

Case Report

## Successful Extracorporeal Life Support for Life-threatening Hypercapnia with Bronchiolitis Obliterans after Allogeneic Hematopoietic Stem Cell Transplantation

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Bronchiolitis obliterans (BO) is a disease with a poor prognosis, and a key factor that limits long-term survival after allogeneic hematopoietic stem cell transplantation (HSCT). We here report a case of a 31-year woman with acute lymphatic leukemia, which was treated by chemotherapy and HSCT, and consequently developed BO 2 years after HSCT. A non-tuberculous mycobacterial infection occurred and showed gradual exacerbation. She started taking anti-mycobacterial drugs, but lost appetite, felt tired and finally lost consciousness one month after beginning medication. Arterial blood gas revealed marked hypercapnia. Using extracorporeal life support (ECLS), the carbon dioxide concentration was reduced and her consciousness recovered. To our knowledge, this is the first case in which ECLS was successfully used for hypercapnia in a patient with BO.

**Key words:** extracorporeal life support, hypercapnia, bronchiolitis obliterans, noninvasive positive pressure ventilation

**B**ronchiolitis obliterans (BO) is the most common late noninfectious pulmonary complication following allogeneic hematopoietic stem cell transplantation (HSCT), and is characterized by the onset of air flow obstruction. It was first described following HSCT by Beschorner *et al.* in 1978 [1], who reported lymphocytic bronchitis in 10% of autopsies from patients who died following HSCT. In 1982, Roca *et al.* described fatal BO in a patient with a severe chronic GVHD following HSCT [2]. Since then, many reports have described this complication follow-

ing HSCT. Recent data suggest that bronchiolitis obliterans syndrome may affect up to 6% of HSCT recipients and dramatically alters survival, with overall survival of only 13% at 5 years. We report a case of a 31-year woman with BO after HSCT, who presented with life-threatening hypercapnia and showed improvement under extracorporeal life support (ECLS), which could be safely discontinued after 7 days.

### Case Report

A 31-year woman with a history of acute lymphocytic leukemia (ALL) and who underwent chemotherapy and HSCT was affected with bronchitis obliterans

(BO) 2 years after HSCT. She had become aware of an increase of sputum and dyspnea on exertion about one and a half years after HSCT. A diagnosis of BO was made by the findings of a chest X-ray film (Fig. 1), CT scan, ventilation-flow scintigraphy, respiratory function test, and clinical history. She needed oxygen inhalation at a flow of 5L/min through a nasal cannulas in the daytime and 4L/min with non-invasive positive pressure ventilation (NIPPV) at night. The level of carbon dioxide was relatively stable around 100mmHg.

She had other complications of pulmonary infection caused by the non-tuberculous mycobacterium (NTM) *M. kansasii*, diabetes due to steroids, and sinus tachycardia. She had also once experienced left pneumothorax. A month before admission to our hospital, antimycobacterial drugs, including isoniazid (INH), rifampicin (RFP) and ethambutol (EB), were given because of the mild aggravation of pulmonary *M. kansasii* infection. She gradually lost appetite, felt lazy and at last became unconscious. Physical examination on admission revealed a temperature of 37.5°C, blood pressure 147/99mmHg, pulse 124/min, oxygen saturation 84% (O<sub>2</sub> 4L/min with NIPPV), and respiratory frequency 25/min. On auscultation, breath

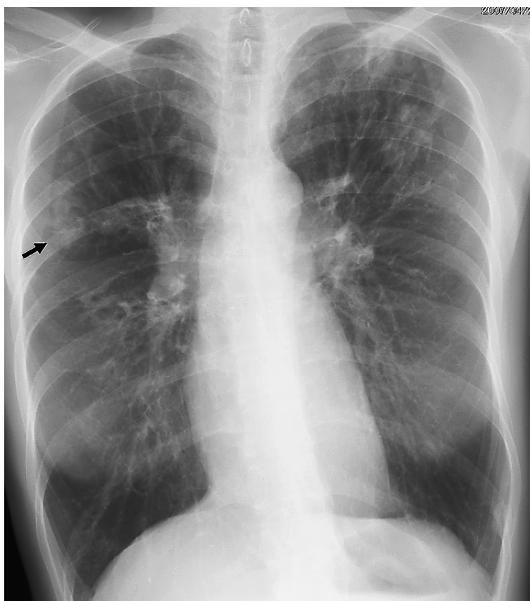


Fig. 1 An X-ray film of the chest just before admission showed overinflation of both lungs and a newly occurred small cavity in the right upper lung field (arrow). There were no findings of exacerbation of BO itself or relapse of pneumothorax.

sounds were hardly detected in both lungs, and no systolic or diastolic murmurs were detected. A chest X-ray film revealed a small cavity with reticulonodular shadows around the right upper lung field due to NTM infection newly occurred a month before admission (arrow). There were no findings of exacerbation of BO itself or relapse of pneumothorax. Arterial blood gases immediately after her transport to the intensive care unit (FiO<sub>2</sub> 100% with NIPPV) were pH7.18, PaO<sub>2</sub> 236.8mmHg, and PCO<sub>2</sub> 161.2mmHg. Pulmonary function and head CT scan could not be assessed because of her severe condition. Regarding laboratory findings, renal and liver function tests were normal. On the basis of these findings, the patient was diagnosed as having disturbance of consciousness with hypercapnia.

We first tried to control respiration with NIPPV. Her oxygenation was well maintained with NIPPV, and the carbon dioxide density, which had temporarily risen to 235mmHg, gradually decreased to around 150mmHg. On the third day of hospitalization, however, the carbon dioxide density suddenly increased beyond 200mmHg and her consciousness got worse. A chest X-ray film showed no findings of new infection or pneumothorax. We decided upon the additional use of ECLS to reduce carbon dioxide density without exchanging NIPPV for invasive ventilation, because we wanted to avoid respiratory complications given the diagnosis of BO and her previous history of pneumothorax. ECLS was initiated via both femoral veins, the left femoral vein for blood transmission and right femoral vein for blood retransfusion, 16 Fr and 18 Fr, 35 centimeters and 20 centimeters in length, respectively, with a blood flow of 1.5L/min, sweep gas flow 100% O<sub>2</sub> 5L/min.

The carbon dioxide density, which had increased to around 200mmHg at the beginning of ECLS, gradually lowered. Ten h later, the level of carbon dioxide was 129mmHg, acidosis had improved to pH7.278, and the patient was able to communicate. The level of carbon dioxide was kept around 100mmHg with a 1.0-1.5L/min flow 3 days after adopting ECLS. Blood transfusion was needed for progressive anemia. ECLS was discontinued a week later, and no re-increase of the carbon dioxide level was seen (Fig. 2).

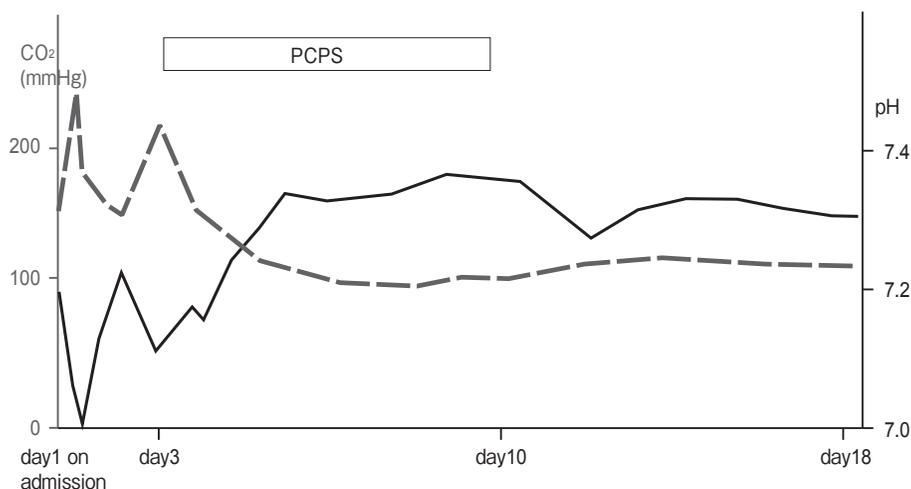


Fig. 2 The course of the patient during hospitalization. Carbon dioxide density gradually reduced to the level she had had before admission, and acidosis was corrected by the use of extracorporeal life support (ECLS).

## Discussion

The ECLS system, first used clinically by Phillips *et al.* in 1983 [3], is generally used to contribute to hemodynamic stabilization. It is widely used for cardiopulmonary resuscitation and is valued in emergency cases due to its easy and quick application [4-6]. It is also used in thoracic surgery such as sleeve pneumonectomy, to assist ventilation [7-9]. In this report, we introduced successful ECLS for severe hypercapnia in a patient with BO. One report exists in which ECLS was used on patients with hypercapnia and severe emphysema as a support during operation [10]. To our knowledge, however, no case of hypercapnia with BO treated by ECLS has been previously reported.

BO is the most common late noninfectious pulmonary complication following allogeneic HSCT, characterized by the onset of air flow obstruction. Patients with BO often develop hypercapnia through an imbalance of the delicate respiratory dynamic state due to events such as infection or progression of BO itself. In our case, the patient had taken antimycobacterial drugs (INH/RFP/EB) because of the exacerbation of pulmonary non-tuberculous mycobacteriosis a month before she presented with general fatigue and appetite loss, well known as adverse effects of RFP. Sufficient examinations, including CT scan and pulmonary function test, could not be done because of her severe condition, but a chest X-ray film and clinical course

showed no manifest progression of the BO itself. We concluded that her disturbance of consciousness was reversibly induced by marked hypercapnia, and decided to use ECLS with NIPPV.

No clear indications for the use of ECLS have been determined because there is no objective evaluation regarding the relationship between the use of ECLS and the severity of shock in patients with acute circulatory failure, much less in patients with respiratory failure. In our case, the patient showed uncorrectable hypercapnia with pH < 7.1 under the use of NIPPV; further, she was affected with respiratory disease and had a previous history of pneumothorax. These conditions induced us to use ECLS to improve severe hypercapnia. ECLS may be strongly indicated for treatment of hypercapnia if invasive mechanical ventilation is not recommended. Hypercapnia that cannot be corrected by mechanical ventilation should also be considered as an indication for ECLS.

The patient achieved spontaneous and stable breathing after the correction of the carbon dioxide density and recovery of consciousness. In our case, antimycobacterial drugs including RFP might have caused fatigue and resulted into hypercapnia, and the cessation of these drugs improved the patient's condition, with help from ECLS.

Using ECLS, we experienced the progression of anemia, which we could handle with blood transfusion. Other complications with ECLS include systemic thrombosis, leg ischemia, renal insufficiency, or sys-

temic inflammatory response, but our patient did not have these complications because the ECLS duration was short.

In conclusion, we successfully adopted an ECLS system for a patient with life-threatening hypercapnia due to severe BO.

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