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Interventional Treatment of Massive Hemoptysis in an ARDS Patient on Extracorporeal Membrane Oxygenation Support: A Case Report

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Abstract

Extracorporeal Membrane Oxygenation [1] is a rescue therapy for patients with refractory hypoxemia which requires an anticoagulant during operation. When patients have life-threatening hemoptysis, the causes should be identified, and an appropriate treatment should be instituted. Here, we report a case of massive hemoptysis in a patient with Acute Respiratory Distress Syndrome (ARDS) on ECMO support that was successfully treated by interventional embolization for hemostasis. A 56-year-old male patient received immunosuppressive therapy (prednisone and cyclosporine A) for nephrotic syndrome, and subsequently developed severe pneumonia and progressed to ARDS. Oxygenation began to deteriorate continuously, even after standard lung protective ventilation, and required ECMO support. During ECMO support he suffered massive hemoptysis, which could not be controlled by routine medications, and heparin withdrawal. Bronchial arteriography was carried out immediately, and demonstrated an enlarged and tortuous right bronchial artery with disorganized new blood vessels and leakage of contrast agent. The bleeding was successfully controlled after embolization of the diseased blood vessel, the patient was successfully weaned off ECMO, and finally discharged.

***Keywords*:** *Extracorporeal membrane oxygenation; hemoptysis; acute respiratory distress syndrome; bronchial arteriography*

Case Description

Over time, there have been gradual improvements in the treatment of severe respiratory failure or acute respiratory distress syndrome (ARDS) in recent years. Included in this improvement are processes known as lung recruitment maneuver, prone position ventilation, high frequency oscillatory ventilation, and inhaled nitric oxide [1]. However, these methods may not reverse serious hypoxemia in patients with severe ARDS, which results in an increased need to use extracorporeal membrane oxygenation [1]. Heparin-based anticoagulation is generally required during ECMO, making it difficult in treating patients with massive hemoptysis. Unfortunately, hemoptysis is commonly seen in ARDS patients as it is often asssociated with infections which are a major source of ARDS. The case study below describes a reported case in which the use of interventional hemostasis successfully treated a patient who had ARDS with a massive hemoptysis and was on ECMO support.

A 56-year-old male had been diagnosed with nephrotic syndrome, and stage I membranous nephropathy based on a renal biopsy in another hospital 5 months before transffered to our ICU. The male was treated with prednisone and cyclosporine A, with a history of hypertension with a peak blood pressure of 180/100 mmHg. He was admitted to our hospital with complaints of a persistent cough, a

fever, and progressive shortness of breath for 6 days. The physical examination revealed a temperature of 38.6°C, heart rate of 100 bpm, respiratory rate of 30 bpm, and blood pressure of 151/100 mmHg. Inspiratory crackles were auscultated bilaterally. The blood test analysized the following: white blood cell counts 10.74×10^9/L, neutrophils 95.9%, hemoglobin 83 g/L, and platelet count 323×10^9/L. Arterial blood gas analysis under non-invasive ventilation (FiO_2 40%) revealed the following: pH 7.442, $PaCO_2$ 32.11 mmHg, PaO_2 70.60 mmHg, HCO_3 21.5 mmol/L. Chest X-ray and CT scan showed bilateral infiltration, and consolidation. The patient was diagnosed with severe pneumonia, ARDS, and nephrotic syndrome. Anti-microbial treatment with imipenem/cilastatin, ganciclovir, and voriconazole was initiated, and non-invasive ventilation (CPAP mode) was applied. The patient deteriorated on the second day of admission, respiratory distress was apparent, and increased consolidation in both lungs was shown on chest X-ray. As a result, endotracheal intubation, and mechanical ventilation were initiated. The ventilator setting was set IPPV mode (autoflow, Evita XL, Drager, Germany), FiO_2 100-75%, PEEP 12 cmH_2O, Vt 450 ml, and plateau pressure (Pplat) was 20 cmH_2O. On the 17th day of admission, the P/F decreased to 58, the Pplat increased to 37 cmH_2O, and ECMO support was initiated. Cannulation was performed using a 15F arterial and 19F venous cannula via the right internal jugular and femoral veins, respectively. We ran VV-ECMO (Medtronic, USA), blood flow 3.0L/min and gas flow 2.8-3 L/min, ACT was maintained about 180-200s. On the 7th day of ECMO support, the patient had massive hemoptysis. An abundance of blood (about 150ml) was aspirated from the airway in an hour, continuous suctioning was performed to keep the airway clear, and to maintain ventilation. While fresh frozen plasma was transfused and the heparin infusion rate was reduced, the ACT was restored to a normal level, and medications including pituitrin were administrated.

However, bleeding was not controlled. As a result, heparin was withdrawn. Bronchoscopy showed active bleeding in the right lower lobe, resulting in an obstruction of the right lower lobe bronchus by a large amount of blood clots. As hemodynamic and SpO_2 became unthreatening, we immediately transferred the patient to the intervention room for interventional therapy. Angiography revealed two enlarged, tortured bronchial arteries in the right lung with disorganized new blood vessels, and leakage of the contrast agent (Figure 1). However, after embolization, the diseased blood vessels did not re-develop (Figure 2). The patient returned to the ICU and heparin was restarted after 6 hours of withdrawal. The ACT was maintained at 160-180s, and no new onset of bleeding was observed. After identified without active bleeding through bronchoscopy on the next day, the blood clots in the airway were gradually removed. Under proper and active anti-infection and supportive treatment, the patient was successfully weaned off ECMO after 10 days of ECMO support, and finally discharged. In a one year follow up, the patient was able to take care of himself and travel with friends by train without dyspnea. A 6-minute walking test was completed with 500 meters. Chest CT scans had shown some bullae, but no infiltration in the lungs.

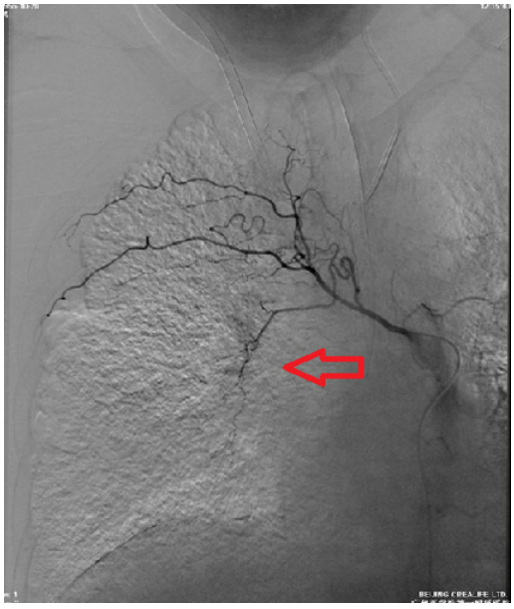

Figure 1: *Findings of interventional angiography: The red arrow indicates abnormal blood vessels and leakage of the contrast agent*

Figure 2: *Abnormal blood vessels disappeared after embolization and no leakage of contrast agent was observed*

Discussion

Ever since Dr. Hill [2] successfully rescued an ARDS patient using ECMO in 1971, ECMO has been used in the treatment of respiratory failure for more than 40 years. Even the CESAR study, which focus on ECMO as a combine treatment bundle in acute respiratory failure (ARF) patients, generated positive results. However, its limitations made it impossible to draw a convincing conclusion regarding the positive effect of ECMO in ARF patients [3]. In 2009, the H1N1 flu became a global pandemic and gave rise to a large number of ARDS patients. Physicians in different countries successfully rescued many ARDS patients by using ECMO, which enhanced the application and development of ECMO in the treatment of patients with respiratory failure [4-6].

ECMO is a version of extracorporeal circulation and requires anticoagulation to avoid thrombosis within the circuit during the process of support. At the same time, bleeding is the most common complication of ECMO. Some life-threatening bleeding disorders, such as intracranial hemorrhage, are included in the contraindications of the ECMO support [7]. However, for pulmonary hemorrhage, application of ECMO depends on etiology. Some scholars have successfully treated a number of patients with massive hemoptysis and acute respiratory failure caused by autoimmune diseases [8], such as Wegener's granulomatosis [9-10], Goodpasture syndrome [11], or systemic lupus erythematosus (SLE) [12]. Bleeding due to these diseases is mainly associated with autoimmune factors and is not closely related to anticoagulation or vascular malformation. The underlying diseases can be managed using corticosteroids, immunosuppressants, or plasma replacement therapy, while extensive pulmonary hemorrhage can be controlled. However, antinuclear antibodies, anti-DNA antibodies and anti-GBM antibodies were not found in our patient.

The patient described herein was presented with massive hemoptysis during ECMO support, which might have been caused by heparin-based anticoagulation. However, bleeding continued even after heparin withdrawn or transfusion of fresh frozen plasma, suggesting that the cause of bleeding was not related to anticoagulation. For patients with severe pneumonia or ARDS, infection is the main cause of hemoptysis, pathogens including M. tuberculosis, Aspergillus, and gram-positive cocci [13]. These pathogens can directly or indirectly injure the lung tissue and invade the blood vessels to induce hemoptysis. The underlying disease of our patient was nephrotic syndrome. He was presented with a lung infection during immunosuppressive therapy and developed into severe ARDS. Although there is no culture-based evidence that supports fungal infections in clinical practice, the diagnosis of fungal infections can be obtained by combining the risk factors for a fungal infection in a patient and specific changes on the imaging examination. After the onset of hemoptysis, a bronchoscopy showed that the bleeding sites were mainly located in the segments of the right lower lung, which

is in accordance to the results acquired through an image finding of the diseased region. It was quite different from the diffuse pulmonary hemorrhage caused by excessive anticoagulation or autoimmune diseases. The bleeding stopped after isolating and embolizing the affected blood vessel with bronchial arteriography. This suggsets that differential diagnosis is necessary during the management of hemoptysis in patients on ECMO support. The various causes of hemoptysis should be meticulously identified; timely interventional examinations and subsequent hemostasis can save the lives of patients with massive hemoptysis from vascular malformations.

There have been only a few reports about interventional hemostasis for hemoptysis in patients on ECMO support, yet none of these patients demonstrated the case for severe pulmonary infections. The current case is the first case with a successful intervention utilizing hemostasis for massive hemoptysis caused by a severe pulmonary infection in an ARDS patient on ECMO support. The ELSO guidelines [7] for the management of bleeding includes maintaining an appropriate ACT level, transfusion of fresh frozen plasma, application of EACA in the case of fibrinolysis, and local treatment of various bleeding sites. However, there is no specific recommendation for massive hemoptysis. In 2010, Hsu., *et al*. [14] reported a successful case of interventional hemostasis in a 42-year-old patient with bronchiectasis using ECMO support without heparin. This patient was presented with severe hemoptysis and hypoxemia due to the communicating branch between the left inferior phrenic and pulmonary arteries.

In 2008, Elisabeth et al. [15] reported a successful case of intervention through hemostasis in a child with tricuspid atresia using ECMO support. The patient was presented with fatal massive hemoptysis 14 years after a Foton surgery. In these rare cases, respiratory support was obtained by short-term application of ECMO without heparin, and the ECMO support was weaned off quickly after successful hemostasis. Patients with ARDS usually require extended ECMO support, a process that is nearly impossible to implement without heparin. As this process can easily lead to fatal complications which include obstruction of the circuit or membrane, and hemolysis. Mongero et al. [16] also reported a case of pulmonary hemorrhage in a patient using VV-ECMO without heparin who presented with circuit obstruction by blood clots, and the entire circuit had to be changed. Changing the circuit is highly risky for a patient completely depending on ECLS, which may cause death. A challenge still remains for us to balance the relationship between anticoagulation and prevention of hemorrhage. In the current case, we had discontinued the heparin infusion for 6 hours after interventional hemostasis and maintained a relatively low ACT level after restarting anticoagulation. Fortunately, when this patient received an application of a low-dose anticoagulants did not result in secondary bleeding after interventional embolization of the offending blood vessel.

It was recommended by some experts' opinion that the endotracheal tube could be clamped in case of massive hemotypsis. At the same time, the blood flow of ECMO should increased, and the ACT level decreased. Heparin could be withdrawn to induce blood clot formation within the trachea until the bleeding stopped completely, after which the blood clots were gradually removed. Gorjup., *et al*. [17] reported a case of massive left pulmonary hemorrhaging in a patient with acute lymphoblastic leukemia on ECMO support due to acute respiratory failure. A double-lumen endotracheal tube was placed to prevent reverse infusion of the blood from the left lung to the right lung, and isolated lung ventilation was carried out. The bleeding stopped with the restoration of bone marrow function and the patient was successfully cured. For patients with severe lung infection, blocking the entire tracheal with blood clots does not facilitate drainage of infectious secretions, and the pathogens can proliferate in the blood clots leading to aggravated infection and even sepsis. Therefore, this method may not be suitable for patients with severe underlying pulmonary infections.

The diagnosis and treatment of the patient in the current case suggests that we should meticulously identify the cause of hemoptysis in patients on ECMO support and perform an interventional examination and achieve hemostasis if the hemoptysis is not related to anticoagulation or there are definite local bleeding sites. For patients with massive hemoptysis, short-time withdrawal of heparin or application of low-dose heparin-based anticoagulation can be used under close monitoring, and if long-term heparin withdrawal is required, pre-primed circuits should be prepared.

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