replacement therapy was stopped after 6 days of treatment and extubated 5 days later. He stayed for 13 days in ICU and 22 days in the cardiovascular department. Finally he was discharged home with normal renal and pulmonary functions (**Figure 2B**).

DISCUSSION

Anti-GBM antibodies observed in serum or renal tissues are typical conditions in Goodpasture's syndrome, but cases of anti-GBM disease without detectable serum antibodies have been reported in many series. This phenomenon may be attributed to several possible reasons; one of the most accepted theories is that the half-life of circulating antibodies (21 days) is much shorter than that of tissue-bound antibodies (several months). Subsequently, if the blood sample for determining anti-GBM antibody is taken when the production of autoantibody has ceased, the assay would be truly negative.[3]

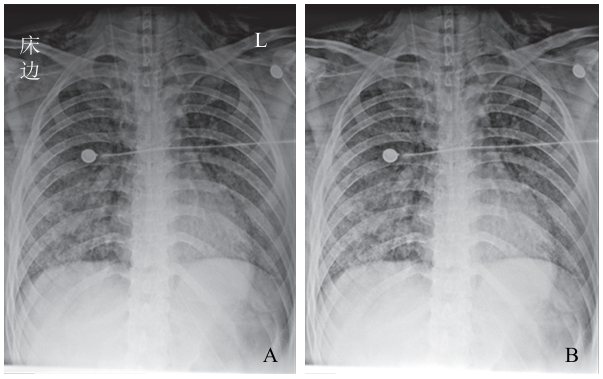

Figure 2. A. Three days after treatment with venoarterial extracorporeal membrane oxygenation, methylprednisolone pulse therapy and plasma exchange, chest X-ray showed resolution of the bilateral infiltrate. B. On the day before he went home chest X-ray showing that both sides of the lung field were clear.

For this case, despite no detectable anti-GBM antibody in serum and no renal biopsy (the patient's family members refused to allow him undergo renal biopsy), the facts, such as ANA being positive, the rapidly progressive deterioration of renal function as well as pulmonary hemorrhage, and numerous erythrocytes in urine on the 1st day of hospitalization, may be the case for diagnosis of Goodpasture's syndrome. It has been accepted that Goodpasture's syndrome usually has a rapidly deteriorating course,[4] so we initiated methylprednisolone pulse therapy and plasma exchange as soon as the diagnosis was made, which turned out to be effective.

As for the type of ECMO, traditionally, venovenous (VV)-ECMO has been used to support patients suffering respiratory failure; while VA-ECMO is utilized to temporarily support severe patients with cardiac and pulmonary failure. Flow support by the VA-ECMO can augment the reduced 'native' cardiac output with retrograde blood flow from the ECMO, and unload the failing heart by decreasing preload.[5]

Pulmonary hemorrhage has been considered as a contraindication to ECMO support for coagulation-related adverse events induced by anticoagulation protocol used for ECMO. However, the technology is being successfully applied to mitigating hypoxemia of Goodpasture's syndrome patients with pulmonary hemorrhage, acting as a bridge to resolution of an initial insult. Balke *et al*.[6] reported that they successfully treated a young woman with ARDS derived from Goodpasture's Syndrome using VV-ECMO as a bridge to recovery. In Dalabih *et al*.'s study,[7] VV-ECMO was applied to supporting the end-organ perfusion of a child with a new onset of Goodpasture's Syndrome and saved her life. In addition, Herbert *et al*.[8] creatively used VV-ECMO without therapeutic anticoagulation, as a bridge to recovery, to treat a teenager with Goodpasture's syndrome-related pulmonary hemorrhage, who finally recovered.

In short, we demonstrate that ECMO could be a useful supporting means to controlling severe pulmonary bleeding secondary to Goodpasture's-like and Goodpasture's Syndrome when no adequate oxygenation is provided by mechanical ventilation.

Conflicts of interest statement

All authors declare no conflicts of interest.

REFERENCES

1. Hellmark T, Segelmark M. Diagnosis and classification of Goodpasture's disease (anti-GBM). J Autoimmun 2014; 48-9:108-12. doi: 10.1016/j.jaut.2014.01.024.
2. Lahmer T, Heemann U. Anti-glomerular basement membrane antibody disease: a rare autoimmune disorder affecting the kidney and the lung. Autoimmun Rev 2012; 12(2):169-73. doi: 10.1016/j.autrev.2012.04.002.
3. Ohlsson S, Herlitz H, Lundberg S, et al. Circulating anti-glomerular basement membrane antibodies with predominance of subclass IgG4 and false-negative immunoassay test results in anti-glomerular basement membrane disease. Am J Kidney Dis 2014; 63(2):289-93. doi: 10.1053/j.ajkd.2013.08.032.
4. Levy JB, Turner AN, Rees AJ, et al. Long-term outcome of anti-glomerular basement membrane antibody disease treated with plasma exchange and immunosuppression. Ann Intern Med 2001; 134(11):1033-42. doi: 10.7326/0003-4819-134-11-200106050-00009.
5. Napp LC, Kuhn C, Hoeper MM, et al. Cannulation strategies for percutaneous extracorporeal membrane oxygenation in adults. Clin Res Cardiol 2016; 105(4):283-96. doi: 10.1007/s00392-015-0941-1.
6. Balke L, Both M, Arlt A, et al. Severe adult respiratory distress syndrome from Goodpasture syndrome. Survival using extracorporeal membrane oxygenation. Am J Respir Crit Care Med 2015; 191(2):228-9. doi: 10.1164/rccm.201409-1625IM.
7. Dalabih A, Pietsch J, Jabs K, et al. Extracorporeal membrane oxygenation as a platform for recovery: a case report of a child with pulmonary hemorrhage, refractory hypoxemic respiratory failure, and new onset Goodpasture syndrome. J Extra Corpor Technol 2012; 44(2):75-7.
8. Herbert DG, Buscher H, Nair P. Prolonged venovenous extracorporeal membrane oxygenation without anticoagulation: a case of Goodpasture syndrome-related pulmonary haemorrhage. Crit Care Resusc 2014; 16(1):69-72.