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ECMO Support in HIV/AIDS with Pneumocystis Jirovecii Pneumonia: A Case Report and Short Review

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Case report

Keywords: PJP,ARDS, HIV, ECMO,Post-ECMO ART.

Posted Date: June 17th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-608244/v1

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Abstract

Background

We report a case of a patient with novel human immunodeficiency virus (HIV) and Pneumocystis jirovecii pneumonia (PJP) was successfully treated with veno-venous (V-V) ECMO owing to refractory hypoxemia and pneumomediastinum, and eventually discharged. In addition to the case report, several previous reports were reviewed for the discussion of some key therapies.

Case report:

A 30-year-old male patient was admitted to the our hospital presented with the shortness of breath. The patient showed a deteriorated oxygenation due to increasing pulmonary infiltrates and development of pneumomediastinum, necessitating ECMO. The diagnosis of ARDS, HIV, PJP was made. Trimethoprim/sulfamethoxazole (TMP/SMX) was provided for the treatment of PJP. After 7 days of ECMO therapy, the patient was successfully decannulated and eventually discharged.

Conclusions

ECMO may benefit adult patients with HIV/AIDS and refractory hypoxemia due to severe PCP. Post-ECMO antiretroviral therapy could improve outcomes.

Background

Acute respiratory failure (ARF), caused by *pneumocystis jirovecii* pneumonia (PJP), is the major cause of hospitalization in patients with human immunodeficiency virus (HIV)[1]. PJP is a serious HIV complication, carrying a mortality rate of 43%, and a critical need for mechanical ventilation (MV) [2].

Extracorporeal life support (ECLS) is a useful salvage therapy approach for treating severe acute respiratory distress syndrome (ARDS) in patients fail to respond to MV[3,4]. Till date, the Extracorporeal Life Support Organization (ELSO) has not offered any absolute contraindications to extracorporeal membrane oxygenation (ECMO). However, ECMO is typically avoided in HIV/AIDS patients, due to poor outcomes and absence of obvious clinical guidelines for HIV-infected or AIDS patients. However, emerging evidences demonstrated the successful usage of ECMO in HIV-positive patients with ARF and PJP infection. The development of highly active antiretroviral therapies (HAART) contribute to the significant prolongation of life expectancy of HIV-infected patients[5,6]. Therefore, now, there is a growing interest in ECLS usage for ARF therapy in HIV patients.

Herein, a HIV-infected patient with ARDS, complicated by PJP, was effectively treated with veno-venous (VV) ECMO. Meanwhile, a literature review was performed to discuss the major therapeutic factors, such as MV parameters, ECMO requirements, and duration of highly active antiretroviral therapy (HARRT).

Case Presentation

A male, aged 30 years, with height 170cm and weight 65kg, and no previous history of severe illness, visited the Emergency Department of our hospital in June 2020 for treatment of worsening shortness of breath for one week, fever (> 40°C), and productive cough. Laboratory examination revealed significant alterations in hemoglobin (9.6 g/dL), hematocrit (28.8%), and lymphocyte (0.8 g/L) levels. Moreover, diffused ground glass bilateral opacities (DGGBO) were observed on chest X-ray. Hence, the patient was hospitalized at our care center.

During hospitalization, the patient received oxygen supplementation via nasal cannula at 3 L/min, conservative fluid management, and empirical antibiotic treatment with piperacillin/tazobactam, yet there was no amelioration of respiratory status. Considering the aggravation of respiratory function, on the 3nd day after hospitalization, the patient was provided with non-invasive positive pressure ventilation (NPPV) to sustain arterial oxygen saturation. On Day 5 after admission, the patient exhibited further deterioration in respiratory status (respiratory rate of 40 breaths/min; PaO_2 of 50 mmHg on FiO_2 of 0.6). Thus, the patient was moved to the intensive care unit (ICU) and was provided with endotracheal intubation with MV support. Computerized tomography (CT) (Fig. 1) scan of the chest revealed DGGBO with massive basal consolidation and mediastinal emphysema.

Despite optimal sedation, analgesia, and neuro-muscular paralysis, adequate oxygen was not achieved with lung protective ventilation and the patient developed hypoxia refractory to MV. The PaO_2/FiO_2 was 73.70 mm Hg on 100 % of FiO_2 and 10 cm H_2O of positive end-expiratory pressure (PEEP).

A therapy decision of using V-V ECMO was made considering the value of PaO_2/FiO_2 of < 80 mmHg on 100% of FiO_2 and to enable lung protective ventilation, stop progression of mediastinal emphysema and maintain arterial oxygen saturation. A 23 French drainage cannula was placed percutaneously into the inferior vena cava via the femoral approach and another 19 French return cannula was positioned inside the right internal jugular vein. Subsequently, the patient was started on a circuit flow of 4.5 L/min and sweep gas of 4.0 L/min of oxygen (FiO_2 of 100%). Moreover, MV was replaced with ultra-protective strategy using Pressure Control Ventilation (Table 1).

Table 1
Ventilator and ECMO parameters

	Pre-Intubation	Post-Intubation	ECMO introduced							Decannulated
			ECMO Day1	ECMO Day2	ECMO Day3	ECMO Day4	ECMO Day5	ECMO Day6	ECMO Day7	
mode	NPPV	PCV	PCV	PCV	PCV	PCV	PSV	PSV	PSV	PSV
PIP		38	27	22	20	15	15	15	15	15
PEEP	6	10	7	6	6	6	6	6	6	6
FiO2	0.6	1.0	0.4	0.4	0.3	0.3	0.3	0.35	0.35	0.35
RR	40	35	14	12	12	12	12	12	20	22
Blood Flow			4.5	4.10	3.87	3.77	3.63	3.65	3.58	
Sweep Flow			4.0	4.0	4.0	4.0	4.0	4.0	0	
pH	NR	7.33	7.39	7.44	7.47	7.42	7.44	7.48	7.47	7.46
PaO_2	NR	73.70	89.40	73.70	72.0	115	132	137.50	135.20	113.20
$PaCO_2$	NR	45.80	43.50	44.10	37.1	40.8	41.8	42.20	40.10	34.20

Note: ECMO = Extracorporeal membrane oxygenation; NPPV = Non-invasive positive pressure ventilation; PCV = Pressure control ventilation; PSV = Pressure support ventilation; PIP = Peak Inspiratory Pressure (cm H_2O); PEEP = Positive End Expiratory Pressure ((cm H_2O); NR = not recorded;

The patient was suspected to have HIV infection on admission, owing to a positive HIV antigen–antibody screening test. This was further verified with CD4 + T-cell count of 8 cells/L and an HIV viral load of 405,000 copies/mL. Simultaneously, three pathogens were found using next-generation sequencing (NGS) in the bronchoalveolar lavage fluid (BALF), namely, *Pneumocystis jirovecii*, *Human betaherpesvirus 7*, and *Acinetobacter baumannii*. The patient was treated for PJP with Trimethoprim/sulfamethoxazole (TMP/SMX). In addition, the patient received methylprednisolone at a daily dose of 80mg.

In time, the chest X-ray and arterial blood gas analysis demonstrated amelioration of the respiratory symptoms and a successful decannulation was performed 7 days after VV ECMO support. The following day, the patient was weaned off of ventilator support. 13 days after decannulation, ART was adopted for the patient after successful therapeutic regimens to prevent immune reconstitution inflammatory syndrome (IRIS). Eventually, the patient was discharged from the hospital 13 days after the withdrawal of ECMO (a total of 25 days after admission).

Discussion

In this study, ECMO was adopted successfully in a patient with ARF and PJP infection, with newly diagnosed AIDS. The course of the patient highlighted some important therapeutic factors.

VV ECMO is a last effort treatment for patients with severe ARDS, who no longer respond to MV [4.7]. Despite no description of absolute contraindications in ELSO guidelines to ECMO, treatment of HIV/AIDS patients with VV ECMO may be controversial, owing to the uncertainties regarding HAART efficacy and high mortality rate. Limited reports exist on ECMO therapy in treating ARF in patients with PJP and HIV/AIDS. However, the reported discharge rate of these patients were comparable to other patients receiving V-V ECMO (Table 2).

Table 2
Adult patients with HIV/AIDS and severe Pneumocystis jirovecii pneumonia requiring ECMO therapy

Authors	Year	Age	CD4 (cells/mm^3)	HIV viral load (copies/mL)	Air leak syndrome	Type of ECMO	Timing of HAART initiation (Pre-, On-, Post-ECMO)	Pre-ECMO invasive ventilation (days)	Duration of ECMO (days)	Outcome
Gutermann. et al[8]	2005	55/M	9	80,235	No	VA	Post	4	4	Survived to hospital discharge
Stepan. et al[9]	2009	39/M	69	6,297	No	VV	Pre	8	14	Died on ECMO
Goodman. et al[10]	2013	25/M	36	622,234	No	VV	Pre	NR	69	Died on ECMO
Goodman. et a[10]	2013	30/F	13	976,631	Pneumomediastinum (Pre-ECMO)	VV	Post	3	7	Survived to hospital discharge
De Rosa. et al[11]	2014	21/F	2	118,330	Pneumomediastinumand Subcutaneous emphysema (Pre-ECMO)	VV	NR	NR	20	Survived to hospital discharge
De Rosa. et al[11]	2014	24/M	3	50,728	No	VV	On	NR	24	Died in hospital post ECMO
Cawcutt. et al[12]	2014	45/M	33	113,000	bilateral pneumothoraces (Post-ECMO)	VV	Pre	NR	57	Died in hospital post ECMO
Ali. et al[13]	2016	26/M	84	907,302	Pneumomediastinum (Pre-ECMO)	VV	Post	1	6	Survived to hospital discharge
Guedes. et al[14]	2016	65/F	9	4,050,000	No	VV	Post	13	10	Alive 6 mo after DFH
Park. et al [15]	2016	59/M	89	442,000	No	VV	Pre	NR	5	Survived to hospital discharge
Horikita.et al[16]	2017	23/M	8.5	550,000	No	VV	On	3	26	Survived to hospital discharge
Simpson. et al[17]	2017	35/M	NR	1,269,866	No	NR	NR	7	27	Survived for 6months
Lee. et al[18]	2017	54/F	12	1,075,072	right pneumothorax (Post-ECMO)	VV	On	10	33	Survived to hospital discharge
Hernandez Conte AT. et al[19]	2018	29/M	4	131,000	pneumomediastinum and left pneumothorax (Pre-ECMO)	VV	Pre	2	19	Survived to hospital discharge
Obata. et al[20]	2018	47/M	6	140,000	No	VV	Post	5	19	Survived to hospital discharge

Authors	Year	Age	CD4 (cells/mm^3)	HIV viral load (copies/mL)	Air leak syndrome	Type of ECMO	Timing of HAART initiation (Pre-, On-, Post-ECMO)	Pre-ECMO invasive ventilation (days)	Duration of ECMO (days)	Outcome
Capatos. et al[21] (15 cases)	2018	39	19.5	190,574	NR	NR	NR	NR	12	60% Survived to hospital
Morley.et al[22]	2018	33/M	133	83,000	bilateral pneumothoraces (Before ECMO)	VV	Pre	5	21	Survived to hospital discharge
Rilinger. et al[23] (6 cases)	2019	36.8 ± 9.7	NR	NR	NR	NR	NR	9.3 ± 6.5	13.8 ± 11.0	50% Survived to hospital discharge
Waqas. et al[24]	2020	40/F	40	59737	Rihgt sides pneumorhorax (Before ECMO)	VV	Pre	18	8	Survived to hospital discharge
Celesia. et al[25]	2020	43/M	10	469654	No	VV	NR	NR	12	Survived to hospital discharge
Our report	2020	30/M	8	405,000	Pneumomediastinum (Pre-ECMO)	VV	Post	1	7	Survived to hospital discharge

Note: ECMO = Extracorporeal membrane oxygenation; F = female; M = male; HAART = highly active antiretroviral therapy; NR = not recorded; VA = veno-arterial; VV = veno-venous

In all published cases, patients received V-V ECMO for ARF, except for a case in the Gutermannet et al [8] study, who was given VA ECMO therapy after cardiac arrest. The timing of V-V ECMO in ARF is still under debate. According to past reports, ECMO initiation within 7 days of MV is highly effective, as recommended by the ELSO guideline and Respiratory ECMO Survival Prediction (RESP) score [26]. The only criteria that is contraindicated for this therapy was reported in the CESAR trial, and it was high pressure (> 30 cm H_2O of peak inspiratory pressure) and/or high FiO_2 (> 0.8) ventilation > 7 days [7].

As for the timing of ECLS initiation in PJP, Goodman [10] reported that apart from higher survival rates, the early usage of ECMO during the course of MV can result in a shorter duration of ECMO support in patients. Similarly, Obata [20] also reported that early ECMO introduction can produce early achievement of lung rest management. Capatos G[21] suggested an approach of early ECLS introduction in ARDS patients with AIDS. He proposed that if patients fail to respond to MV, they should be placed on ECLS within 24 hours, without delay. In this case, the duration between MV and ECMO was minimal and this could have contributed to the enhanced clinical outcome of our patient.

PJP infections often produce airflow constriction, due to cyst formation and pneumotoceles, which, when ruptured, can cause air leak syndrome. In the Table 3, 9 out of 19 patients had developed pneumothorax or pneumomediastinum, which deteriorated the respiratory failure, necessitating ECMO. In contrast, ECMO facilitates a decrease in mean airway pressure and respiratory rate, which reduces barotrauma and accelerates lung rest management, is highly beneficial in patients with PJP. Therefore, early introduction of ECMO is advantageous and should be considered in such patients.

As shown in Table 2, all cases who received post-ECMO ART Survived to hospital discharge, whereas 3/7 of the patients with pre-ECMO ART died. Notably, ART inhibits HIV replication, and may produce immune reconstitution inflammatory syndrome [27], which can worsen PJP, particularly in those requiring ECMO support. In this regard, post-ECMO ART is an effective candidate for ARDS therapy in HIV/AIDS patients with PJP.

Conclusions

Early ECMO introduction and aggressive mobilization on ECLS may benefit adult HIV/AIDS patients with refractory hypoxemia owing to acute PJP. Additional investigations are warranted to explore approaches that improve ECMO therapy in these patients.

Declarations

Ethics approval and consent to participate

The patients signed the informed consent form to participate in this study and allow the publication of the results.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that there have no conflicts of interests.

Funding

Not applicable

Authors' contributions

All authors contributed to the study conception and design.ALL were leading members of ECMO team and were responisble for ECMO care during treatment in ICU. JLL and KH were were responsible for main treatment during patients stay in ICU. JLL and YFL were responsible for data collection, analysis and drafting the manuscript.KH and ALL reviewed manuscript. All authors read and approved the final manuscript.

Acknowledgements

The authors thank all medical staff for their important contributions to the care of the patient.

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Table 3

Table 3 is not available with this version

Figures

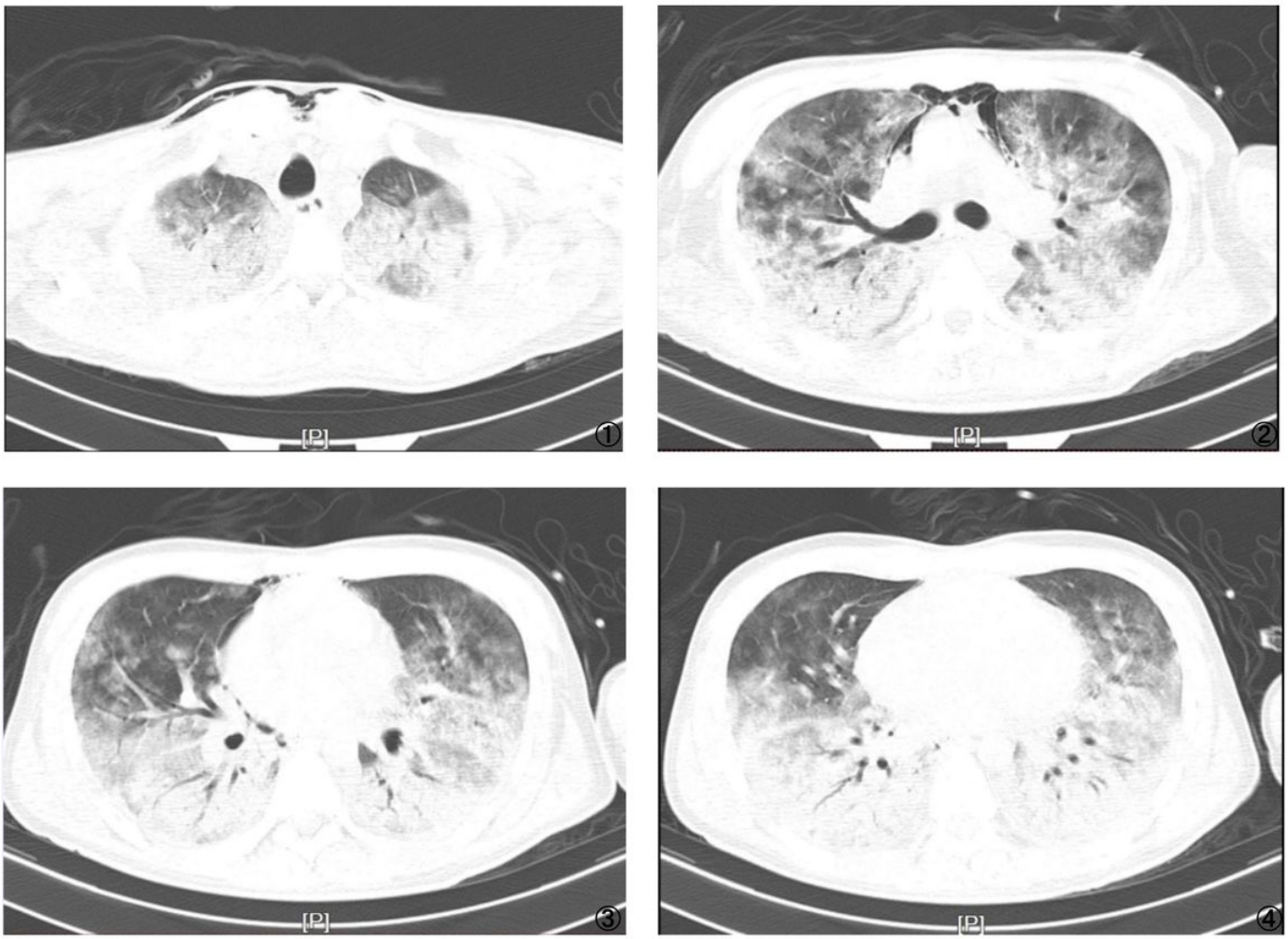

Figure 1

CT scan of the patient.□lung apices □level of bifurcation of carina. □and□lung bases. CT scan showed bilateral diffuse ground glass opacities with extensive basal consolidation. Pneumomediastinum: air in the anterior mediastinum.