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Successful use of Extracorporeal Membrane Oxygenation (ECMO) in postpartum as rescue therapy in a woman with Covid-19

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Abstract

Clinical manifestations of coronavirus disease 2019 (COVID-19) in pregnant women, in contrast to last outbreaks, seem to be similar to those of non-pregnant women. During severe acute respiratory syndrome (SARS), SARS influenza A (H1N1), and Middle East respiratory syndrome (MERS) outbreaks an increased severity of disease among pregnant women was observed.

In some pregnant women, respiratory failure can occur and quickly progress to acute respiratory distress syndrome (ARDS) requiring extracorporeal membrane oxygenation (ECMO) as a rescue therapy. Despite a lack of current guidelines on the use of ECMO in pregnant or postpartum women, this support therapy is an effective salvage therapy for patients with cardiac and/or respiratory failure, and is associated with favorable maternal and fetal outcomes. Herein, we report a case of severe COVID-19 disease in a pregnant patient after urgent cesarean section, who was successfully treated with ECMO during the postpartum. ECMO should be considered early when conventional therapy is ineffective and it is essential to refer to ECMO expert centers.

Introduction

A new viral disease, caused by a novel coronavirus (CoV-2), was identified at the end of 2019 in China. Since then, the disease has expanded rapidly worldwide and the World Health Organization (WHO) has characterized the disease as coronavirus disease 2019 (COVID-19), declaring it as a pandemic on March 2020¹. Although most of COVID-19 patients are asymptomatic or mildly symptomatic, **several** patients can experience respiratory failure and quickly progress to acute respiratory distress syndrome (ARDS). Clinical manifestations of COVID-19 in pregnant women seem **to** be similar to those **of** non-pregnant individuals. Pregnancy does not appear to promote infection or worsen the clinical course²⁻⁴. However, in some cases, severe or critical forms can occur requiring advanced and rescue therapies **such as** extracorporeal membrane oxygenation (ECMO).

The fundamental role of ECMO is the transient support of cardiac and/or lung function in the management of potentially reversible effects, providing time necessary for recovery of cardiac and/or respiratory function. In the past decade, **the** use of ECMO therapy has significantly increased in adults, especially during the last outbreaks [influenza A (H1N1) ARDS in 2009 and Middle East respiratory syndrome (MERS) in 2012], and **currently** is considered a lifesaving treatment when conventional therapies fail.

We report a case of **severe** COVID-19 disease in a **pregnant woman who underwent** urgent caesarean section and required ECMO **therapy in the postpartum**.

Case Report

A previously healthy 31-year-old black woman (gravida 5, para 2) presented to the labor and delivery unit, at 31-weeks of gestation, with 1-week of dry cough and fever without dyspnea. Her medical history was remarkable for obesity (body mass index 31), heterozygote Sickle cell disease, unoperated small restrictive perimembranous ventricular septal defect and **prior** thyroidectomy. On examination, she was found to be febrile (39 °C) with a normal respiratory rate and tachycardia. Breath sounds were normal and she had good oxygen saturation. Laboratory tests and chest radiograph were within normal limits. Obstetric examination and fetal ultrasonography were normal. A **COVID-19** infection was suspected and a nasopharyngeal swab was obtained for the detection of **severe acute**

respiratory syndrome coronavirus 2 (SARS-CoV-2), which was reported as negative on the next day. An antibiotic therapy was started. After 3 days, her clinical conditions rapidly deteriorated requiring oxygen supplementation and admission to intensive care unit (ICU). Acute chest syndrome of sickle cell disease, cardiogenic pulmonary edema or infective endocarditis secondary to perimembranous ventricular septal defect was differential diagnosis.

A transthoracic echocardiography excluded cardiogenic pulmonary edema and infective endocarditis and demonstrated good biventricular function, no valvular abnormalities and a small perimembranous interventricular defect with left-to-right shunt, with a gradient of 50 mmHg across the defect and normal pulmonary arterial pressure. A chest computed tomography scan ruled out the presence of pulmonary embolism, but showed bilateral extensive pulmonary involvement with ground glass opacities in lower lobes and in the peripheral areas. These radiologic findings were found specific for COVID-19 infection and second positive nasopharyngeal swab confirmed this hypothesis. Antibiotic therapy was implemented and a prophylactic dose of anticoagulant was started by subcutaneous injection once a day of low molecular weight heparin (enoxaparin 4000IU). Worsening of dyspnea, an increase necessity of oxygen and a deterioration of arterial blood gas results (pH 7,3, PaO₂ 62 mmHg, PaCO₂ 45 mmHg, SpO₂ 90%) required the induction of fetal lung maturation with 24 mg betamethasone (12 mg given intramuscularly 24 hours apart). Over the subsequent 24 hours, the patient was intubated with specific precautions to prevent contamination and was placed on mechanical ventilation. Urgent caesarean section was performed and a baby girl of 1680 g was born. Nor complications of the placenta or chorioamniotic membrane inflammation were reported. Three successive nasopharyngeal swab tests for the infant were done at 24 hours, 48 hours and 1 week of age which were negative.

After delivery, the patient was referred to our hospital. Despite optimization of mechanical ventilation (MV), use of neuromuscular blockade, inhaled nitric oxide (80 ppm for the first 48 hours) and prone positioning to improve oxygenation for ARDS, all these advanced strategies were ineffective being a ratio of arterial oxygen tension to fraction of inspired oxygen (PaO₂/FiO₂) lower than 70 mmHg. Cardiovascular status was unchanged and a week after the delivery, the decision was made to initiate veno-venous ECMO (Oxygenator EOS, pump REVOLUTION™, Livanova UK). A classic

configuration with a double cannulation of the right internal jugular vein and the right femoral vein was established. ECMO flow (about 5 L/min flow) was adjusted to maintain optimal oxygenation and hemodynamic conditions remained satisfactory. After 7 days of ECMO support, the respiratory function improved to allow a successful weaning off ECMO therapy. The hemodynamic status was unchanged and she was extubated 1 week later, after 20 days of MV. The patient was transferred to the maternity ward one week later. On follow up, the patient and the baby had gone home, the baby was in good health and the mother had only a moderate shortness of breath upon effort.

Discussion

After the first cases in China, the COVID-19 pandemic has rapidly spread around the world. Although most COVID-19 patients are asymptomatic, the clinical manifestations of disease can be of the most varied, but are generally respiratory. An undefined proportion of patients can experience respiratory failure and quickly progress to acute respiratory distress syndrome (ARDS). SARS-CoV-2 is associated with higher mortality, compared to the two recent outbreaks, influenza A (H1N1) ARDS and MERS, combined⁵. This mortality is related to the direct and indirect effects of disease and to the lack of effective therapies.

It is well known that pregnant women are particularly predisposed to respiratory pathogens and severe Pneumonia when compared to non-pregnant women, due to pregnancy-related immunoalterations and physiologic maternal adaptations to pregnancy, with subsequent higher maternal and fetal morbidity and mortality⁶. Recent reports indicate that in contrast to the last outbreaks, SARS, influenza A (H1N1) ARDS and MERS, the clinical manifestations of COVID-19 in pregnant women seem to be similar to those in non-pregnant women. Pregnancy does not appear to promote infection or worsen the clinical course²⁻⁴. However, as in non-pregnant cases, ARDS can occur, requiring advanced and rescue therapies such as ECMO.

To date no drug has demonstrated a universally accepted effect against COVID-19, but a preliminary report (Recovery trial) suggest that the steroid dexamethasone can reduce mortality in COVID-19 patients⁷. Another study shows that the administration of antenatal corticosteroids has a higher combined maternal and infant outcome compared with expectant management for women at high risk

of preterm birth with COVID-19 infection⁸. In the **present** case the administration of betamethasone may have played an important role in association with ECMO therapy.

The **widespread use** of ECMO therapy is due on the one hand to **the** improved technology, making its use simpler and safe, and on the other hand to **its** extensive utilisation **during the** outbreak of influenza A (H1N1) ARDS and MERS. The real benefit of ECMO in ARDS seems to be controversial in the influenza A (H1N1) ARDS and more evident in MERS with a clear lower mortality in the latter^{9,10}. It is clear that ECMO may be helpful in selected patients, but the optimal timing of ECMO initiation is still debated. During pregnancy and postpartum period, the use of ECMO for severe influenza A (H1N1) ARDS was associated with a 66% survival rate while no data is available for MERS¹¹.

Despite a lack of current guidelines on the use of ECMO in pregnant or postpartum patients, several observational studies have reported that ECMO is an effective salvage therapy for patients with cardiac and/or respiratory failure, and is associated with encouraging maternal and fetal outcomes with high rate of survival and low rate of major complications¹²⁻¹⁴. The most common complication remains bleeding that contributes to significant maternal morbidity and mortality^{11,14}. The indication and type of ECMO (veno-veinus or veno-arterial) seem to be unrelated to survival^{12,14}.

The optimal timing for ECMO assistance is crucial and outcomes may be related to its very early use. This is far more important in pregnancy, where it is essential to limit maternal hypoxia, hypercarbia and acidosis. Early referral to an ECMO expert center, with a dedicated ECMO team, should also be discussed, either directly or after rescue implementation by a mobile ECMO team. The case described confirms the potential value of the ECMO in severe forms of ARDS and extreme levels of hypoxia in COVID-19 patients.

Figure Legend

Figure 1. Computed Tomography (CT) scan features **at different interval**. A, A1: axial and frontal view at admission to the intensive care unit, before induced delivery. B, B1 axial and frontal view after weaning off mechanical ventilation. C, C1 axial and frontal view after 1 month **after** discharge.

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