A patient with leptospirosis associated severe pulmonary haemorrhagic syndrome successfully managed with Extra Corporeal Membranous Oxygenation

Palliyaguruge NU, Egodage UK, Gunasinghe G, Harischandra DVT, Weerakoon RR

Teaching Hospital Karapitiya, Galle, Sri Lanka.

Correspondence: Dr. NU Palliyaguruge
e-mail: nupalliyaguruge@gmail.com

<https://orcid.org/0000-0002-3912-3273>

Introduction

Leptospirosis is a zoonosis caused by *Leptospira interrogans*. Severe pulmonary haemorrhagic syndrome (SPHS) is the major cause of mortality in leptospirosis (1). Incidence of pulmonary haemorrhages in leptospirosis varies from 20 – 70% of patients (2). Contemporary theory suggests the pathogenesis of SPHS is immune mediated (1). Membranous depositions of linear immunoglobulins (IgA, IgG, IgM) and complement on alveolar surface may trigger fatal pulmonary haemorrhage (1). Here we describe a case of SPHS successfully managed with Veno-Venous Extra Corporeal Membranous Oxygenation (V-V ECMO) at Teaching Hospital Karapitiya.

Case report

A previously well, 48 year-old mason was transferred from a local hospital for the management of fever of 5 day duration. In addition, he had arthralgia, myalgia and reduced urine output for 12 hours. He did not have haemoptysis, cough, or shortness of breath. He gave a history of exposure to mud prior to the onset of fever. Examination revealed generalized muscle tenderness, conjunctival injection, icterus, pulse rate of 122 bpm, blood pressure of 90/60 mmHg, and respiratory rate of 26 cycles per minute. SaO₂ on room air was 100%. There was vesicular breathing and occasional scattered fine crepitations over both lung fields. Investigation findings are summarized in table 1.

Table 1: Lab findings of the patient on admission

Investigation	Result
WBC	7750 /μL
Neutrophil	86.2%
Platelets	21000 /μL
CRP	299 mg/dL
Blood urea	87 mg/dL
Serum creatinine (SCr)	195 μmol/L
Serum sodium	135 mmol/L
Serum potassium	2.2 mmol/L
Total bilirubin	157 μmol/L
Direct bilirubin	127.5 μmol/L
UFR	red cells 4 - 6/hpf

ABG: pH 7.48; PCO₂ 30 mmHg; PO₂ 72 mmHg. Chest radiograph was normal. Bedside ultrasound scan showed no free fluid or B lines but collapsible inferior vena cava. A presumptive diagnosis of leptospirosis complicated with acute kidney injury, septic shock and possible pulmonary haemorrhages was made. Intravenous (IV) benzylpenicillin 2 MU 6 hourly and oral doxycycline 100mg 12 hourly were started. IV noradrenaline infusion was started because blood pressure did not improve with adequate fluid resuscitation. IV methylprednisolone 1g daily, IV tranexamic acid 1g 8 hourly and tranexamic acid nebulizations 8 hourly were also started suspecting pulmonary haemorrhages. Platelets were transfused to maintain platelet count > 50,000/μL. Within next 12 hours patient became

more tachypnoeic and bilateral end inspiratory fine crepitations became more prominent. He needed O₂ via nasal prongs. Repeat chest radiograph showed bilateral diffuse alveolar infiltrates suggestive of pulmonary haemorrhages (Figure 1).

Figure 1: Chest radiograph; bilateral diffuse alveolar infiltrates suggestive of pulmonary haemorrhages.

Figure 2: Chest radiograph; worsening pulmonary haemorrhages diffusely involving all zones of bilateral lung fields

Total plasma exchange (TPE) was started after a multidisciplinary team discussion among medical team, nephrologist and transfusion physician. The patient was transferred to medical ICU and CPAP was started. Bilateral alveolar infiltrates increased (Figure 2), haemoglobin dropped (10.4g/dL) and ABG deteriorated indicating worsening pulmonary haemorrhages.

Despite optimizing CPAP settings patient further deteriorated and we had to intubate him on the 3rd day of admission. Bronchoscopy showed blood clots in the bronchial tree. On the 4th day respiratory acidosis worsened (Figure 3) and Murray's acute lung injury score was 3. The patient was referred to cardiothoracic surgeon for ECMO. V-V ECMO was instituted via 20 Fr and 28 Fr percutaneous single lumen cannulae inserted into right internal jugular vein and right femoral vein respectively. ECMO settings are summarized in table 2. Activated partial thromboplastin time was maintained between 190 – 210 seconds with IV heparin infusion. During ECMO, mechanical ventilation was set at the lung rest settings. IV noradrenaline infusion titrated to maintain mean arterial pressure around 80 mmHg and gradually weaned off. IV ceftriaxone 1g 12 hourly was added. Fever and inflammatory markers improved with treatment and serum creatinin became normal on the 5th day. IV immunoglobulin 0.4 g/kg daily was given after each plasmapheresis. Methylprednisolone and immunoglobulin were omitted after completing 5 doses.

Alveolar infiltrates in chest radiograph started to improve on the 7th day of admission (Figures 4 & 5).

Tidal volume improved from 240 ml to 419 ml. Since chest radiograph, ABG and ventilator support gradually improved, trial off ECMO was performed. Oxygen flow through oxygenator was stopped at the 114th hour. Since the trial off was successful, decannulation of ECMO was done at the 143rd hour i.e.; 10th day after admission.

The patient was extubated on the 14th day and discharged from the hospital 8 days later. Pulmonary infiltrates were totally cleared from chest x-ray on discharge.

Table 2: ECMO settings

ECMO day	1	2	3	4	5	6
Flow (L/min)	4.8	5.0	4.65	4.93	3.8	3.2
Gas Flow (L/min)	5	10	11	12	4	2
Motor RPM	4000	4000	3800	3500	3400	3200

Figure 3: Graphic presentation of ABG values **Figure 3 & 4:** Chest radiographs disappearance of pulmonary infiltrates

The patient received a total of 7 packs of red cell concentrate and 34 packs of platelet concentrate. He never needed renal replacement therapy. ECG, troponin I and 2D Echocardiogram did not show features of myocarditis. MAT on days 10 and 24 after the onset of symptoms showed a fourfold or higher increase in antibody titres for *Leptospira interrogans* serovars Australis, Bangkinang, Bakeri, Cynopteri, and Patoc, confirming the diagnosis of leptospirosis. Lung function test performed 2 months after discharge was normal.

Discussion

Progressive lung injury increases the demand of pressure support which may in turn cause barotrauma and ventilator induced lung injury (7) leading to a vicious cycle. In addition high levels of PEEP may cause reduction in cardiac output and blood pressure (8). High-frequency oscillatory ventilation has been used to treat SPHS successfully when the response to maximal support with conventional mechanical ventilation (CMV) was poor. But the disadvantage was associated significant haemodynamic instability (3). ECMO is an alternative treatment which uses cardio-pulmonary bypass technology to temporarily provide gas exchange (9). There are several case reports where SPHS was successfully treated with V-V ECMO (4-6). In our case we initiated V-V ECMO on the 8th day of illness, continued for 6 days and were able to extubate 4 days after the decannulation.

In conclusion, we suggest that V-V ECMO can be used as a treatment option for patients with leptospira SPHS and poorly responding to CMV. Since SPHS leading to ARDS is the major cause of death in leptospirosis, ECMO should be considered early when it is difficult to maintain oxygenation with CMV.

Acknowledgements

Authors gratefully acknowledge Dr. R. K. Firmin who shared his knowledge and experience in managing this patient and preparing the case report.

References

1. J Crodaa, Netoa, RA Brasila, C Pagliaria, AC Nicodemob, MIS Duartea. Leptospirosis pulmonary haemorrhage syndrome is associated with linear deposition of immunoglobulin and complement on the alveolar surface. *Clinical Microbiology and Infection*, 2010; **16**(6): 593-9.
2. Carvalho CR, Bethlem EP. Pulmonary complications of leptospirosis. *Clin Chest Med*, 2002; **23**(2): 469-78.
3. Nor MBM, Md Ralib A, Ibrahim NA, Abdul-Ghani MR. High frequency oscillatory ventilation in leptospirosis pulmonary haemorrhage syndrome: A case series study. *Indian Journal of Critical Care Medicine*, 2016; **20**(6): 342-8.
4. Nao Umei and Shingo Ichiba. A Case of Leptospirosis - associated severe pulmonary haemorrhagic syndrome successfully treated with venovenous extracorporeal membrane oxygenation. *Case Reports in Critical Care*, 2017; 5369267.
5. Liao CY, Ben RJ, Wu HM, *et al.* Acute respiratory distress syndrome manifested by leptospirosis successfully treated by extracorporeal membrane oxygenation (ECMO). *Internal Medicine*, 2015; **54**(22): 2943-6.
6. Arokianathan D, Trower K, Pooboni S, Sosnowski A, Moss P, Thaker H. Leptospirosis: A case report of a patient with pulmonary haemorrhage successfully managed with extra corporeal membrane oxygenation. *The Journal of Infection*, 2005; **50**(2): 158-62.
7. T Whitehead, AS Slutsky. The pulmonary physician in critical care: *Ventilator induced lung injury*. *Thorax* 2002; **57**: 635-42.
8. Thomas Luecke and Paolo Pelosi. Clinical review: Positive end-expiratory pressure and cardiac output. *Crit Care*, 2005; **9**(6): 607-21.
9. Giles J Peek, Felicity Clemens, Diana Elbourne, Richard Firmin, Pollyanna Hardy, *et al.* CESAR: conventional ventilatory support vs extracorporeal membrane oxygenation for severe adult respiratory failure. *BMC Health Serv Res*. 2006; **6**: 163.