

Addition of a bilateral access form of peripheral extracorporeal membrane oxygenation rescued a patient with idiopathic pulmonary arterial hypertension who developed circulatory collapse immediately after childbirth

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Abstract

Pregnancy is not advised for patients with Pulmonary hypertension (PH) because of high risk of PH crisis. However, some patients have undiagnosed idiopathic pulmonary arterial hypertension (IPAH) before pregnancy. Upfront combination therapy has high efficacy for patients with IPAH. However, some patients are unable to stand until upfront combination therapy has worked sufficiently. The extracorporeal membrane oxygenation (ECMO) system has been proposed as a bridging therapy to recovery for patients with IPAH. Here, we report a case where a novel form of peripheral ECMO assist plus upfront combination therapy containing intravenous epoprostenol rescued a female patient diagnosed with IPAH just after childbirth. Following this treatment, the patient could successfully transition from intravenous epoprostenol to oral selexipag.

Keywords

pulmonary arterial hypertension, upfront combination therapy, childbirth, peripheral extracorporeal membrane oxygenation

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Pregnancy is not advised for patients with PH because of high risk of PH crisis. However, some patients have undiagnosed idiopathic pulmonary arterial hypertension (IPAH) before pregnancy. Upfront combination therapy (UCT) has high efficacy for patients with IPAH.^{1,2} However, in patients who present with PAH late in pregnancy, or following delivery, there may not be time to fully optimize their condition with an adequate dose of intravenous epoprostenol.

The extracorporeal membrane oxygenation (ECMO) system has been proposed as a bridging therapy to recovery for patients with IPAH.^{3,4} Here, we report a case where a novel form of peripheral ECMO assist plus UCT containing

intravenous epoprostenol rescued a female patient diagnosed with IPAH just after childbirth. Following this treatment, the patient could successfully transition from intravenous epoprostenol to oral selexipag.

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Case description

A previously active 25-year-old female presented with dyspnea on the third day (day 0) after her first childbirth. She was transferred from the gynecology clinic to a general hospital because of acute circulation failure on the same day. Blood pressure, heart rate, and oxygen saturation were 82/56 mmHg, 105 beats per minute, and 80% under 10 L/min oxygen inhalation with oxygen mask at transportation. Hemodynamics parameter values obtained by right heart catheterization (RHC) before treatment were as follows (day 1): pulmonary arterial pressure (PAP) (s/d/m), 103/48/75 mmHg; pulmonary wedge artery pressure, 14 mmHg; right atrium pressure, 13 mmHg; cardiac index (CI), 2.39 L/min/m²; pulmonary vascular resistance, 13.6 Wood unit under ambient air. Arterial blood pressure simultaneously measured during RHC was 132/92/106 mmHg. Oxygen step-up was not observed in blood sampling. Diuretics and dobutamine were initiated for right heart failure (day 1). Despite these treatments, dyspnea was rapidly progressive and subsequent circulatory and respiratory failure required a ventilator and veno-arterial (VA-) ECMO with 20-Fr venous line and a 10-Fr artery line on day 3. The patient then was transferred to our institution for further investigation and treatment. We found no thrombus in the pulmonary artery on contrast Computed tomography (CT), and no signs of connective tissue disease, liver cirrhosis, lung disease, or left heart disease. UCT was adopted because IPAH was strongly suspected. Oral macitentan (10 mg once a day) and inhaled nitric oxide (40 ppm) were initiated together with diuretics plus dobutamine treatment on day 3. Intravenous epoprostenol via a peripherally inserted central venous catheter was simultaneously initiated at 0.5 ng/kg/min, and then being increased rapidly to 10 ng/kg/min over a period of seven days; epoprostenol was continuously administered at this final concentration (day 8) in an intensive care unit under a respirator and VA-ECMO. However, mPAP (81 mmHg) still remained higher than mean arterial pressure (mAP, 61 mmHg) under VA-ECMO delivered at a flow of 3.2 L/min with UCT. Therefore, we considered that higher flows were necessary for this patient. To this end, on day 11 we increased the gauge of the venous line from 20 to 24 Fr and added a new 14 Fr arterial line at the opposite side to the previous 10 Fr-line; the arterial cannulas were connected in a Y configuration (day 10). This refined system using bilateral femoral arterial access, hereafter called VAA-ECMO, increased the flow to ~4 L/min, decreased mPAP to ~40 mmHg, and increased mAP to ~70 mmHg on day 12. Epoprostenol was increased to 31 ng/kg/min within a month and the VAA-ECMO was successfully withdrawn on day 30. Inhaled nitro oxide therapy was changed to oral tadalafil treatment just after extubation (day 31).

On day 37, mPAP was 39 mmHg and CI was 3.9 L/min/m², a substantial improvement compared with day 1. On day 72, mPAP was 29 mmHg and CI was 6.3 L/min/m², indicating high cardiac output due to excessive dilation of the pulmonary

artery. Therefore, epoprostenol was reduced to 15 ng/kg/min; after one month of this reduced dosage, no worsening signs were observed (mPAP, 15 mmHg; CI, 4.0 L/min/m²). Therefore, we switched treatment from intravenous epoprostenol to oral selexipag (day 121). Selexipag was initiated at 200 µg twice a day and up-titrated, while epoprostenol was further down-titrated. On day 181, epoprostenol was withdrawn and selexipag was administered at 1000 µg twice a day. On day 186, RHC revealed mPAP of 14 mmHg and CI of 2.6 L/min/m².

Discussion

This case demonstrated the usefulness of employing a novel peripheral VAA-ECMO system for a postpartum woman who underwent a PH crisis and was diagnosed with IPAH. This case also shows that intravenous epoprostenol could be switched to oral selexipag once the PH crisis was overcome. Pregnancy in women with IPAH is associated with a high maternal mortality,⁵ and when IPAH manifests with cardiogenic shock, as in the case described here, the chances of rescuing the patient are very low. Clinical deterioration and increased mortality manifest in the late stages of pregnancy, during delivery, in the puerperium, and in the postpartum period. Therefore, the treatment regimen outlined here could be particularly beneficial for postpartum women with PAH. It has been previously reported that VA-ECMO should be considered to save IPAH patients with cardiogenic shock.^{3,4} Central ECMO is recommended over peripheral ECMO to prevent leg ischemia, insufficient blood flow, and an increase in left ventricular afterload.⁴ However, the use of central ECMO depends on the patients' condition because central ECMO is invasive and associated with major bleeding. Peripheral ECMO has lower bleeding risk but sometimes cannot achieve adequate flow due to small aortic diameter in patients with low cardiac output. We previously reported that increasing the flow rate of peripheral ECMO by concomitant use of vasodilation, rather than transitioning to central EMCO, could deliver high-flow and overcome the disadvantage of peripheral ECMO in a patient with severe myocarditis.⁶ Indeed, when peripheral ECMO was first applied in the patient in the current study, mPAP remained elevated and exceeded mAP, and the right ventricle remained enlarged, all of which indicated insufficient ECMO flow. After increasing the gauge of the venous line and adding another arterial line through the other femoral artery, the peripheral VAA-ECMO system was established. Using this system, right ventricular (RV) preload was reduced, RV dysfunction was ameliorated, and PAP was rapidly decreased. To avoid the increase in the left ventricular afterload that inevitably occurs after an increase in blood flow, we concomitantly administered vasodilator and managed hemodynamics very carefully. This VAA-ECMO system could overcome the disadvantage of inadequate blood flow in the ordinary peripheral VA-ECMO. We demonstrated that the refined VAA-ECMO

system has the potential to rescue a PAH patient with cardiogenic shock with refractory hypotension and/or signs of progressive secondary organ dysfunction. Previous report revealed that cardiogenic shock during pregnancy dramatically increased mortality. Although the mortality rate was 18.8%, early initiation of mechanical support such as intra-aortic balloon pumping, mechanical ventilation, and ECMO within less than or equal to six days after the diagnosis of cardiogenic shock were associated with the lower mortality rate. Delayed initiation of mechanical support was an independent risk factor for inpatient mortality.⁷ In the present patient, VA-ECMO was decided to initiate on day 3. This early decision might contribute to dramatical improvement.

The patient described here could eventually switch from continuous intravenous epoprostenol to oral selexipag. At present, few patients have been reported to safely transit from intravenous or subcutaneous treprostinil to selexipag; in these cases, reasons for switching were mostly patients' preference and line infection.⁸ In contrast, the decision to transition this patient was based on a stable hemodynamics followed by UCT with intravenous epoprostenol therapy. The effects of orally administered selexipag at a dosage of 1600 µg twice a day is reported to be equivalent to those of 20.1 ng/kg/min subcutaneous infusion of treprostinil,² and the volume of treprostinil required is reported to be 1.2 times that of epoprostenol.⁹ Therefore, in this case, 15 ng/kg/min of epoprostenol was gradually down-titrated to 1000 µg twice a day of selexipag.

Conclusion

A postpartum patient who experienced cardiopulmonary collapse after delivery and was diagnosed with PAH at this time survived to leave hospital after treatment with novel peripheral VAA-ECMO procedure. Furthermore, the patient could be switched from continuous intravenous epoprostenol to oral selexipag, highlighting the importance of critical care management in PAH patients during the perinatal period.

Conflict of interest

Takahisa Kondo and Yoshihisa Nakano belong to the endowed department of Actelion Pharmaceuticals, Japan.

Ethics approval

We obtained a written consent from the patient.

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