J Extra Corpor Technol. 2020;52:237–41
The Journal of ExtraCorporeal Technology

Case Reports

ECMO Membrane Lung Failure due to Hypertriglyceridemia: A Case Report and Review of the Literature

Jenelle H. Badulak, MD;* Eleanor Curtis, MD, MPVM;† Eileen M. Bulger, MD‡

**Department of Emergency Medicine, University of Washington School of Medicine, Seattle, Washington; †Division of Trauma, Acute Care Surgery & Surgical Critical Care, University of California Davis School of Medicine, Sacramento, California; and ‡Division of Trauma, Burn & Critical Care Surgery, Harborview Medical Center, University of Washington School of Medicine, Seattle, Washington*

Abstract: The deleterious effects of high serum lipid content on the membrane lung (ML) during extracorporeal membrane oxygenation (ECMO) are sparsely documented, and the threshold of lipemia-induced membrane failure is poorly described. We present a case of a patient on venovenous ECMO who developed ML failure after 7 days due to moderate to severe hypertriglyceridemia (700–800 mg/dL). ML failure was exhibited by impaired gas exchange and high transmembrane pressures, and there was notable lipemic layering in the circuit immediately after decannulation. This case demonstrates that in addition to patients with extreme lipemia, ML failure can also occur in patients with moderate to severe hypertriglyceridemia. Hypertriglyceridemia should be suspected in patients with high transmembrane pressures and ML failure not attributable to thrombosis, and these patients may require frequent ML changes if a prolonged ECMO run is required. **Keywords:** ECMO, VV ECMO, ECLS, membrane lung failure, oxygenator failure, hypertriglyceridemia, lipid, lipemia. *J Extra Corpor Technol. 2020;52:237–41*

Lipemia is known to cause membrane lung (ML) dysfunction during extracorporeal membrane oxygenation (ECMO); however, the published in vivo experience is small, and the threshold at which ML failure occurs is unknown (1–5). Lipemia can be due to parenteral infusions of lipids as well as hereditary and acquired causes, such as ethanol ingestion, poorly controlled diabetes, nephrotic syndrome, beta-blockers, antiretrovirals, and immunosuppressants. The following report will detail a case of ML failure due to moderate to severe hypertriglyceridemia thought secondary to hereditary dyslipidemia. We will also review the current state of the literature for lipemia-induced ML failure.

Received for publication April 25, 2020; accepted August 3, 2020.
Address correspondence to: Jenelle H. Badulak, MD, Acting Assistant Professor, University of Washington, 328B NW 41ST ST, Seattle, WA 98107. E-mail: badulakj@uw.edu
The senior author has stated that the authors have reported no material, financial, or other relationship with any healthcare-related business or other entity whose products or services are discussed in this paper.

DESCRIPTION

A 22-year-old previously healthy man suffered a motor vehicle collision and was found to have multiple injuries including subdural hematoma, subarachnoid hemorrhage, skull fracture, blunt aortic injury with pseudoaneurysm, bilateral hemopneumothorax, left diaphragmatic rupture, grade 5 splenic injury, grade 3 renal injury, grade 3 liver injury, and pneumoperitoneum. There were no long-bone fractures. Shortly after arrival to the emergency department, the patient was taken urgently to the operating room where he underwent exploratory laparotomy, diaphragmatic repair, splenectomy, bilateral tube thoracostomy, thoracic endovascular aortic repair, and temporary abdominal closure. On arrival to the intensive care unit, an intracranial pressure monitor was placed to guide management of intracranial hypertension. He returned to the operating room 48 hours after laparotomy for abdominal washout and closure and was noted to have pancreatic contusions. Lipase levels were initially elevated 1,200 U/L on admission because of pancreatic injury but decreased to 200 U/L on hospital day 3.

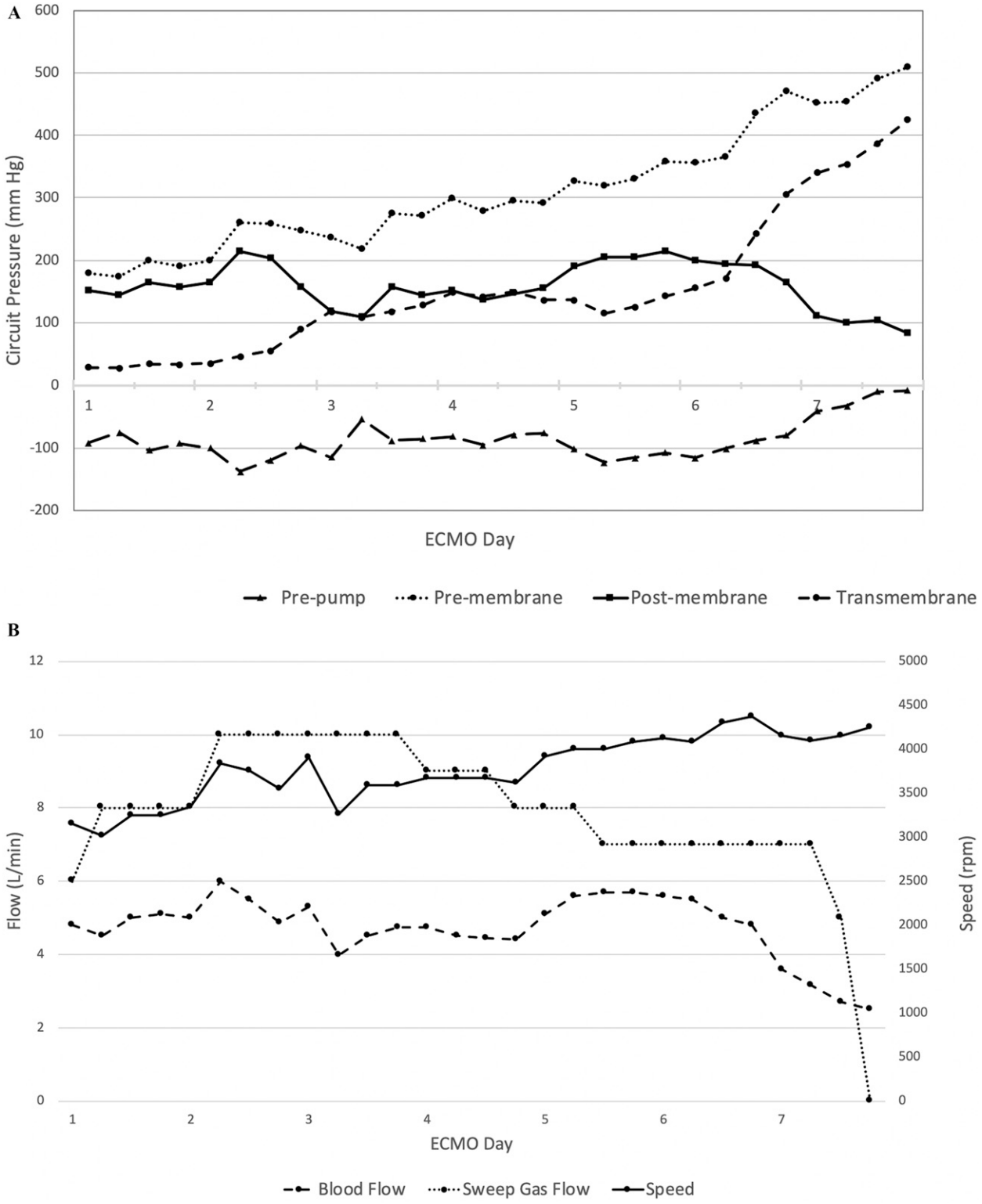

Figure 1. (A) Circuit pressures throughout the ECMO run. (B) Speed, blood flow, and sweep gas flow rate throughout the ECMO run.

Within 24 hours of abdominal closure (hospital day 3), he developed severe acute respiratory distress syndrome due to *Enterobacter cloacae* pneumonia. He was managed with sedation, positive end-expiratory pressure (PEEP) optimization, neuromuscular blockade, and inhaled epoprostenol. Despite these interventions, his hypoxemia continued to worsen, and on hospital day 9, he was emergently cannulated for venovenous ECMO using the

Cardiohelp™ (Maquet, Wayne, NJ) system. Pre-cannulation ventilator settings were volume control 4.5 cc/kg (ideal body weight), respiratory rate 35/min, PEEP 14 cm H_2O, FiO_2 100%, and plateau pressure 35 cm H_2O. Arterial blood gas showed pH 7.23, $PaCO_2$ 66 mmHg, with P:F 62, and SpO_2 nadir 79%.

After initiation on the ECMO circuit, the patient was transitioned to "rest" ventilator settings: pressure control, PEEP 10 cm H_2O, driving pressure 10 cm H_2O, respiratory rate 10/min, and FiO_2 40%. Initial circuit settings included ECMO blood flow 4.5–5.5 L/min, FdO_2 (fractional delivered oxygen percentage of sweep gas) 100% achieving SpO_2 92–100% with pre-membrane O_2 saturation 60% and sweep gas flow rate 8 L/min targeting normal pH. Triglycerides were noted to be elevated at 667 mg/dL on the day of cannulation; therefore, propofol infusion was stopped. Over the next 5 days, the transmembrane pressure gradually increased, requiring increased speed, revolutions per minute (RPM), to maintain blood flow (Figure 1).

On ECMO day 7 (hospital day 15), the transmembrane pressure increased dramatically (peak 428 mmHg) with associated flow reduction, despite increases in speed. Using FdO_2 100% and sweep gas flow rate 7 L/min, blood gases revealed pre-membrane PO_2 29 mmHg and PCO_2 57 mmHg, with post-membrane PO_2 160 mmHg and PCO_2 51. Over the next 24 hours, free hemoglobin increased from 5 to 23 mg/dL, hyperkalemia developed (5.3 mEq/L), and lactate dehydrogenase increased from 994 to 1,804 units/L, all suggesting possible hemolysis. There were no extremes of pump inlet pressures (range −150 to −50 mmHg) or post-membrane pressures (range 100–220 mmHg) during the ECMO run, and there was no circuit chatter. There were no significant clots visible on the ML (Figure 2) or elsewhere in the circuit. Anticoagulation was maintained at goal activated partial thromboplastin time (aPTT) 45–55 seconds for the duration of the run except on ECMO day 4 with a single low aPTT value of 31 seconds. Triglycerides remained elevated 808 mg/dL.

At this time, pulmonary function had significantly improved and sweep gas flow rate was weaned to zero over 4 hours with concomitant transition in ventilator settings to volume control, tidal volume 6 cc/kg (ideal body weight), respiratory rate 26/min, PEEP 10 cm H_2O, and FiO_2 40%. Arterial blood gases demonstrated adequate native lung gas exchange with a sweep gas flow rate set to zero for 4 hours, and the patient was successfully decannulated on ECMO day 7 (hospital day 15).

Shortly after the circuit was clamped during decannulation, a lipemic layer formed throughout the tubing, cannulas, and ML (Figure 3). The patient received a tracheostomy and continued to improve to tracheostomy decannulation and eventual discharge to home, ambulatory and neurologically intact without supplemental oxygen requirement, after a 49-day hospital stay. Triglyceride levels were not rechecked.

Figure 2. ML window before decannulation without evidence of clot to explain high transmembrane pressure (sweep gas 0 L/min and blood flow 2.4 L/min).

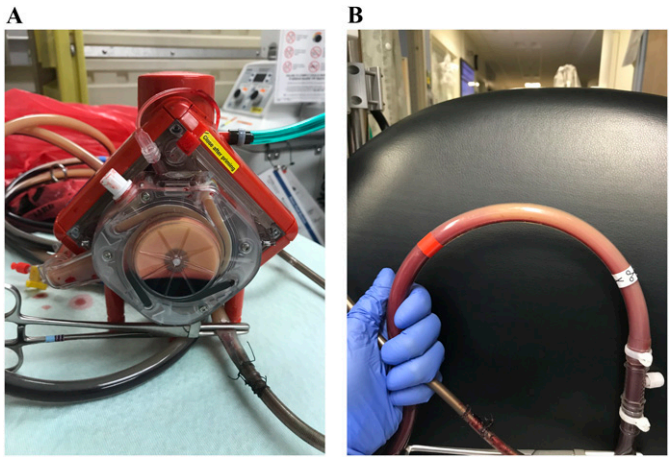

Figure 3. Lipemic layering of static blood in the ECMO circuit immediately after decannulation. (A) Pump head after disconnection from the pump. (B) Circuit tubing.

COMMENT

Hypertriglyceridemia is the likely cause of ML failure in this patient. Support for this conclusion includes significant lipemic layering in the circuit noted post-decannulation (Figure 3), elevated triglycerides in serum assay, high transmembrane pressures, and impaired ML gas exchange with no identified alternative cause such as clot or fibrin deposition. There was no evidence of thrombosis in the ML window or circuit, and anticoagulation was maintained throughout the ECMO run.

ML failure due to hypertriglyceridemia has been described previously in a pregnant Korean ECMO patient at 23-week gestation with acute pancreatitis due to very severe hypertriglyceridemia (1). In this case, the triglyceride level was >10,000 mg/dL on cannulation, which resulted in high resistance limiting flow through the circuit to 100 mL/min. A patient with a triglyceride level of 5,618 mg/dL undergoing cardiopulmonary bypass had significant lipemic layering throughout the circuit but did not have circuit component failure (2). These cases combined with our patient's course suggest that there are likely a number of variables that determine whether hyperlipidemia will lead to ECMO (or cardiopulmonary bypass) circuit component failure including severity of hyperlipidemia, duration of extracorporeal therapy, and the individual types of circuit components used. The threshold at which lipemia interferes with the ML is unknown, and our case is the first to demonstrate that ML failure can occur at triglyceride levels less than 1,000 mg/dL.

Similar to hypertriglyceridemia, the use of intravenous lipid emulsion (ILE) therapy to treat toxic ingestions has been shown to impair flow through continuous renal replacement therapy filters and limit ECMO blood flow to less than 1 L/min, resulting in inadequate support (3). Case reports of ILE use during ECMO are varied in their concern regarding the dose of ILE that should be given if ECMO is being considered for a patient. Low doses of ILE (10 mL/kg over 60 minutes) appear to have no major effect on ECMO circuits, however, large doses (as low as 20 mL/kg for visual layering) and certainly at 4,200 mL (850 g) may lead to severe circuit dysfunction and laboratory interference many hours after initial dosing (3–7). An in vitro study of six ECMO circuits with 20% ILE of 3 mL/h up to 4 hours showed deposition of lipid at all points of stasis in the circuits; five ECMO circuits ended up clotting, despite anticoagulation, and one of the circuits could not maintain flows due to elevated pressures (5). These ILE findings mirror the potential deleterious effects of lipid interaction with the ECMO circuit observed in patients with other causes of hypertriglyceridemia.

In addition to ECMO blood flow limitation from high transmembrane pressures and impaired gas exchange, this patient exhibited signs of hemolysis with elevated free hemoglobin, lactate dehydrogenase, and mild hyperkalemia (bilirubin was not tested). This is unlikely to be due to high transmembrane pressures as previous studies have indicated high transmembrane pressure in a modern ML is not an independent risk factor for hemolysis (8). Although no clots were visualized within the circuit, lipid deposition at points of stasis may promote clot formation, which could cause hemolysis (5). It is also important to note that Venado et al. (9) have previously described two cases of spurious elevation of free hemoglobin in ECMO likely due to medication-induced hypertriglyceridemia: one case attributed to sirolimus and another secondary to prolonged infusion of propofol. By altering the turbidity of the blood, triglycerides may cause interference with photometric laboratory analysis used to quantify free hemoglobin (7,9). Therefore, use of free hemoglobin is limited in hypertriglyceridemic patients and other markers of hemolysis should be used.

Propofol infusion is a known cause of hypertriglyceridemia; however, it was an unlikely cause for this patient as it was discontinued on hospital day 9 before cannulation and triglyceride levels remained unchanged throughout the ECMO run. With the known lipophilicity of the ECMO circuit and ML, as well as the risk of propofol-induced hypertriglyceridemia, one may question the safety of propofol use during ECMO; however, Hohlfelder et al. (10) observed no curtailment of ML life span with propofol use.

This patient did not have an elevated ethanol level on admission; was not given any other medications associated with hypertriglyceridemia; did not have diabetes, hyperglycemia, or proteinuria; and did not have any long-bone fractures to suspect fat emboli syndrome. Hereditary dyslipidemia is the most likely cause of this patient's hypertriglyceridemia.

We recommend providers assess for moderate to severe hypertriglyceridemia in the setting of high transmembrane pressures and premature ML failure, as well as anticipate the need for more frequent circuit exchanges in patients with hypertriglyceridemia.

REFERENCES

1. Son KH, Lee SI, Choi CH, et al. Mechanical failure of extracorporeal membrane oxygenation induced by hypertriglyceridemia. Ann Thorac Surg. 2017;104:e85.
2. Burstedt D, Tippett JC. Severe hypertriglyceridemia during cardiopulmonary bypass. J Cardiothorac Vasc Anesth. 2019;33:3418–22.
3. Sin JH, Tom A, Toyoda A, et al. High-dose intravenous lipid emulsion affecting successful initiation of continuous venovenous hemofiltration and extracorporeal membrane oxygenation. Clin Toxicol. 2017; 56:149–50.
4. Albrecht E, Baeriswyl M, Orrit J, et al. Lipid emulsion layering in extracorporeal membrane oxygenation circuit. Intensive Care Med. 2016;42:1806–7.
5. Lee HMD, Archer JRH, Dargan PI, et al. What are the adverse effects associated with the combined use of intravenous lipid emulsion and

extracorporeal membrane oxygenation in the poisoned patient? Clin Toxicol. 2015;53:145–50.
6. Schroeder I, Zoller M, Angstwurm M, et al. Venlafaxine intoxication with development of takotsubo cardiomyopathy: Successful use of extracorporeal life support, intravenous lipid emulsion and CytoSorb (R). Int J Artif Organs. 2017;40:358–60.
7. Johnson-Arbor K, Salinger L, Luczycki S. Prolonged laboratory interference after administration of intravenous lipid emulsion therapy. J Med Toxicol. 2015;11:223–6.
8. Venema LH, Sharma AS, Simons AP, et al. Contemporary oxygenator design relative to hemolysis. J Extra Corpor Technol. 2014;46: 212–6.
9. Venado A, Wille K, Belott SC, et al. Unexplained hemolysis in patients undergoing ECMO: Beware of hypertriglyceridemia. Perfusion. 2014;30:465–8.
10. Hohlfelder B, Szumita PM, Lagambina S, et al. Safety of propofol for oxygenator exchange in extracorporeal membrane oxygenation. ASAIO J. 2017;63:179–84.