# **Case Report**

# Preparedness for rapid veno-venous extracorporeal membrane oxygenation introduction for pediatric severe acute respiratory distress syndrome: a case report

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*Case:* Previous research has suggested that venovenous extracorporeal membrane oxygenation (vvECMO) is useful for patients refractory to conventional therapy. We report a pediatric case of influenza A(H1N1)pdm09 infection with a good outcome following rapid initiation of vvECMO.

This patient was a 13-year-old boy with severe acute respiratory distress syndrome due to influenza virus. Severe acute respiratory distress syndrome according to the Berlin definition, Murray score of 3.3, and severe air leak syndrome were found.

**Outcome:** Puncture for the cannula began 67 min after admission, and vvECMO management was rapidly initiated within 90 min after admission. Introduction of vvECMO required 23 min to complete. The patient was weaned from vvECMO on day 5 and he was discharged home without any complication.

Conclusion: It is essential to prepare a system that enables the rapid introduction of vvECMO for children in the emergency center.

Key words: Acute respiratory failure, critically ill pediatric patient, emergency center

## BACKGROUND

**P**ATIENTS INFECTED WITH influenza A(H1N1) pdm09 virus have been reported to experience symptoms much more severe than those caused by other seasonal influenza viruses.<sup>1–3</sup> Previous research suggested that venovenous extracorporeal membrane oxygenation (vvECMO) is useful for patients who are refractory to conventional therapy.<sup>4,5</sup> To improve the quality of pediatric vvECMO management, it is important to prepare essential equipment and protocols and to develop an education and training program.<sup>7–9</sup> We report a pediatric case of influenza A(H1N1) pdm09 infection that showed a good outcome following rapid initiation of vvECMO.

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#### CASE

T HE PATIENT WAS a 13-year-old boy who was 148 cm in height and weighed 46 kg. He presented with high fever, disturbance of consciousness, and respiratory distress. He had no medical history of immunosuppression and no developmental delay. He was transferred to our emergency center 14 h after exhibiting fever. His Glasgow Coma Scale score was E1V1M4. He was tachypneic with a respiration rate of 40 breaths/min. Oxygenation was impaired, with an SpO<sub>2</sub> of 93% on oxygen at a flow rate of 10 L/min. His heart rate was 133 b.p.m. The patient underwent tracheal intubation.

Laboratory results were  $27,840/\mu$ L for leucocytes, 7.09 mg/dL for C-reactive protein, 1.53 for prothrombin time – international normalized ratio, 47.5 s for activated partial thromboplastin time, 7.4 µg/mL for fibrin degradation products, and 2.7 µg/mL for p-dimer. Blood gas analysis revealed pH 7.05, PaCO<sub>2</sub> 109 mmHg, PaO<sub>2</sub> 84 mmHg, HCO<sub>3</sub><sup>-</sup> 28.8 mmol/L, and lactate 1.6 mmol/L. Bilateral consolidation and left pneumothorax were observed on the chest X-ray and computed tomography (CT) (Fig. 1). The brain

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CT scan was suggestive of cerebral edema. Electroencephalography revealed that reaction to stimulation was weak, and theta waves were present. An electrocardiogram revealed ST-segment elevation in leads V4–6, II, III, and aVF. Echocardiography showed no abnormal findings. He tested positive for influenza A virus, and he had not been previously vaccinated against influenza.

Under the mechanical ventilation (MV) setting (synchronized intermittent mandatory ventilation mode: peak inspiratory pressure/positive end expiratory pressure 32/ 12 cmH<sub>2</sub>O; ventilation rate 20/min; F<sub>I</sub>O<sub>2</sub> 1.0), the total and minute volumes were 3 mL/kg and 1.3 L/min, and the lung compliance was 65-75 mL/cmH<sub>2</sub>O. The oxygenation index and P<sub>a</sub>O<sub>2</sub>/F<sub>I</sub>O<sub>2</sub> ratio were 24 and 84, respectively. Moreover, the patient had a pH level of <7.25 with a P<sub>a</sub>CO<sub>2</sub> of >60 mmHg, which is one of the criteria for the initiation of ECMO in the EOLIA trial.<sup>10</sup> The air leakage from the thoracic drain inserted for the left pneumothorax continued. The patient had a Murray score of 3.3 and was diagnosed with the Berlin definition of severe acute respiratory distress syndrome and severe air leak syndrome. According to the Pediatric Index of Mortality 2, the predicted mortality was 16.7%. His acute respiratory distress syndrome was difficult to treat using conventional therapy. Puncture for the cannula began 67 min after hospital admission, and vvECMO management was rapidly initiated within 90 min after hospital admission and required 23 min to complete.

A vvECMO cannula was punctured and inserted under real-time ultrasound guidance in our angiography room. For blood return, an 18-Fr, 15-cm cannula (Flexmate, Toyobo Ltd, Osaka, Japan) was inserted in the right internal jugular vein and advanced into the right atrium. For blood drainage, a 22-Fr, 52-cm cannula (Flexmate) was inserted in the right femoral vein and advanced into the inferior vena cava.

A centrifugal pump was used. The pump and gas flow rates were to 80-100 mL/kg/min and  $F_IO_2$ , 1.0, respectively. Anticoagulant therapy involved the continuous i.v. injection of heparin targeting an activated clotting time level of 180-200 s. During vvECMO management, the MV setting was adjusted targeting  $SaO_2 \ge 75\%$  and  $PaCO_2 \le 60 \text{ cmH}_2O$ . Within 12 h after the initiation of vvECMO, the MV setting needed adjustment because the control by vvECMO was insufficient for oxygenation and ventilation (Fig. 2). We continued continuous renal replacement therapy from day 1 to 5 because the patient developed oliguria and his metabolic acidosis had progressed. Peramivir



Fig. 1. Imaging findings at hospital admission of a 13-year-old boy with severe acute respiratory distress syndrome. A, Chest and abdominal X-ray. B, Chest computed tomography (CT). C, Brain CT.

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**Fig. 2.** Clinical course of a 13-year-old boy with severe acute respiratory distress syndrome from day 1 to 10 of his intensive care unit (ICU) stay while being treated with venovenous extracorporeal membrane oxygenation (vvECMO). The top part of this figure shows the ventilator settings (mode, peak inspiratory pressure [PIP], and respiratory rate [RR]) and duration of ECMO and continuous renal replacement therapy (CRRT). The middle part of the figure shows medication doses. The bottom part shows changes in vital signs, PaCO<sub>2</sub> level, pH level, oxygenation index, and  $P_aO_2/F_1O_2$  (P/F) ratio. ABPC/SBT, Ampicillin/Sulbactam; APRV, airway pressure release ventilation; CLDM, Clindamycin; CTRX, Ceftriaxone; HR, heart rate; MV, mechanical ventilation; PEEP, positive end expiratory pressure; PS, pressure support; sBP, systolic blood pressure; SIMV, synchronized intermittent mandatory ventilation; VCM, Vancomycin.

(10 mg/kg/day) was given for 3 days. Due to the risk of developing bacterial infection and/or encephalitis, prophylactic antibiotics (ceftriaxone 60 mg/kg/day + clindamycin 25 mg/kg/day), steroid pulse (30 mg/kg/day), and immunoglobulin (150 mg/kg/day) were given for 3 days. The results of reverse transcription–polymerase chain reaction at admission yielded influenza A(H1N1)pdm09 virus.

The patient was weaned from vvECMO on day 5 and MV on day 9. He was discharged from the intensive care unit on day 10. He was discharged to home on day 20 with a Pediatric Cerebral Performance Category score of 1.

# DISCUSSION

S IMILAR TO PREVIOUS research, this case report reaffirms that vvECMO is useful for a patient refractory to conventional therapy. An emergency center should accept critically ill patients regardless of age. Therefore, these centers should develop a system of vvECMO management for children. Prompt vvECMO introduction may be required because respiratory insufficiency can rapidly worsen, as in our case.<sup>6</sup>

Our center prepared the following systems for rapid pediatric vvECMO introduction:

1. Essential equipment and protocols for pediatric vvECMO.

*Cannulation technique*: The blood drainage cannula is inserted in the internal jugular vein if the patient weighs  $\leq$ 30 kg and in the femoral vein if the patient weighs >30 kg. The blood return cannula is inserted in the internal jugular vein regardless of body weight. The cannula size and insertion length in children vary with body weight (Table 1). Because neonates or infants rarely undergo vvECMO in the

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Body weight (kg)	Cannula size (Fr)/insertion length (cm)			
	Blood drainage cannula (site of puncture)		Blood return cannula (site of puncture)	
	8	11.5 (internal jugular vein)	6	6.5 (internal jugular vein)
3–5	10		8	
5–10	12		10	
10–15	14		12	
15–30	18	55 (femoral vein)	14	15 (internal jugular vein)
>30	20		18	, , ,

**Table 1.** Cannula size and insertion length in children according to body weight, as used at Yokohama City University Hospital (Yokohama, Japan)

emergency center, it is not cost-effective to stock several cannula sizes, especially smaller sizes for neonates or infants. Therefore, we substitute hemodialysis catheters for vvECMO cannulas in patients weighing <5 kg.

*Management technique*: We use collateral flow for children weighing <10 kg to stabilize vvECMO flow in order to avoid the need to lower the pump frequency while using a centrifugal pump. Collateral flow acts an as AV shunt (the pathway from postoxygenator to prepump). If a patient weighs <15 kg, we undertake blood priming.

2. Education and training program.

Because few pediatric patients undergo ECMO, on-thejob experience is limited. Several reports indicated that a simulation training program effectively provided a standardized education experience for all members of an ECMO care team.<sup>7,8,11</sup> A future need for our hospital is the development of a simulation training program for pediatric ECMO.

A previous study found an association between higher hospital ECMO volume and lower mortality.<sup>9</sup> When the duration of ECMO management is predictably prolonged for a pediatric patient, transfer to another hospital with highvolume pediatric ECMO management will be considered to improve the outcome.

## CONCLUSION

**T** IS ESSENTIAL to prepare a system enabling the rapid initiation and management of ECMO for children in the emergency center.

## DISCLOSURE

Approval of the research protocol: This study was approved by the ethics committee of Yokohama City University. Informed consent: Written informed consent was obtained from the subject and/or guardians for publication of this case report.

Registry and registration no. of the study/trial: N/A.

Animal studies: N/A.

Conflict of interest: None.

## REFERENCES

- Minchole E, Figueredo AL, Omenace M *et al.* Seasonal influenza A H1N1pdm09 virus and severe outcome: a reason for broader vaccination in non-elderly, at-risk people. PLoS ONE 2016; 11: e0165711.
- Webb SA, Pettila V, Seppelt I *et al.* Critical care service and 2009 H1N1 influenza in Australia and New Zealand. N. Engl. J. Med. 2009; 361: 1925–34.
- 3 Randolph AG, Vaughn F, Sullivan R *et al.* Critically ill children during the 2009-2010 influenza pandemic in the United States. Pediatrics 2011; 128: e1450.
- 4 Zangrillo A, Biondi-Zoccai G, Landoni G et al. Extracorporeal membrane oxygenation (ECMO) in patients with H1N1 influenza infection: a systematic review and meta-analysis including 8 studies and 266 patients receiving ECMO. Crit. Care 2013; 17: R30.
- 5 Noah MA, Peek GJ, Finney SJ *et al.* Referral to an extracorporeal membrane oxygenation center and mortality among patients with severe 2009 influenza A (H1N1). JAMA 2011; 306: 1659–68.
- 6 Maslach-Hubbard A, Vratton SL. Extracorporeal membrane oxygenation for pediatric respiratory failure: History, Development and current status. World J. Crit. Care Med. 2013; 2: 29–39.
- 7 Short BL, Williams L (eds). ECMO Specialist Training Manual, 3rd edn. Michigan: Extracorporeal Life Support Organization, 2010.

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- 8 Johnston L, Oldenburg G. Simulation for neonatal extracorporeal membrane oxygenation teams. Semin. Perinatol. 2016; 40: 421–9.
- 9 Barbaro RP, Odetola FO, Kidwell KM *et al.* Association of hospital-level volume of extracorporeal membrane oxygenation cases and mortality. Analysis of the extracorporeal life support organization registry. Am. J. Respir. Crit. Care Med. 2015; 191: 894–901.
- 10 Combes A, Hajage D, Capellier G *et al.* Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. N. Engl. J. Med. 2018; 378: 1965–75.
- 11 Sakamoto S. Simulation-based training for handing extracorporeal membrane oxygenation emergencies. J. Thorac. Dis. 2017; 9: 3649–51.