Case Report

COVID-19 and ECMO support after neonatal congenital heart surgery: a case report

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Short Title: COVID-19 after congenital heart surgery
Abstract

Coronavirus disease 2019 (COVID-19) causes respiratory and systemic disease and has led to a sudden epidemic affecting people of all ages. Patients with congenital heart disease represent a high-risk population. In this article, we present a newborn who required extracorporeal membrane oxygenation (ECMO) support for acute respiratory failure in the early postoperative period due to exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) after aortic arch repair and ventricular septal defect closure. To the best of our knowledge, this patient represents the first neonatal case of SARS-CoV-2 infection after congenital heart surgery and is the youngest patient to need ECMO support.

Keywords: SARS-CoV-2; neonate; congenital heart surgery; ECMO
Introduction

Coronavirus disease 2019, the illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first announced in an adult in China on 17 November 2019, and the World Health Organization (WHO) classified the epidemic of SARS-CoV-2 as an emergency of international concern on January 30, 2020 (1,2).

Babies with congenital heart disease (CHD) continue to be born at the rate of 1 in 100 live births during the pandemic, and approximately 25% of these are considered to have critical CHD requiring surgery or other interventions in the first year of life (3). A history of cardiac surgery may be associated with the risk of hospitalization in an intensive care unit (ICU), intubation and mechanical ventilation, particularly more severe form of the disease in newborns and children (4).

In this report, we present the management of a SARS-CoV-2 infection in newborns after successful repair of the aortic arch and ventricular septal defect (VSD) closure surgery. We performed this operation approximately 6 months after the epidemic was declared. Although extracorporeal membrane oxygenation (ECMO) support was applied twice due to respiratory failure, the patient died due to multiorgan failure. To our knowledge, this patient was the first newborn to receive ECMO support for SARS-CoV-2 infection after congenital heart surgery. Consent was obtained from the family for the publication of this study.

Case Report

A full-term 16-day-old newborn boy weighing 3.5 kg was admitted to our department with an absence of femoral pulses and suspected coarctation of the aorta. Echocardiography (ECHO) revealed aortic arch hypoplasia with important aortic coarctation (35-40 mmHg gradient with diastolic extension), the diameter of the proximal transverse arch was 4.9 mm (z-score -3.27), the diameter of the distal transverse arch was 4 mm (z score -2.62), and the diameter of the isthmus was 2.8 mm (z-score -4.29). She also had a restrictive muscular outlet ventricular septal defect with no evidence of left ventricular volume overload, a bicuspid aortic valve with mild stenosis, left aortic arch, and systemic pulmonary hypertension. There were no abnormalities in the patient's preoperative laboratory values, and she did not have a fever or cough preoperatively.
The patient underwent surgery with a median sternotomy, and cardiopulmonary bypass (CPB) was performed. During arch repair, selective antegrade cerebral perfusion (ASCP) was initiated, and del Nido cardioplegia was given. The aortic arch incision was started from the descending aorta and extended to the midportion of the ascending aorta, and the aortic arch was reconstructed with the anterior patch augmentation technique using an autologous pericardial patch. The VSD was closed with the pericardial patch via right atriotomy. After the cessation of CPB, modified ultrafiltration was performed, and the skin was closed with a patch, leaving the sternum open. The patient was transferred to the intensive care unit with moderate doses of inotropic support and was in stable haemodynamic condition. The CPB, aortic cross-clamping, and ASCP times were 152 min, 75 min, and 35 min, respectively. In the control ECHO examination, no significant gradient was observed on the aortic arch, and no residual VSD was detected. Peritoneal dialysis was started postoperatively. The sternum was closed uneventfully on postoperative day 2. Laboratory test results included a normal white blood cell (WBC) count (6.2 kU/ul, ref range <= 4 kU/ul) with elevated polymorphonuclear neutrophils of 77.9% and a low lymphocyte count of 750 cells/mm^3 (ref range <=800 cells/mm^3) on postoperative day 2. The lymphocyte count (570 cells/mm^3) was lower than that on the previous day, and the C-reactive protein (CRP) level (7.7 mg/dL, ref interval <= 0.5 mg/dL) was higher on postoperative day 3.

Acute respiratory deterioration occurred with refractory hypoxemia and worsening hypercapnia despite lung protective ventilation and high positive end-expiratory pressure (PEEP) therapy on postoperative day 3 (Figure 1). ECMO support was used because of acute respiratory dysfunction on postoperative day 4. Venoarterial ECMO support was initiated via a 14 Fr venous cannula inserted into the right atrium and an 8 Fr arterial cannula inserted into the ascending aorta. The support was started at a flow rate of 100 ml/kg/min (80-140 ml/kg/min), and the arterial waveform demonstrated normal pulsatility. The WBC count decreased to 4 kU/ul with an elevated polymorphonuclear neutrophil percentage of 72% and a low lymphocyte count of 690 cells/mm^3. The patient’s reverse transcription-polymerase chain reaction (RT-PCR) test for SARS-CoV-2 was positive, with the sample taken from the endotracheal tube on postoperative day 4. Hydroxychloroquine and favipiravir therapy was started immediately and given for 7 days. A heparin infusion was started, and the activated clotting time was maintained in the target range of 180-220. We did not see major complications such as thrombosis or bleeding during the ECMO support. The initial echocardiogram on ECMO showed normal left ventricle systolic function. The patient was
weaned from ECMO after 6 days of support. Since oxygen saturation decreased and respiratory functions deteriorated 7 days after weaning from ECMO, the support was applied again. After 18 days of care, including hydroxychloroquine and favipiravir therapy, the RT-PCR test for SARS-CoV-2 was negative; however, there was no significant improvement in the patient's clinical condition. During this period, the patient's sternum being open also made the patient vulnerable to infections in addition to COVID-19. *Candida parapsilosis* mediastinitis occurred, and *Sterotrophomonas maltophilia* was found to have reproduced in blood culture obtained during the second ECMO support. Unfortunately, the patient was unable to survive and died on ECMO due to sepsis and multiorgan failure despite extended antibiotic therapy on postoperative day 28.

**Discussion**

It is necessary to understand that although the majority of children are not seriously affected, there may be a subset of group children for whom COVID-19 can progress rapidly, leading to respiratory function deterioration (5). Our patient is the youngest patient ever reported with a progression of SARS-CoV-2 to severe disease requiring ECMO support after cardiac surgery. The respiratory deterioration in this case is important for understanding SARS-CoV-2 disease in newborns undergoing cardiac surgery. Our patient, who developed a rapid respiratory disorder in the early postoperative period, required ECMO support within the next 24 hours despite lung protective ventilation and high PEEP therapy.

Current evidence shows that excessive inflammation, oxidation and an extreme immune reaction play significant roles in the pathogenesis of COVID-19 (6). Direct myocardial damage via angiotensin-converting enzyme 2, viral pneumonia, acute respiratory distress syndrome (ARDS), acute lung injury, hypoxia-induced myocardial damage, CPB-related systemic inflammatory response syndrome, and pulmonary hypertension related to CHD may contribute to the inflammation course (6). Moreover, these events cause a cytokine storm and result in ARDS (6). The immunity of the patient has a major influence on COVID-19 severity, and those with low immune function, such as neonates, may be more susceptible, especially after CPB (6).
According to the Extracorporeal Life Support Organization (ELSO) registry, as of 5 December 2020, ECMO support has been used in 3543 confirmed SARS-CoV-2 patients, and the in-hospital mortality is 45% (7). Thrombosis and bleeding complications are well-known risks of ECMO support. Some studies have indicated a 70% incidence of bleeding and a 37% incidence of thrombosis complications in children supported by ECMO (8). However, the experience with ECMO and the corresponding literature are limited with regard to SARS-CoV-2 (9). Kaushik et al. reported a 5-year-old male patient who underwent ECMO support with carotid artery cannulation due to SARS-CoV-2 multisystem inflammatory syndrome (9).

Unfortunately, right anterior and middle cerebral artery infarction occurred on ECMO day 6, and finally, the patient succumbed to the disease. The cause of stroke in the present case may be multifactorial and could include SARS-CoV-2-associated thromboembolic complications or the carotid artery cannulation strategy. A single centre reported a 5% incidence of acute ischaemic stroke in 221 patients with SARS-CoV-2, and in addition, the incidence of ECMO-associated stroke in children is known to be between 5.6% and 7.8% (10,11).

In our case, the ARDS findings were first observed on the 3rd postoperative day, and the respiratory functions of the patient deteriorated rapidly. Given that the thromboembolic complications associated with SARS-CoV-2 could increase, venoarterial ECMO support was applied with central cannulation. Perhaps for this reason, we did not observe thromboembolic neurological complications, which may produce symptoms such as anisocoria or a decrease in NIRS values over a total of 17 days of ECMO support.

CPB circuit complications during cardiac surgery are another critical issue in COVID-19. A multicentre study showed that the rate of coagulation complications (4.1% versus 0.2%) and oxygenator gas exchange complications (2% versus 0.2%) during adult cardiac surgery were higher in patients who tested positive for COVID 19 than negative ones (12).

ECMO support in ARDS due to COVID-19 is associated with high mortality. Henry et al. reviewed 234 COVID-19-related ARDS patients in China, 17 of whom (7.25%) received ECMO, with a mortality rate of 94.1% versus 70.9% in conventional patients (13). In our opinion, in addition to having undergone cardiac surgery in the neonatal period, the high mortality rate of ECMO in ARDS due to COVID-19 negatively affected survival in our patient.
On the other hand, several multicenter studies have demonstrated that ECMO can play a helpful role in rescuing selected seriously ill adult patients with COVID-19 (14,15). Jacobs et al. conducted a prospective study on 100 adult patients with COVID-19 who needed ECMO support. Of these, 50 patients weaned from ECMO and 49 were discharged from hospital. Although the rate of survival with veno-arterial ECMO was 25% (1 of 4 patients), that with veno-venous was 51% (49 of 96 patients). These studies show that ECMO may facilitate salvage, and provides a sensible rescue strategy.

**Conclusion**

Because little is known about the clinical course and progression of SARS-CoV-2 infection in newborns after cardiac surgery, the duration of ECMO support, cannulation and anticoagulation strategy, and the recovery timetable for guiding treatment are unclear. Our case emphasizes the clinical course of this disease leading to mortality, as well as the difficulties in managing ARDS and ECMO in the context of SARS-CoV-2 syndrome, especially in newborns who undergo cardiac surgery.

**Financial support**

None

**Conflict of interest**

None

**Ethical standards**

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the institutional committees.
References


Figure Legends

Chest radiography (CXR) during hospitalization. A) CXR on postoperative day 2 after sternum closure. B) CXR on the postoperative day 3. C) CXR after central cannulation for VA ECMO. Venous cannula in the right atrium and arterial cannula in the ascending aorta. D) CXR after weaning from the first ECMO support.