MyJA .pub

© Malaysian Journal of Anaesthesiology 2023; 2:173-181
Case report
https://doi.org/10.35119/myja.v2i2.29

Successful utilization of blood purification therapy with Oxiris® haemofilter for the management of severe leptospirosis with multiorgan involvement: a case report

Nurul Izzah Binti **Azmi**, Shahir Asraf Bin **Abdul Rahim**, Azrina Binti **Md Ralib**

Department of Anaesthesiology and Intensive Care, Sultan Ahmad Shah Medical Centre, Kuantan, Pahang, Malaysia

Abstract

Severe leptospirosis is associated with excessive proinflammatory and anti-inflammatory cytokines that lead to multiorgan failure. Oxiris® haemofilter is a blood purification therapy that can be utilized to control these inflammatory responses during early phase of sepsis-associated acute kidney injury (AKI) that requires renal replacement therapy. We present a case of a 15-year-old male with severe leptospirosis with multiorgan involvement who was admitted to our intensive care unit (ICU). He had septic shock with myocarditis, respiratory failure, AKI with metabolic acidosis, and transaminitis. We started him on continuous veno-venous haemofiltration with the Oxiris haemofilter for metabolic acidosis and cytokine absorption for a total duration of 35 hours. A rapid decrease of vasopressor requirement, lactate, and procalcitonin levels was observed following therapy initiation. He was extubated on day 5 of ICU admission and discharged well to the general ward after 7 days in the ICU. This case highlights the potential benefits of the Oxiris haemofilter

Correspondence: Nurul Izzah Binti Azmi, Department of Anaesthesiology and Intensive Care, Sultan Ahmad Shah Medical Centre @ IIUMMC, Jalan Sultan Haji Ahmad Shah, Bandar Indera Mahkota, 25200, Kuantan, Pahang.
E-mail: drnurulizzah87@gmail.com

as an adjunct in the management of septic shock in severe leptospirosis with multiorgan involvement. Randomized clinical trials are warranted to validate the clinical benefits of this therapy.

Keywords: haemofiltration, leptospirosis, Oxiris, septic shock

Introduction

Leptospirosis is a zoonosis caused by pathogenic gram-negative spirochetes of the genus *Leptospira*. In Malaysia, the incidence of leptospirosis is increasing, with national mortality rates between 0.01 to 0.31 per 100,000 population from 2006 to 2015, as reported by the Malaysia Ministry of Health.[1]

A multicentre observational study from central Malaysia has identified lung, liver, and renal dysfunction as well as septic shock as prognostic factors of severe and fatal leptospirosis.[2] At the biochemical level, cytokine markers including tumour necrosis factor (TNF)-α, interleukin (IL)-6, and IL-10 were significantly higher in severe and fatal leptospirosis.[3] Based on this knowledge of the host immune response mechanism during sepsis, extracorporeal blood purification therapy has been proposed as an alternative treatment. Various techniques are available, including high adsorption haemofiltration such as the Oxiris® haemofilter (Baxter, Deerfield, IL, USA). In addition to renal support, this haemofilter removed cytokines, endotoxins, and inflammatory mediators.[4]

Case presentation

A 15-year-old Malay boy with underlying obesity class II presented to our emergency department with a 4-day history of fever, loose stools, vomiting, and reduced oral intake associated with abdominal pain and dry cough. Upon presentation, his blood pressure was 99/30 mmHg, pulse rate was 110 beats per minute, oxygen saturation was 99% under room air, and temperature was 37.8°C. His initial haemoglobin was 12 g/L, white blood cell count was 4.7 x 10^9 L, platelet count was 199 x 10^9 L, with evident of lymphopenia of 1.9%. As he complained of chest pain, a serial electrocardiogram was performed which showed ischemic changes. Troponin I was significantly elevated at 14,215 pg/mL. The diagnosis of leptospirosis was made based on World Health Organization Modified Faine criteria, fever, proteinuria, and epidemiological information from Pahang associated with the rainfall season. The patient had a history of swimming in the river in Kuantan, Pahang.

He was admitted that same day to the intensive care unit (ICU) for septic shock. His arterial blood gas (ABG) showed deterioration of metabolic acidosis with lactate increasing to 4 mmol/L. Hemodynamically, he was started on intravenous infusion (IVI) noradrenaline of 0.5 mcg/kg/min. In the ICU, he was intubated because of acute respiratory failure. Post-intubation, IVI vasopressin was added. He was persistently oliguric, with urine output ranging from 0.3 to 0.5 ml/kg/hr. The patient was diagnosed with septic shock secondary to possible leptospirosis with multiorgan involvement due to myocarditis, respiratory failure, AKI with metabolic acidosis, and transaminitis.

Post-intubation, the patient appeared to have pulmonary haemorrhage based on imaging, blood-stained secretion from his endotracheal tube, shortness of breath, cough, anaemia, and thrombocytopenia. The lowest platelet count was 30

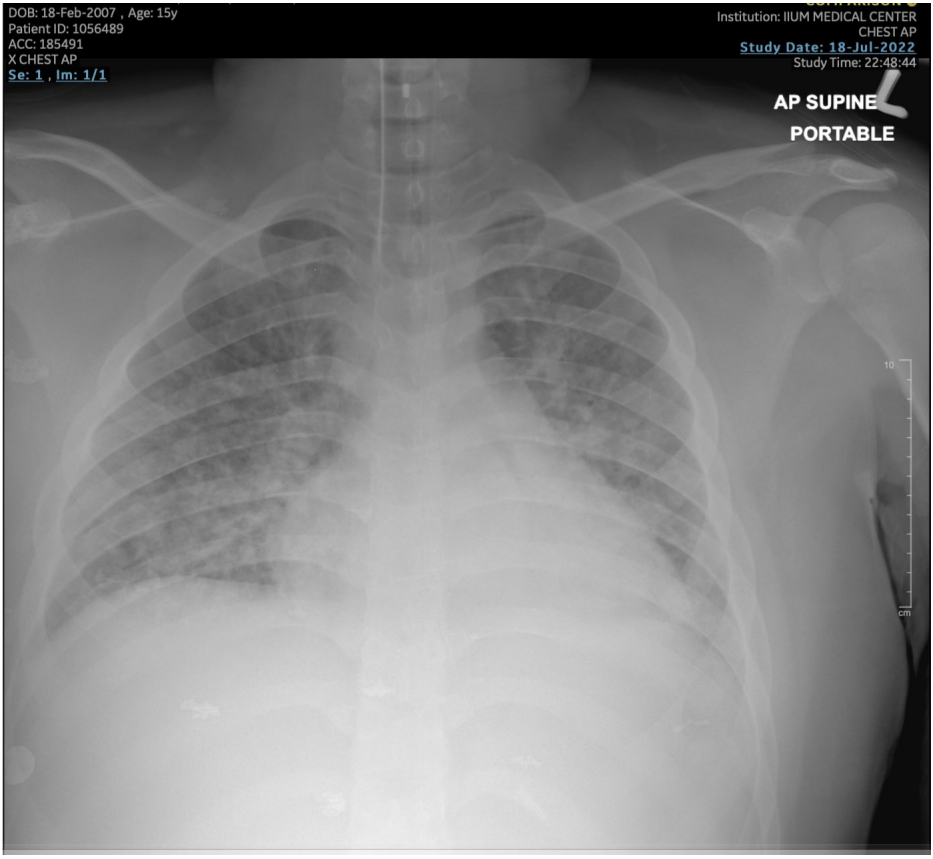

Fig. 1. Anterior-posterior view of chest radiograph post-intubation showing bilateral air space opacification with blunted left costophrenic angle on day 1 of ICU admission.

x 10^9/L. The initial ventilator setting post-intubation was FiO_2 0.6, pressure control was 16 mmHg, pressure support was 12 mmHg, positive end-expiratory pressure was 10 mmHg, and rate was 20 breaths per minute using synchronised intermittent mandatory ventilation mode. His ABG showed pH 7.182, pCO_2 51.9 mmHg, pO_2 104 mmHg, HCO_3- 17.3, BE -8.2, SPO2 96%, and lactate 3.0 mmol/L with a PaO_2: FiO_2 ratio of 173. His chest radiograph post-intubation showed bilateral air space opacification, with blunted left costophrenic angle (Fig. 1). He was empirically treated with intravenous piperacillin-tazobactam and azithromycin for severe leptospirosis and atypical pneumonia.

Continuous veno-venous hemodiafiltration (CVVH) was indicated to treat severe metabolic acidosis and initiate cytokine absorption. On the Prismaflex machine (Baxter, Deerfield, IL, USA), we initiated CVVH with the Oxiris haemofilter as a cytokine absorber at the 7th hour of ICU admission. The Prismaflex flow settings used were blood flow of 200 ml/min, pre-blood pump infusion of 1,000 ml/min, with nil pre-filter replacement flow rate, and 1,000 ml/hr of post-filter. We chose CVVH as the mode of RRT for the purpose of removing low molecular weight proteins as cytokine. After initiation of the Oxiris haemofilter, IVI noradrenaline was gradually reduced and completely stopped on day 3 of ICU admission (Fig. 2a). IVI vasopressin was stopped after 24 hours of ICU admission (Fig. 2a). Notably, the patient's lactate levels reduced significantly after initiation of the Oxiris haemofilter (Fig. 2b).

During the patient's 7-day ICU stay, the Sequential Organ Failure Assessment (SOFA) score decreased by 50%, going from 10 (upon ICU admission) to 5 (upon discharge to the ward). (Fig. 2b). A significant reduction of serum procalcitonin level from 37.6 ng/mL to 6.7 ng/mL (82% clearance) was observed after 35 hours of Oxiris initiation. We discontinued the CVVH after 35 hours due to the marked resolution of septic shock and metabolic acidosis, and recovery of kidney function. His biochemical parameters showed improvement upon discharge from ICU (Table 1). He was extubated on day 5 of the ICU stay and discharged to the ward 2 days following that.

Leptospirosis serology on day 7 of illness confirmed leptospirosis infection. On day 8 of illness, leptospirosis microscopic agglutination test was sent but the result was still pending during the patient's stay in ICU. Although laboratory confirmation of leptospirosis was not available at the time, we treated empirically for leptospirosis based on laboratory parameters. Other than thrombocytopenia, AKI, and elevation of troponin, there was evidence of transaminitis, and hyperbilirubinemia (Table 1). Dengue and malaria investigations were negative.

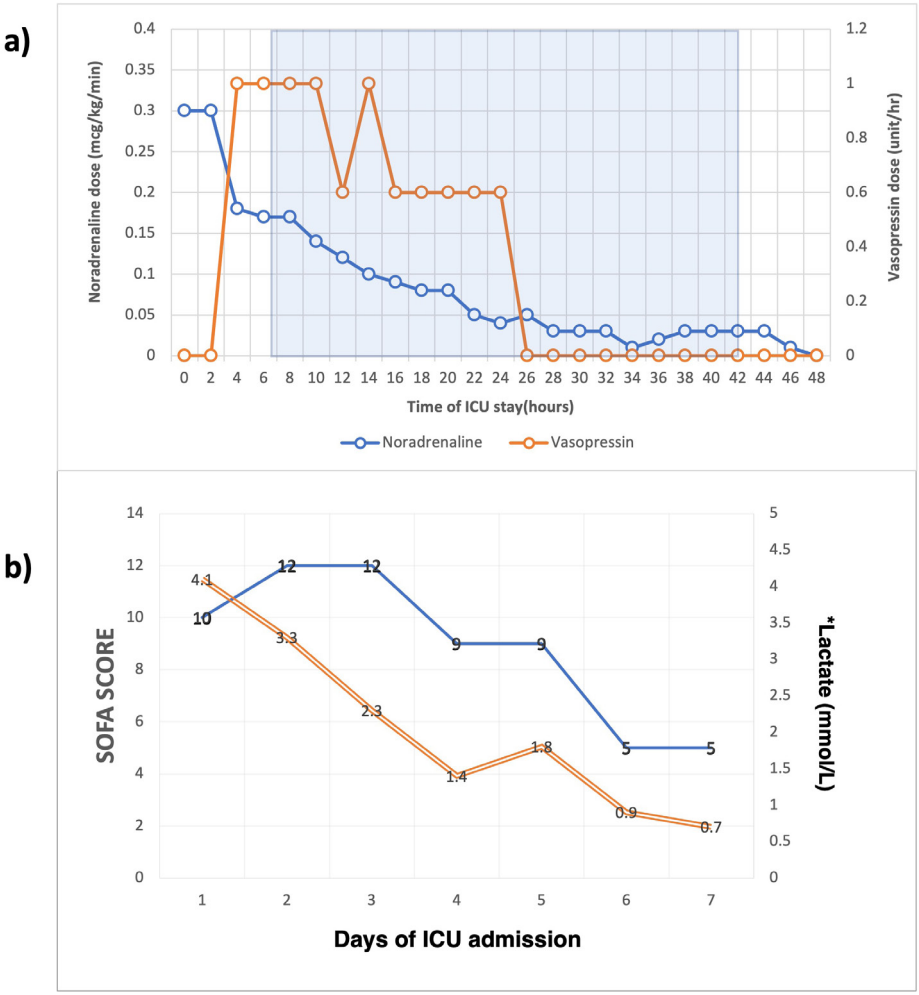

Fig. 2. (*a*) Trend of IVI noradrenaline (µg/kg/min) and IVI vasopressin (unit/hr) dose during CVVH with the Oxiris for a total duration of 35 hours (shaded). After initiation of the Oxiris haemofilter, IVI noradrenaline reduced gradually and was completely ceased on day 3 of ICU admission. IVI vasopressin was off after 24 hours of ICU admission. (*b*) Both SOFA score and lactate levels showed the same reduction trend throughout the ICU stay. The graph shows the highest lactate level from daily ABG.

Table 1. Clinical and laboratory parameters following 35 hours of Oxiris

Blood parameters	***Pre-Oxiris**	**24 hours post Oxiris**	**On day of ICU discharge**
Full blood count			
Hb, g/dL	8.6	8.6	9.0
TWC, x 10^9/L	21.0	15.8	23.2
Platelets, x 10^9/L	47.0	77.0	271.0
Renal profile			
Urea, mmol/L	16.4	20.8	11.0
Creatinine, µmmol/L	246.0	250.0	111.0
Potassium, mmol/L	3.1	3.6	4.1
Sodium, mmol/L	133.0	140.0	157.0
Urine volume, ml/24hr	895	2690.0	3770.0
Coagulation profile			
PT, s	13.0	10.9	10.6
APTT, s	34.8	26.6	25.9
INR	1.0	0.82	< 0.8
Liver function test			
AST, U/L	120.0	122.0	42.0
ALT, U/L	140.0	196.0	96.0
Bilirubin, µmol/L	85.0	197.0	139.0
Direct, µmol/L	58.5	128.6	73.7
Indirect, µmol/L	26.8	68.4	65.3
Procalcitonin, ng/mL	37.6	6.7	-

*Pre-Oxiris parameters were taken upon ICU admission
Hb: haemoglobin; TWC: total white cell, PT: prothrombin time; APTT: activated partial thromboplastin time; INR: international normalized ratio; AST: aspartate transferase; ALT: alanine transaminase; s: seconds

Discussion

To the best of our knowledge, this is the first report from Malaysia showing the successful use of the Oxiris haemofilter as an adjunct in the treatment of severe leptospirosis with multiorgan involvement. We observed rapid improvement of haemodynamic stability within 72 hours and early reduction of vasopressor dose within the first 12 hours of initiating Oxiris treatment, similar to findings in Europe.[5]

Organ function as reflected by SOFA score during ICU stay improved significantly after initiation of the Oxiris haemofilter. Our patient's highest SOFA score during the ICU stay was 12, which predicted a mortality rate as high as 80%, as reported in a previous prospective study.[6] Despite the high mortality risk, our case has shown successful intervention using CVVH with the Oxiris haemofilter, very possible due to early treatment. Broman *et al* found in their randomised crossover double-blind study that continuous renal replacement therapy (RRT) using Oxiris effectively removed endotoxins such as TNF-α, IL-6, IL-8, and interferon-α during the first 24 hours of treatment in patients with septic shock-associated AKI.[7] Mitigating the "cytokine storm" in the early phase of the illness is beneficial in preventing immunoparalysis where sepsis-associated mortality is observed.[8]

We chose the Oxiris haemofilter blood purification therapy as an adjunct in the management of septic shock with multiorgan failure in our patient for several reasons. The Oxiris haemofilter is comprised of an AN69-based membrane which can adsorb endotoxin and inflammatory mediators from the blood. This is due to the inner aspect of its membrane that is grafted with polyethyleneimine. Its unique feature includes antithrombogenic characteristics owing to its surface being pre-grafted with heparin.[4] However, this feature is a concern for patients allergic to heparin and those with heparin-induced thrombocytopenia.

Our findings may add insights on the use of the relatively new Oxiris haemofilter for RRT and multiorgan support in patients with septic shock. We believe that our patient benefited from Oxiris treatment, as its membrane filter endotoxins, which are the key component of sepsis due to gram-negative bacteria in leptospirosis. Shum *et al.* reported significant reduction of the SOFA score in 6 patients with sepsis-induced AKI due to gram-negative bacteria within the Oxiris group in comparison to the control group.[9] However, early antibiotic initiation and the young age of our patient could also be contributing factors of the marked improvement in his clinical outcomes.

The usage of Oxiris is convenient as we are familiar with conventional CVVH in our daily practice. No adverse events were observed during the treatment. However, this is a case report of a single patient, and randomized controlled trials are needed

to demonstrate its benefit in clinical practice. This is consistent with the 2021 update of Surviving Sepsis Campaign that to date, no recommendation has been made regarding the use of Oxiris.[10] A limitation of our study is that we were unable to measure the concentration of inflammatory mediators such as IL-6 and IL-10 pre- and post-initiation of Oxiris to establish a direct causal relationship.

Conclusion

Although routine usage of the Oxiris haemofilter is challenging due to its cost, its application should be explored further as it has the potential to increase survival rate and reduce morbidity in septic shock, including those from severe leptospirosis as demonstrated in our case report. Larger clinical studies are needed to establish patient selection, efficacy, and timing for initiation of blood purification therapy with the Oxiris haemofilter.

Declarations

Informed consent for publication
The authors obtained written informed consent from the patient and their next-of-kin for the publication of the images and clinical data contained in this case report.

Competing interests
Dr. Azrina Binti Md Ralib serves as Deputy Chief Editor in Malaysian Journal of Anaesthesiology. She has not been involved in any part of the publication process prior to manuscript acceptance; peer review for this journal is double blind. The remaining authors have no competing interests to declare.

Funding
None to declare.

Acknowledgements
The authors wish to acknowledge the staff in the Department of Anaesthesiology and Intensive Care at Sultan Ahmad Shah Medical Centre for the continuous support in this case report.

References

1. Abdul Wahab Z. Epidemiology and Current Situation of Leptospirosis in Malaysia Ministry of Health Malaysia. [Internet]. Persidangan Kesihatan Persekitaran Pihak Berkuasa Tempatan 2015. [cited 2022 December 20]. Available from: https://jkt.kpkt.gov.my/jkt/resources/PDF/Persidangan_2015/persidangan%20kesihatan/Leptospirosis_in_Malaysia.pdf
2. Philip N, Lung Than LT, Shah AM, Yuhana MY, Sekawi Z, Neela VK. Predictors of severe leptospirosis: a multicentre observational study from Central Malaysia. BMC Infect Dis. 2021;Dec 1;21(1).1081. https://doi.org/10.1186/s12879-021-06766-5
3. Reis EA, Hagan JE, Ribeiro GS, et al. Cytokine Response Signatures in Disease Progression and Development of Severe Clinical Outcomes for Leptospirosis. PLoS Negl Trop Dis. 2013;7(9). https://doi.org/10.1371/journal.pntd.0002457
4. Zhang L, Feng Y, Fu P. Blood purification for sepsis: An overview. Precis Clin Med. 2021 Feb 25;4(1):45-55. https://doi.org/10.1093/pcmedi/pbab005
5. Pickkers P, Vassiliou T, Liguts V, et al. Sepsis management with a blood purification membrane: European experience. Blood Purif. 2019 Apr 1;47(Suppl3):36–44. https://doi.org/10.1159/000499355
6. Ferreira FL, Bota DP, Bross A, Mélot C, Vincent JL. Serial Evaluation of the SOFA Score to Predict Outcome in Critically Ill Patients. JAMA. 2001 Oct 10;286(14):1754–1758. https://doi.org/10.1001/jama.286.14.1754
7. Broman ME, Hansson F, Vincent JL, Bodelsson M. Endotoxin and cytokine reducing properties of the oXiris membrane in patients with septic shock: A randomized crossover double-blind study. PLoS One. 2019 Aug 1;14(8). https://doi.org/10.1371/journal.pone.0220444
8. Venet F, Monneret G. Advances in the understanding and treatment of sepsis-induced immunosuppression. Nat Rev Nephrol. 2018 Feb;14(2):121-137. https://doi.org/10.1038/nrneph.2017.165
9. Shum HP, Chan KC, Kwan MC, Yan WW. Application of endotoxin and cytokine adsorption haemofilter in septic acute kidney injury due to Gram-negative bacterial infection. Hong Kong Med J. 2013 Dec;19(6):491–497. https://doi.org/10.12809/hkmj133910
10. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021 Nov 1;47(11):1181–247. https://doi.org/10.1007/s00134-021-06506-y