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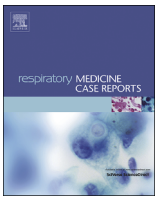

Case Report

Successful use of VA-ECMO in the treatment of an infant with SARS-CoV-2 associated ARDS: A case experience of China and literature review

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1. Introduction

In December 2019, the emergence of a new and highly infectious agent known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) occurred in Wuhan, China. This virus rapidly became a pandemic [1,2]. Although SARS-CoV-2 primarily affects adults, it can also infect children and infants, though incidence rates in these younger populations are comparatively low. When pediatric cases do occur, they are often mild [3]. Data shows that only about 2.5 % of these pediatric patients require hospitalization, and just 0.8 % are severe enough to need intensive care unit (ICU) admission. The mortality rate among the pediatric population with SARS-CoV-2 is less than 0.1 % [4]. The most severe outcomes, including fatalities, in children with SARS-CoV-2 have been associated with acute respiratory distress syndrome (ARDS), multiorgan failure, and multisystem inflammatory syndrome [5].

The lungs are notably vulnerable to SARS-CoV-2, with acute respiratory distress syndrome (ARDS) frequently precipitating patient decline and intensive care unit (ICU) admissions [6]. In cases of severe respiratory failure and refractory hypoxemia, Extracorporeal Membrane Oxygenation (ECMO) becomes the critical intervention. While ECMO's use in pediatric SARS-CoV-2 cases is less common than in adults [7], it is particularly rare among infants. Most severe pediatric ARDS cases linked to SARS-CoV-2 that necessitate ECMO involve older children or adolescents [8]. This report details a rare instance: a 3-month-old infant with SARS-CoV-2-related ARDS who achieved full recovery through ECMO support.

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2. Case presentation

A 3-month-old female infant, weighing 5.5 kg, was presented with symptoms including fever, cough, and dyspnea, as well as peripheral cyanosis. These symptoms developed subsequent to exposure from her mother, who tested positive for COVID-19. On initial assessment, severe pneumonia was visualized on a CT scan and a PCR test confirmed the diagnosis of COVID-19. Despite receiving supplemental oxygen, antibiotics, antipyretics, and other supportive measures, the patient's respiratory distress progressed. With her oxygen saturation levels critically falling between 50 and 60 %, she required endotracheal intubation and mechanical ventilation, which improved her oxygenation to 95 %. Thereafter, she was transferred to our facility for higher-level care.

The patient continued to test positive for the 2019 novel coronavirus (2019-nCoV). Therapeutic interventions encompassed mechanical ventilation, prone positioning, and the administration of methylprednisolone, intravenous immunoglobulin, furosemide, ambroxol, and sulperazone, along with other supportive treatments. Despite these interventions, the patient's condition deteriorated, evidenced by escalating pulmonary infiltrates, decreased oxygenation, and the need for increased ventilatory support. Subsequently, the patient experienced a significant decline in oxygenation, which necessitated the initiation of high-frequency oscillatory ventilation. Oxygen saturation fluctuated between 70 and 82 %, with partial pressure of oxygen (PaO_2) readings of 50–60 mmHg and a PaO_2/FiO_2 ratio within the range of 50–60. Concomitantly, the patient exhibited oliguria and hemodynamic instability with blood pressures oscillating between 50 and 60/20–30 mmHg, requiring the initiation of vasopressor therapy. Imaging studies, including a chest X-ray (Fig. 1) and computed tomography scan (Fig. 2), displayed extensive pneumonia and evidence of mediastinal emphysema. Echocardiography showed right ventricular dilation and pulmonary hypertension. Arterial blood gases were indicative of respiratory acidosis and a persistently low PaO_2/FiO_2 ratio. Given the ongoing hypoxemia, extracorporeal membrane oxygenation (ECMO) was

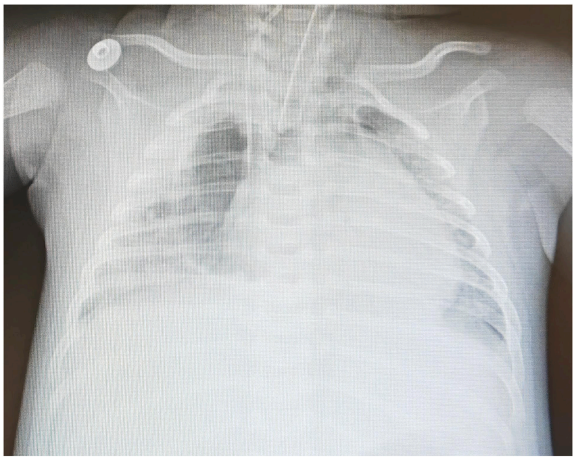

Fig. 1. Chest X-ray before ECMO treatment.

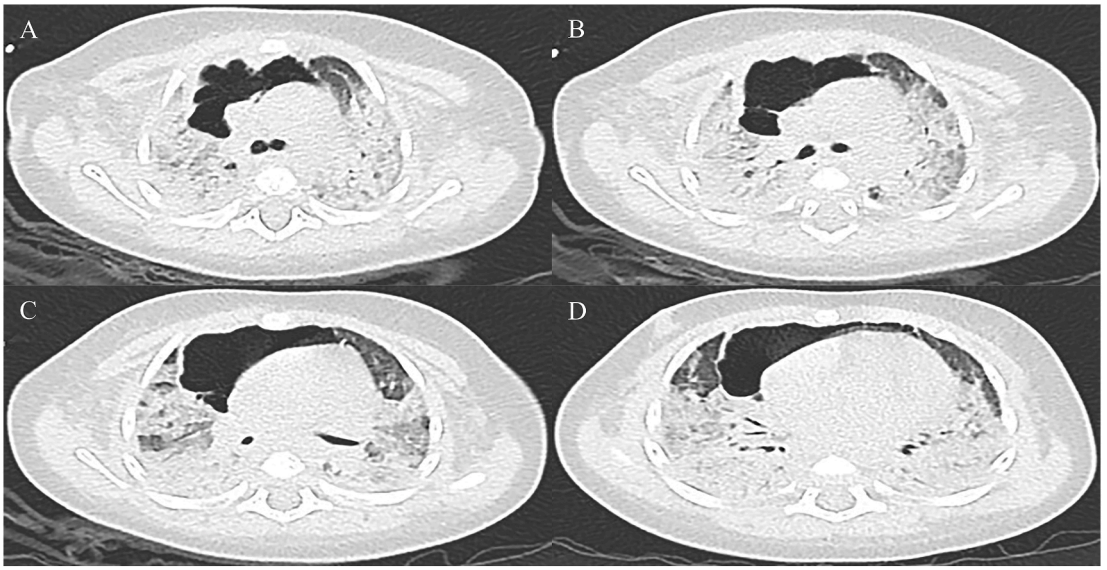

Fig. 2. Chest CT before ECMO treatment.

commenced. Throughout the ECMO therapy, the patient was maintained in a prone position to optimize ventilation and received daily bronchoscopic suctioning. Anticoagulation management with heparin was guided by target ranges for activated clotting time (ACT) between 180 and 220 seconds and activated partial thromboplastin time (APTT) between 60 and 80 seconds. Diuretics were administered to achieve a negative fluid balance, and transfusion of blood products was performed as indicated. Bronchoalveolar lavage fluid analysis returned positive results for SARS-CoV-2 (BA.5.2), Candida parapsilosis, and Pneumocystis jirovecii. These findings prompted the addition of antifungal therapy and sulfamethoxazole to the patient's treatment protocol.

During the period of ECMO support, vigilant management ensured a consistent negative fluid balance, which was regularly monitored through transthoracic echocardiography (TTE) and lung ultrasound assessments (Table 1). On the sixteenth day of admission, coinciding with the eighth day on ECMO, the patient exhibited marked improvements in oxygenation, with partial pressure of arterial oxygen (PaO_2) levels improving to a range of 150–220 mmHg and the ratio of PaO_2/FiO_2 rising to 200–300. Follow-up imaging, including chest X-rays and lung ultrasounds, revealed a decrease in pulmonary infiltrates (Figs. 3 and 4). Cardiac function assessed by TTE also showed significant improvement with reduced pulmonary arterial pressures, enabling the weaning and eventual discontinuation of ECMO support, though dopamine infusion was continued to support blood pressure. Albumin, plasma, and red blood cells were administered to maintain colloid oncotic pressure. Diuretic therapy was utilized to sustain the negative fluid balance. The patient's anti-infective therapy included mepicin and voriconazole, which was complemented by prophylactic anticoagulation with heparin. By the nineteenth day, the patient's clinical status had improved to the extent that mechanical ventilation was no longer necessary, and the ventilator was discontinued (Fig. 5). By the twenty-eighth day, the patient had a negative test result for the novel coronavirus, and a computed tomography (CT) scan showed substantial resolution of the pulmonary abnormalities (Fig. 6).

Table 1
Changes of laboratory examination indexes, arterial blood gas analysis indexes, intake and output volume, and cardiopulmonary function during ECMO treatment.

Item	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
ACT (s)	196	175	186	178	186	196	177	178
APTT (s)	60.3	78.8	75.9	69.1	65	81.9	70.5	68.2
Platelet (10^9/L)	189	178	161	151	140	101	99	94
Hemoglobin (g/L)	111	109	103	105	106	106	98	110
White blood cell (10^9/L)	5.62	5.68	6.25	4.55	5.73	6.47	6.69	6.07
C-reactive protein (mg/L)	15.6	17.02	27.76	23.90	19.75	26.68	37.60	31.98
Heparin (IU/Kg h)	4.5	11.3	10.3	11.5	14.8	15.9	13.6	12.5
Output (mL)	680	661	555	521	570	513	524	610
Intake (mL)	590	620	506	490	497	518	499	607
EF%	20.6	30	35	40	50	55	59	62
Pulmonary ultrasound score	30	31	25	27	24	21	19	17
ECMO FiO_2 (%)	80	80	70	60	50	50	40	40
Ventilator FiO_2 (%)	40	40	40	40	40	40	40	40
PaO2 (mmHg)	90	109	120	140	177	186	226	237

Pulmonary ultrasound score: Images were acquired by using a portable vivid ultrasound machine. Based on the parasternal line, anterior axillary line, posterior axillary line and paravertebral line, the left and right lungs were divided into 12 regions: anterior superior, anterior inferior, lateral superior, lateral inferior, posterior superior and posterior inferior. The pulmonary ultrasound images of each region were divided into 0–3 points according to the condition of B-line and lung consolidation. The total score is the sum of 12 domains (on a scale of 0–36).[26].

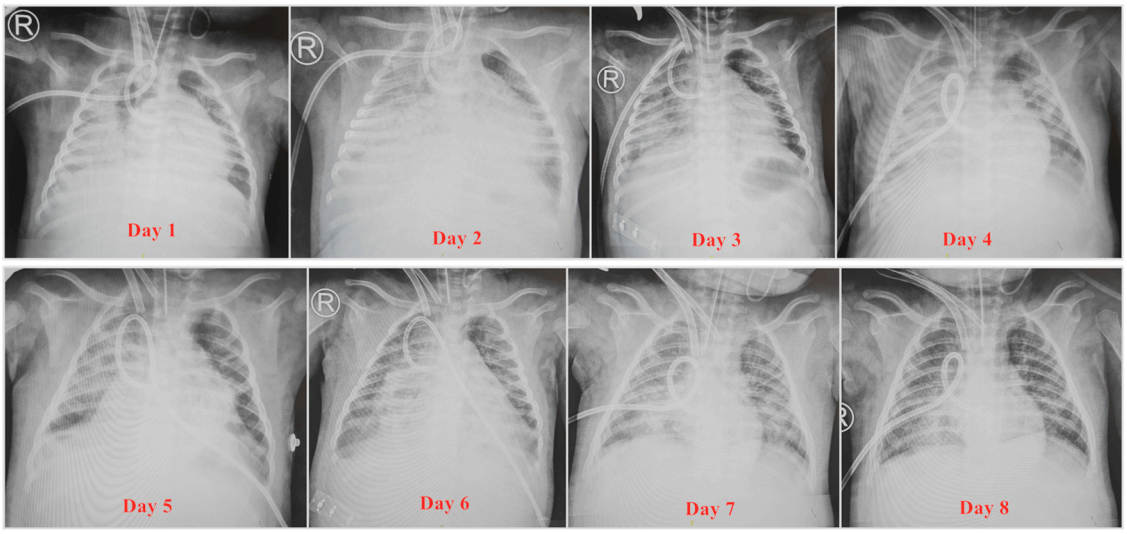

Fig. 3. Changes in chest X-rays during ECMO treatment.

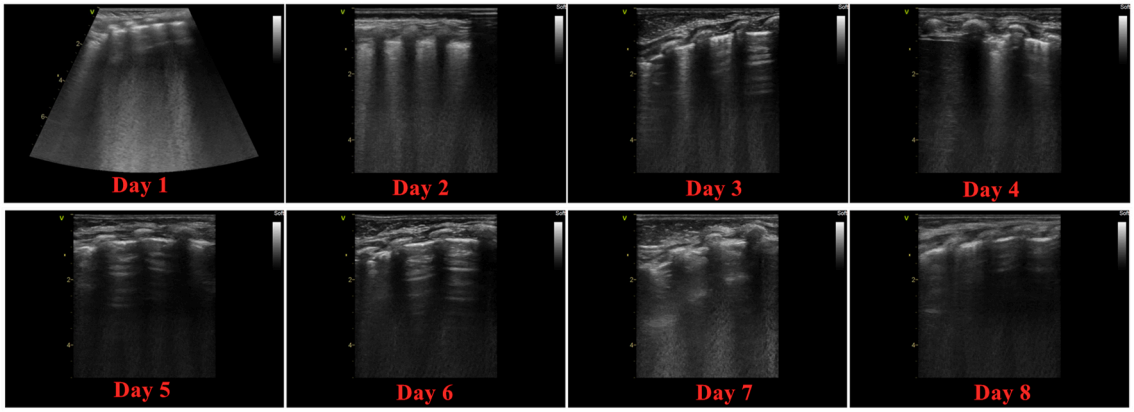

Fig. 4. Changes in pulmonary ultrasound scores during ECMO treatment.

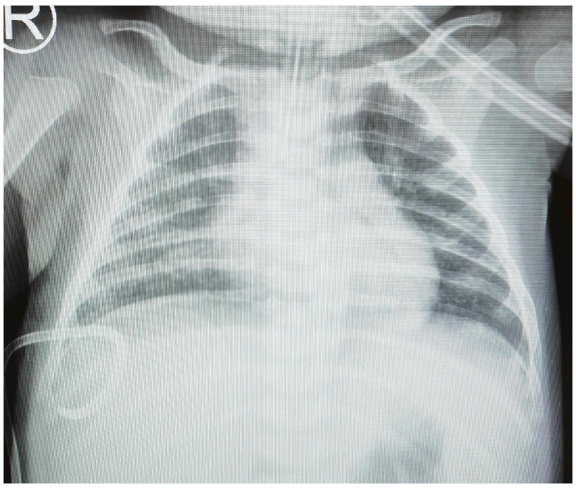

Fig. 5. Chest X-ray before endotracheal tube extubation.

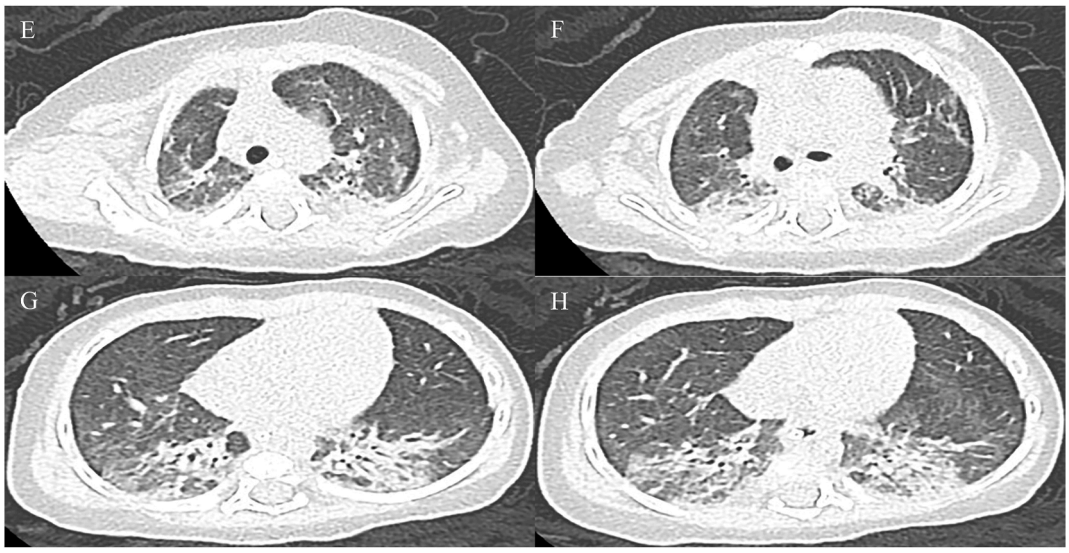

Fig. 6. Chest CT after nCoV test turned negative.

3. Discussion

Extracorporeal Membrane Oxygenation (ECMO) has emerged as a vital lifesaver for patients with severe respiratory and circulatory failure, particularly in cases of ARDS with refractory hypoxemia where traditional management strategies fail. Data from the Extracorporeal Life Support Organization (ELSO) indicates that only a small fraction, 0.5–1%, of SARS-CoV-2 ICU admissions required ECMO during the peak of the pandemic [9]. Although SARS-CoV-2 pneumonia spans all pediatric age groups, severe cases necessitating ECMO are uncommon [10]. Prior case reports have underscored the judicious use of ECMO in pediatric ARDS. Stasiv et al. reported successful venovenous ECMO (VV-ECMO) in two patients, ages 3 and 17, with initiation seven days after diagnosis [11]. Shannon et al. detailed a 16-year-old girl, previously diagnosed with an intracranial tumor, who developed ARDS secondary to SARS-CoV-2 infection and underwent venoarterial ECMO (VA-ECMO) therapy [12]. Unfortunately, she succumbed to intracranial hemorrhage. Cicek et al. narrated the experience of a patient who developed SARS-CoV-2-related ARDS post-congenital heart surgery and was managed with VA-ECMO [13]. Regrettably, after 18 days of intensive care, he passed away due to sepsis and multi-organ failure. Cavalcante et al. analyzed 6 patients (median age of 1.8 years, range: 0.4−14.5 years) who were supported with ECMO for SARS-CoV-2-induced ARDS [14]. Of these, 2 were managed with VV-ECMO and 4 with VA-ECMO. Each patient was provided with lung protective ventilation, glucocorticoid therapy, and gamma globulin support. Two of the six patients died — one from extensive bleeding and another from multi-organ dysfunction. In this report, we highlight the successful ECMO treatment of a 3-month-old infant diagnosed with SARS-CoV-2 (BA.5.2) related ARDS.

Patients who require mechanical ventilation for over two weeks, present with multiorgan failure, or suffer from severe complications are at a higher risk of mortality during ECMO support. Consequently, ECMO should be considered early, before irreversible organ damage occurs. According to ELSO guidelines, the decision to initiate pediatric respiratory ECMO should be based on deteriorating oxygenation trends, rather than waiting for critical PaO_2/FiO_2 thresholds to be crossed [15]. ELSO also advises that for SARS-CoV-2 management, patients should be transferred to an ECMO-capable center when the PaO_2/FiO_2 ratio drops below 100, rather than delaying until it falls below the more critical level of 80 [16]. At our center, we opted to initiate ECMO for this infant when the PaO_2/FiO_2 ratio fell below 80, accompanied by unstable blood pressure, increasing need for vasopressors, and a drop in urine output, despite the absence of significant renal injury at the time. Post-ECMO initiation, liver and renal functions remained within normal ranges.

In the management of ARDS-induced severe respiratory failure, the primary objective of ECMO support is to reduce ventilator-induced lung injury, diminish pulmonary inflammation, and promote the clearance of interstitial fluid to aid in lung recovery. The cornerstone of ARDS treatment is the application of lung-protective ventilation strategies, which include low tidal volumes [17]. Key elements of this approach involve preventing overdistention of alveoli and maintaining optimal positive end-expiratory pressure (PEEP) to prevent the collapse of alveoli at the end of expiration. Such a strategy not only protects the lungs from further damage but also facilitates more rapid resolution of the underlying disease.

High-frequency oscillatory ventilation (HFOV) delivers continuous small volume breaths with oscillatory waveforms, effectively enhancing oxygenation and carbon dioxide clearance while minimizing the risk of barotrauma. The lung-protective benefits of HFOV are well-established in the literature [18,19]. Prone positioning has become a recognized intervention for severe hypoxemia due to ARDS, improving oxygenation by redistributing lung density, promoting the opening of dorsal lung regions, increasing chest wall compliance, decreasing shunting, improving ventilation-perfusion matching, reducing ventilator-associated lung injury, and aiding in alveolar recruitment [20–22]. Following the initiation of ECMO, we utilized HFOV for lung protection and continued prone positioning to further promote lung recovery. We also employed albumin and plasma infusions to maintain colloid osmotic pressure and administered torsemide to achieve diuresis, ensuring a negative fluid balance and reducing pulmonary interstitial edema. An 8-day course led to significant resolution of pulmonary edema and inflammation, resulting in improved pulmonary oxygenation and the successful weaning off ECMO.

Thrombotic and hemorrhagic complications are common during ECMO, with bleeding events reported in 70 % of pediatric cases, including a 16 % incidence of intracranial hemorrhage, and thrombotic events occurring in 37 % [23]. Current literature on anticoagulation protocols during ECMO for SARS-CoV-2-related ARDS is limited. Stasiv et al. reported maintaining APTT between 80 and 100 seconds without thrombotic complications, although they observed significant bleeding related to vascular trauma during cannulation [11]. Cicek et al. aimed for an ACT target of 180–220 seconds, and encountered no major bleeding or clotting events [13]. Kaushik et al. documented a case of right anterior and middle cerebral artery infarction on the sixth day of ECMO in a 5-year-old with VA-ECMO for SARS-CoV-2 associated ARDS [24]. Adult patients with SARS-CoV-2 may have a prothrombotic tendency, as noted by Spiezia et al. [25] In our management, we rigorously monitored ACT and APTT every 4 h, aiming for an ACT of 180–220 seconds and APTT of 60–80 seconds, with heparin doses adjusted accordingly. Throughout the ECMO treatment, coagulation parameters were maintained within target ranges, and the patient did not experience any thrombotic or hemorrhagic events.

4. Conclusion

For infants afflicted with SARS-CoV-2-associated ARDS, ECMO can emerge as an efficacious treatment recourse when conventional respiratory support proves inadequate.

Data sharing and data accessibility

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Author contributions

Yi-Rong Zheng and Bin Weng designed the study, performed the statistical analysis, participated in the operation, and drafted the manuscript. Qi-Liang Zhang collected the clinical data. Shi-Biao Wang and Qiang Chen supervised the study. All authors read and approved the final manuscript.

Declaration of competing interest

All authors declare that they have no competing interests.

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