Case Report

Severe acute respiratory distress syndrome in a patient with AIDS successfully treated with veno-venous extracorporeal membrane oxygenation: a case report and literature review

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Case: Several successful uses of extracorporeal membrane oxygenation (ECMO) for acute respiratory distress syndrome in patients with novel HIV/AIDS infection have been reported; however, the therapeutic keys have not always been discussed.
A 47-year-old man was admitted with progressive shortness of breath. He was in respiratory failure with a PaO_2/F_IO_2 ratio of 110.8 requiring intubation. Chest computed tomography showed diffuse ground glass opacities. An HIV infection was suspected, and a diagnosis of acute respiratory distress syndrome was made. Based on clinical indications, treatment for *Pneumocystis jirovecii* pneumonia and concomitant bacterial infection was started.

Outcome: Despite broad-spectrum antibiotics, the patient's oxygenation deteriorated, necessitating ECMO. After 19 days of ECMO therapy, the patient was successfully decannulated and was eventually discharged.

Conclusion: In acute respiratory distress syndrome in patients with HIV/AIDS refractory to treatment, ECMO should be considered. Post-ECMO antiretroviral therapy could improve outcomes.

Key words: Acute respiratory distress syndrome, HIV/AIDS, post-ECMO ART, V-V ECMO

BACKGROUND

ALTHOUGH THE FREQUENCY of extracorporeal membrane oxygenation (ECMO) use in respiratory failure is increasing, only half of such cases are discharged or transferred, and high survival rates have not yet been achieved.[1] The indications for ECMO remain controversial, especially in patients who are immunosuppressed or have non-recoverable comorbidities. There are several reports of successful ECMO use for severe hypoxia in patients with HIV/AIDS.[2–10] However, key therapeutic issues, such as mechanical ventilation (MV) settings, indications for ECMO, and the timing of antiretroviral therapy (ART), have not always been discussed in these reports. A case of acute respiratory distress syndrome in a patient with novel HIV/AIDS, who was successfully treated with veno-venous (V-V) ECMO and discharged, is presented.

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Received 7 Nov, 2017; accepted 2 Jul, 2018; online publication 19 Aug, 2018
Funding Information
No funding information provided.

CASE

A 47 -year-old man with an unknown medical history was admitted to our tertiary medical center due to worsening shortness of breath. He had been in his usual state of health until he developed oral white plaques 3 months prior to admission. In the previous month, he had mild chest pain, productive cough, and a mild fever. On the day of admission, he was found lying down with severe shortness of breath. He presented with a respiratory rate of 42 breaths/min and unmeasurable O_2 saturation, and was brought in by ambulance for severe respiratory failure. Physical examination showed coarse crackles over the right lung. Chest computed tomography (Fig. 1A) showed diffuse, bilateral, ground glass opacities. He was in severe respiratory failure with a PaO_2/F_IO_2 ratio of 110.8 requiring intubation and MV.

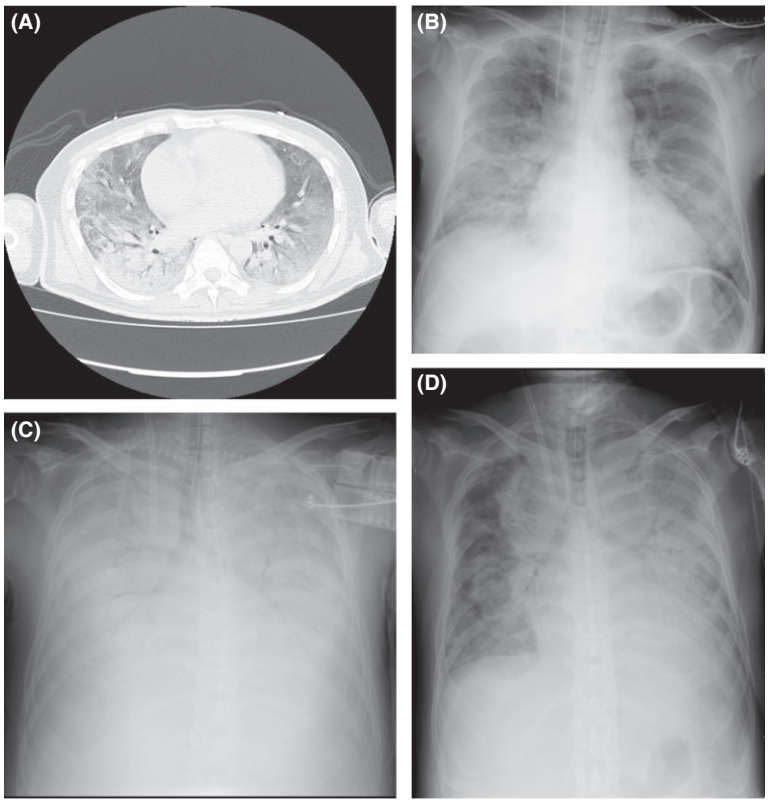

Fig. 1. Chest computed tomography and X-ray findings in a patient with HIV/AIDS and severe acute respiratory distress syndrome treated with veno-venous extracorporeal membrane oxygenation. A, Initial chest computed tomography. B, Portable chest X-ray on hospital day 4. C, Portable chest X-ray on hospital day 11, showing prominent bilateral consolidation. D, Portable chest X-ray on hospital day 17, showing decreased lung consolidation.

Table 1. Mechanical ventilation (MV) settings in a patient with HIV/AIDS and severe acute respiratory distress syndrome treated with veno-venous extracorporeal membrane oxygenation (ECMO)

Hospital day	Mode	F_IO_2	Vt (mL) or PIP (cmH_2O)	PEEP (cmH_2O)	RR (/min)
Day 1	VCV	0.50	420 mL	8	12
Day 2	PCV	0.45	15	8	12
Day 3	PCV	0.40	15	10	8
Day 4	PCV	0.50	15	10	8
Day 5	PCV	0.70	18	15	8
ECMO introduced					
Day 6	PSV	0.40		8	
Day 9	PCV	0.50	18	6	15
Day 11	PCV	0.40	20	10	8
Fixed MV settings and changed only as needed					
Day 23	PCV	0.40	25	8	20
	PCV	0.60	25	8	20
Increased F_IO_2, then ECMO decannulated					

PCV, pressure control ventilation; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure; PSV, pressure support ventilation; RR, respiratory rate; VCV, volume control ventilation; Vt, tidal volume.

The diagnosis of HIV infection was suspected on admission because of positive screening for HIV antigen–antibody (CLIA test), and it was later confirmed by a $CD4^+$ T-cell count of 6/μL and an HIV viral load of 1.4×10^5 copies/mL. Simultaneously, *Pneumocystis jirovecii* pneumonia was highly suspected on admission based on clinical signs, diagnostic imaging, a lactate dehydrogenase level of 1,511 U/L, and an elevated β-D-glucan level of 25.9 pg/mL. His respiratory failure was so severe that we believed it was safer and more appropriate to start treatment for *P. jirovecii* pneumonia than to carry out bronchoalveolar lavage. Polymerase chain reaction test was not available. Although a definitive diagnosis of *P. jirovecii* pneumonia was not made, treatment with trimethoprim/sulfamethoxazole and prednisolone was started appropriately, and piperacillin/tazobactam and vancomycin were started to cover concomitant bacterial infections from admission. Sputum culture was negative for common pneumonia pathogens, urine *Streptococcus pneumoniae* antibody was negative, and blood cultures were negative; therefore, concomitant bacterial infection was considered unlikely, and piperacillin/tazobactam and vancomycin were discontinued after 4 days.

Four days after his admission, the patient developed progressive hypoxia requiring F_IO_2 0.5/positive end-expiratory pressure (PEEP) 10 increasing to F_IO_2 0.7/PEEP 15 within 1 day and worsening consolidation on X-ray (Fig. 1B). The Murray score was 3 points, and progressive respiratory failure was predicted. As he developed progressive symptoms despite appropriate care and had no prospect of improvement within 7 days, beyond which time ECMO use is associated with worse outcomes, and because there have been some case reports of successful ECMO use in cases of acute respiratory distress syndrome with novel HIV/AIDS, it was decided to initiate V-V ECMO (Capiox; Terumo, Tokyo, Japan).

Conventional MV settings ($F_IO_2 < 0.4$ and plateau pressure < 25) were used (Table 1), maintaining $SaO_2 > 80\%$, hemoglobin > 12 g/dL, and platelets $> 10 \times 10^4$/μL with transfusion based on protocols or Extracorporeal Life Support Organization (ELSO) guidelines.[11,12] The patient required two membrane exchanges, and after the second membrane replacement, surgical tracheostomy was carried out following heparin antagonization with protamine; by that time his oxygen demand decreased to F_IO_2 0.3/PEEP 10, and significant X-ray improvement was noted (Fig. 1C, D). His course was further complicated by mediastinal emphysema before ECMO decannulation, which was managed supportively. He was successfully decannulated after 19 days of ECMO, because arterial blood gases were satisfactory for at least 8 hours with a blood flow of 1.5 L/min and a sweep gas of 0.5 L/min (parameters from a previous article).[6]

Table 2. Antibiotic, antimycotic, and antiviral treatment during extracorporeal membrane oxygenation (ECMO) use in a patient with HIV/AIDS and severe acute respiratory distress syndrome

	Admission	Day 5	Day 7	Day 10	Day 18	Day 20	Day 21	Day 23
Bacterial pneumonia								
	Piperacillin/tazobactam and vancomycin	Piperacillin/tazobactam and vancomycin		Levofloxacin	Levofloxacin	Levofloxacin	Levofloxacin	Levofloxacin
Novel HIV/AIDS								
Pneumocystis jirovecii pneumonia	SMX + TMP	SMX + TMP	SMX + TMP	SMX + TMP	Pentamidine	Pentamidine	Pentamidine	Pentamidine
CMV			Ganciclovir	Ganciclovir	Ganciclovir	Ganciclovir		
MAC							Azithromycin	Azithromycin
ECMO		Initiated						Decannulated

CMV, cytomegalovirus; MAC, mycobacterium avium complex; SMX, sulfamethoxazole; TMP, trimethoprim.

Table 3. Review and comparison of previous cases with HIV/AIDS treated with extracorporeal membrane oxygenation (ECMO)

	Age (years)	Sex	New HIV diagnosis	Diagnosis	CD4	HIV viral load (/mL)	Timing of ART initiation (pre-, on-, post-ECMO)	PaO_2 (mmHg)/F_IO_2 (%)	ECMO initiation (hospital day)	ECMO duration (days)	Outcome
Present case	47	M	Yes	HIV/AIDS	6 cells/μL	140,000	Post	54.9/50	5	19	Survived to discharge
Goodman[4]	30	F	Yes	HIV/AIDS, PCP	13 cells/mL	976,631	Post	50.1/100	3	7	Survived to discharge
Simpson[8]	35	M	Yes	HIV/AIDS, PCP	NA	1,269,866	NA	NA/NA	NA (7 days on MV)	27	Survived for 6 months
Ali[10]	26	M	Yes	HIV/AIDS, PCP	84	907,302	Post	200 (P/F ratio)	NA	6	Survived to discharge
Horikita[9]	23	M	Yes	HIV/AIDS, PCP	8.5 cells/μL	550,000	On	48/100	NA (ICU day 3)	12, 14 (2nd course)	Survived to discharge
De Rosa[6]	24	M	Yes	HIV/AIDS, PCP	3 cells/mm^3	50,728	On	100 (P/F ratio)	12 (6 days on MV)	24	Died in hospital, s/p decannulation
Cawcutt[7]	45	M	Yes	HIV/AIDS, PCP	33 cells/mL	113,000	Pre	59/60	5	57	Died in hospital, s/p decannulation
Gutermann[2]	55	M	Yes	HIV/AIDS, PCP	9 cells/mL	80,235	Post	NA/NA	4	4	Survived to discharge
Goodman[4]	25	M	Yes	HIV/AIDS, PCP	36 cells/mL	622,234	Pre	63.6/100	18	69	Died on ECMO
Steppan[3]	39	M	NA	HIV/AIDS, PCP	69 cells/mL	6,297	Pre	NA/100	12	14	Died on ECMO
De Rosa[6]	21	F	No	HIV/AIDS, PCP	2 cells/mm^3	118,330	Non-compliant, restarted	120 (P/F ratio)	10	20	Survived to discharge
Simpson[8]	40	M	No	HIV, disseminated Kaposi's sarcoma	NA	126,947	NA	NA	NA (1 day on MV)	28	Died in ICU
Simpson[8]	20	F	No	HIV, adenovirus	NA	Undetectable	NA	NA	NA (1 day on MV)	5	Survived for 6 months
	25	M	Yes	HIV/AIDS, MDR bacterial PNA	134 cells/μL	2,220,000	Pre	80/90	27 (11 days on MV)	56	Survived to discharge
De Rosa[6]	38	F	No	HIV, HCV, *Legionella pneumophila*	170 cells/mm^3	500	Compliant and continued	90 (P/F ratio)	2	13	Survived to discharge

ART, antiretroviral therapy; F, female; HCV, hepatitis C virus; ICU, intensive care unit; M, male; MDR, multidrug resistant; MV, mechanical ventilation; NA, not applicable; PCP, pneumocystis pneumonia; P/F, PaO_2/FIO_2; s/p, status post.

Several microbial infections concurred during his hospital stay (Table 2). Detection of cytomegalovirus antigen in neutrophils came back positive and ganciclovir was started on hospital day 7. The patient's respiratory status worsened on ECMO and because atypical pneumonia pathogens had not been covered since admission, levofloxacin was added on hospital day 10 and a 14-day course was completed. In addition, *P. jirovecii* pneumonia treatment was switched to pentamidine per recommendation from consultants followed by initiation of prophylactic treatment with azithromycin for mycobacterium avium complex on hospital day 21.

Thirteen days after decannulation, after the successful treatment regimen and to avoid reported immune reconstitution inflammatory syndrome (IRIS), ART was started. Subsequently, the patient was weaned off ventilator support. The patient was then moved to a regular ward and eventually discharged home ambulatory.

DISCUSSION

THE COURSE OF this patient highlighted some important clinical issues. The discharge rate of acute respiratory distress syndrome cases with HIV/AIDS treated with ECMO is reportedly better than that of general patients treated with V-V ECMO (67% versus 58%, Table 3).[1] Although there is no absolute contraindication to V-V ECMO in the guidelines, treating immune-compromised patients, including those with HIV/AIDS, with V-V ECMO is sometimes considered controversial.[11,12] However, previous reports and the present case show that severe respiratory failure with HIV/AIDS can now be treated by V-V ECMO support. In these cases, respiratory status should be closely monitored with evaluations including the Murray score to determine the indication for ECMO.

To our knowledge, there have been 14 reported cases of HIV/AIDS patients with progressive respiratory failure treated with ECMO. Eleven of these 14 cases had *P. jirovecii* pneumonia. As *P. jirovecii* pneumonia was highly suspected in the present case, we managed our patient with novel HIV/AIDS for *P. jirovecii* pneumonia. The focus in the present case was on early achievement of lung rest management by the early introduction of ECMO, which is a novel approach in these types of cases. Boonsarngsuk *et al.* concluded that PEEP on the 3rd day of ventilation management was related to higher mortality in *P. jirovecii* pneumonia,[13] so we hypothesize that lung rest settings achieved by ECMO do have benefits. In the present case, the patient needed higher PEEP settings due to worsening oxygenation before ECMO introduction. In terms of timing of ECMO initiation, it seems ideal to start ECMO within 7 days from ventilator introduction based on the ELSO guideline[12] and Respiratory ECMO Survival Prediction (RESP) score.[14] In addition, as Goodman *et al.*[4] reported, patients given ECMO early during their ventilator management course showed higher survival rates (Table 3).

In addition, post-ECMO ART should be considered in HIV/AIDS patients with acute respiratory distress syndrome. All cases listed in Table 3 that received post-ECMO ART survived. It was difficult to extract all the conditions related to the RESP score, but when age and time to starting ECMO are based on the RESP score, post-ECMO ART achieved survival in all cases. In general, ART is not started in *P. jirovecii* pneumonia cases presenting with high *P. jirovecii* activity, because immune reconstitution induced by ART can worsen *P. jirovecii* pneumonia. Especially in severe *P. jirovecii* pneumonia requiring ECMO support, *P. jirovecii* activity is considered to be very high. Furthermore, as IRIS has been thought to cause deterioration in some cases, we believe it is more effective and safer not to start ART until patients recover to the point where they have sufficient spontaneous oxygenation and ventilation.

CONCLUSION

VENO -venous ECMO achieved a favorable outcome in an HIV/AIDS patient with severe acute respiratory distress syndrome. Post-ECMO ART is likely a key factor for success when treating severe respiratory infection in HIV/AIDS patients requiring ECMO support.

ACKNOWLEDGMENTS

THE AUTHORS ARE grateful to Professor Shiro Mishima from Tokyo Medical University of Emergency and Critical Care Medicine for his instruction and inspiring guidance.

DISCLOSURE

Approval of the research protocol: Ethical approval to report this case was not required.
Informed consent: Written, informed consent was obtained from the patient for publication of this case report and any accompanying images.
Registry and the registration no. of the study/trial: N/A.
Animal studies: N/A.
Conflict of interests: None.

REFERENCES

1 elso.org [homepage on the internet]. ECLS Registry Report (January 2017). [cited 29 Jul 2017]. Available from: https://www.elso.org/Registry/Statistics/InternationalSummary.aspx.

2 Gutermann H, van Roy B, Meersseman W, Meyns B, Herijgers P. Successful extracorporeal lung assistance for overwhelming pneumonia in a patient with undiagnosed full blown AIDS–a controversial therapy in HIV-patients. Thorac. Cardiovasc. Surg. 2005; 53: 252–4.

3 Steppan J, Sikazwe I. Extra-corporeal membrane oxygenation in an adult with severe pneumocystis pneumonia [Abstract]. Baltimore (MD): American College of Physicians Meeting, 2009.

4 Goodman JJ, Goodman LF, Sarvepalli SK, Firstenberg MS, Lustberg ME, Bazan JA. Extracorporeal membrane oxygenation as adjunctive therapy for refractory hypoxemic respiratory failure in HIV-positive patients with severe Pneumocystis jirovecii pneumonia. Clin. Pulm. Med. 2013; 20: 117–20.

5 Samalavicius R, Serpytis M, Ringaitiene D *et al.* Successful use of extracorporeal membrane oxygenation in a human immunodeficiency virus infected patient with severe acute respiratory distress syndrome. AIDS Res. Ther. 2014; 11: 37.

6 De Rosa FG, Fanelli V, Corcione S *et al.* Extra Corporeal Membrane Oxygenation (ECMO) in three HIV-positive patients with acute respiratory distress syndrome. BMC Anesthesiol. 2014; 14: 37.

7 Cawcutt K, Gallo De Moraes A, Lee SJ, Park JG, Schears GJ, Nemergut ME. The use of ECMO in HIV/AIDS with Pneumocystis jirovecii Pneumonia: a case report and review of the literature. ASAIO J. 2014; 60: 606–8.

8 Simpson T, Haidari G, Barrett N *et al.* Severe respiratory failure, extra-corporeal membrane oxygenation and human immunodeficiency virus: a single centre case series. Conference: 14th European AIDS Conference, Brussels, Belgium. [cited 29 Jul 2017]. Available from: https://www.researchgate.net/publication/276887672_Severe_respiratory_failure_extracorporeal_membrane_oxygenation_and_human_immunodeficiency_virus_a_single_centre_case_series.

9 Horikita S, Sanui M, Fujimoto Y, Lefor AK. Successful repeat ECMO in a patient with AIDS and ARDS. BMJ Case Rep. 2017;. https://doi.org/10.1136/bcr-2017-219870.

10 Ali HS, Hassan IF, George S. Extra corporeal membrane oxygenation to facilitate lung protective ventilation and prevent ventilator-induced lung injury in severe pneumocystis pneumonia with pneumomediastinum: a case report and short literature review. BMC Pulm. Med. 2016; 16: 52.

11 Nippon Medical University Surgical ICU series. [cited 29 Jul 2017]. Available from: square.umin.ac.jp/jrcm/pdf/ecmo/ecmotext04.pdf.

12 elso.org. [homepage on the internet]. ELSO Guidelines General v 1.3. [cited 27 Jul 2017]. Available from: https://www.elso.org/Resources/Guidelines.aspx.

13 Boonsarngsuk V, Sirilak S, Kiatbonsri S. Acute respiratory failure due to Pneumocystis pneumonia: outcome and prognostic factors. Int. J. Infect. Dis. 2009; 13: 59–66.

14 Schmidt M, Bailey M, Sheldrake J *et al.* Predicting survival after ECMO for severe acute respiratory failure: the respiratory ECMO Survival Prediction (RESP)-Score. Am. J. Respir. Crit. Care Med. 2014; 189: 1374–82.