

Case Report

Successful cure of a patient with urosepsis using a combination of extracorporeal membrane oxygenation and continuous renal replacement therapy: A case report and literature review

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ABSTRACT

Holmium laser lithotripsy (HLL) is one of the common surgical methods for urolithiasis. It causes minor surgical trauma, but complications are not rare. Extracorporeal membrane oxygenation (ECMO) treatment of sepsis is common, but venoarterial (VA)-ECMO treatment of urosepsis has not been reported yet. In this article, we reported a 67-year-old female patient with refractory septic shock caused by HLL under percutaneous nephroscope, involving breathing, heart, kidney and other organs, and organs support treatment was ineffective for the patient. Finally, we successfully treated the patient under VA-ECMO with continuous renal replacement therapy (CRRT). Combined ECMO and CRRT may provide a solution for addressing refractory sepsis. Here we present the case and review relevant literature, so as to provide a treatment strategy for patients with refractory urogenic sepsis and to reduce the mortality rate.

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Introduction

Because of the continuously updated definitions for sepsis and the improved concept of organ-support therapy, including early use of broad-spectrum anti-infective drugs and fluid resuscitation, the pathogenesis and treatment of sepsis has made great progress. Nevertheless, septic shock remains one of the major causes of death in intensive care patients. The annual incidence is high—in the tens to hundreds of millions—and accounts for 20%–50% of hospital deaths.^{1–3}

Holmium laser lithotripsy (HLL), a common surgical procedure for treating urinary calculi, is characterized by minimal surgical trauma, fast recovery, few complications, and a low incidence of urosepsis. However, the complication urosepsis has the characteristics of acute onset, fast progress, and high fatal disability rate, and thus has attracted attention. Once sepsis-derived acute respiratory distress syndrome (ARDS), cardiomyopathy, and acute renal failure have progressed to refractory septic shock, the situation is difficult to reverse, thus leading to extremely high morbidity and mortality.

For the refractory septic shock patient who has failed traditional therapy, especially when involving the lung and the heart, extracorporeal membrane oxygenation (ECMO) is a remedial measure.⁴ The use of ECMO has improved the prognosis of newborns and children, but there are few reports of its application in adult septic patients. In addition, some adults who have undergone ECMO treatment have had contradictory outcomes. Continuous renal replacement therapy (CRRT) not only replaces the failing renal function and restores electrolyte acid-base equilibrium, it can be also used to treat sepsis.⁵ We report a case of refractory septic shock after HLL that was successfully treated using venoarterial (VA)-ECMO combined with CRRT.

Case report

A 67-year-old woman (body weight 50 kg, height 158 cm) presented to a local hospital complaining of backache. She had no history of hypertension or diabetes. Calculi in both kidneys associated with ureteral calculi was diagnosed via ultrasonography and computed tomography. Then, she was admitted and underwent HLL combined with double J catheterization. Purulent urine, observed intraoperatively, was sampled and sent to the laboratory for culture. She was back in the ward 30 min postoperatively when she exhibited severe fever (body temperature 39.5 °C) associated

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with chill and low blood pressure (60/42 mmHg). Blood and urine samples were sent to the laboratory for culture. Empiric anti-infection drugs were given along with imipenem and Cilastatin sodium (1.0 g per 6 h), fluid resuscitation (30 mL/kg), a vasoactive agent (Norepinephrine), and Hydrocortisone sodium succinate hormone. Despite these measures, the patient's symptoms progressively deteriorated over the next 48 h, at which point she was anuric and diagnosed with ARDS. She was placed on invasive ventilatory support with endotracheal intubation and CRRT, but the symptoms were not alleviated. And then she was transferred to the intensive care unit (ICU) of our hospital.

At the time of admission, the patient was in a sedated state (Richmond agitation-sedation scale -4). Main vital signs included blood pressure 80/62 mmHg (Norepinephrine 1.5 µg/kg/min, Epinephrine 1.0 µg/kg/min), heart rate 139 beats/min, and transcutaneous oxygen saturation 80%. Physical examination revealed cold, clammy extremities, and a loud bubbling sound in the lung. Arterial blood gas analysis revealed oxygen partial pressure 50 mmHg (oxygen concentration 1.0), lactic acid 10.6 mmol/L, bicarbonate 10.8 mmol/L, and central venous pressure 20 cmH₂O. A large area of B lines was monitored in the lung using bedside ultrasonography (Fig. 1). Cardiac function detected through the chest wall indicated diffuse dysfunction, severe functional damage in the left ventricle, left ventricular ejection fraction (LVEF) 20.3%, and normal function in the right ventricle (Fig. 2). Chest wall electrocardiography suggested sinus tachycardia associated with broad ST depression, significantly elevated troponin I (10.2 ng/mL), amino-terminal brain natriuretic peptide precursor increasing beyond the maximum normal range (>35,000 pg/L), creatinine 356 µmol/L, and anuria. The abovementioned examinations supported multiple organ function failure (e.g., heart, lung, and kidney failure).

Lung damage was caused by sepsis—i.e. ARDS. Cardiomyopathy had arisen from sepsis in the heart, and acute renal failure was due to sepsis in the kidney. The patient was considered in refractory

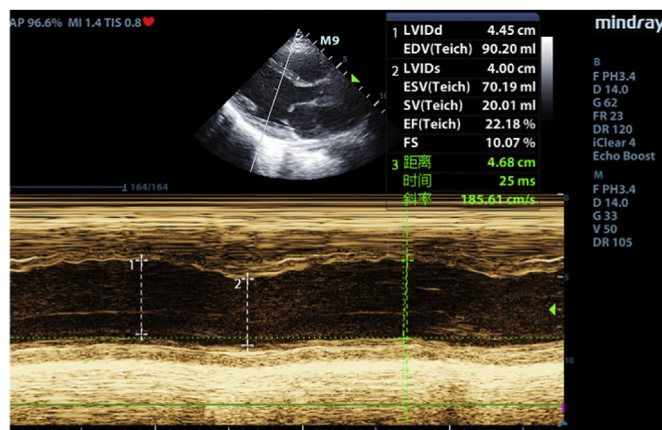


Fig. 2. Echocardiography shows diffuse reduction of motion in the left ventricular chamber wall with a left ventricular ejection fraction of 20.3%.

septic shock, so VA-ECMO treatment was urgently initiated. The ECMO venous leading-out end used a 20F catheter, and the arterial leading-in end used a 17F catheter (DuraFlo Edwards Lifesciences, Irvine, CA, USA). The catheters were placed in the left femoral vein and right femoral artery, respectively. In addition, a No. 6 arterial catheter was placed in the right femoral artery to avoid avascular necrosis in the distal right lower extremity. ECMO (centrifugal pump Maquet Rotaflow RF 32; Maquet Cardiopulmonary AG, Hirrlingen, Germany) ran normally 3000 rpm, blood flow 3.5 L/min, arterial pressure 135 mmHg, venous pressure -29 mmHg. The patient's cyclic dynamics rapidly improved. After 30 min, the Norepinephrine (1.0 µg/kg/min) and Epinephrine were stopped. Because of the anuria, the lactic acid level was high. Hence, bedside CRRT was performed. The leading-in and leading-out ends of CRRT

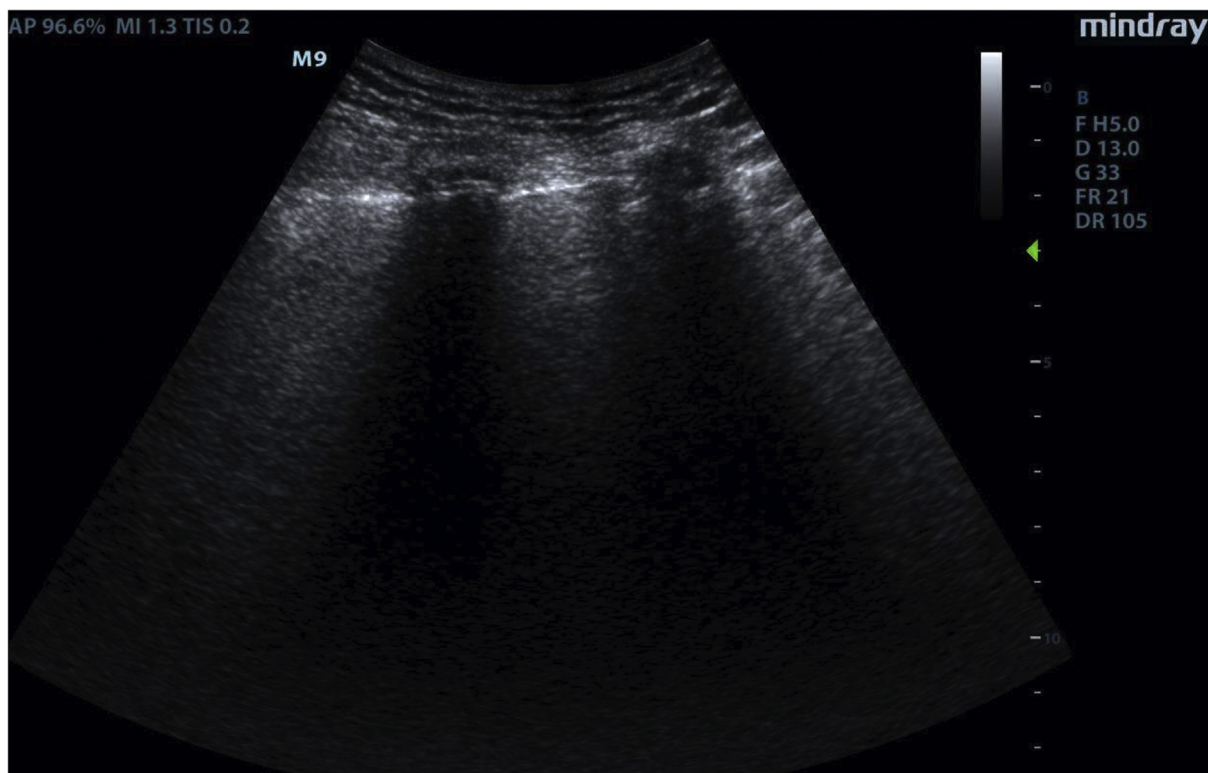


Fig. 1. Pulmonary ultrasonography indicates large areas of line B fusion.

(Jinbao) were connected between the centrifugal pump of the ECMO apparatus and the membrane. Imipenem and Cilastatin sodium combined with Vancomycin were used for anti-infective therapy. After 2 h, the lactic acid level had declined. After 10 h, vasoactive drugs were completely stopped. The arterial blood lactate level had reached the normal range at 12 h. At 2 days after admission, extended-spectrum β -lactamase-positive *Escherichia coli* was found in both blood and urine cultures. Although the inflammatory indices (e.g. leukocytes, calcitonin, C-reactive protein) diminished, the anti-infection regimen continued. The minimum serum trough concentration of Vancomycin was monitored, and it remained within the range of 15–20 $\mu\text{g/mL}$.

Beside echocardiographic patterns were re-evaluated daily. On day 5, the LVEF was 35%, but black and necrotic skin was found at the extremities of both lower limbs and the end of a finger on the right upper limb. The patient was successfully weaned from ECMO therapy on day 6.

Renal function was scaled as acute kidney injury grade 3, so the bedside CRRT was discontinued. The treatment time of each session lasted 10–12 h. The patient began urinating, with its volume gradually increasing to a maximum of 1000 mL/day.

Vascular ultrasonography and computed tomography angiography were performed in the bilateral lower limbs, followed by a vascular surgery consultation. On day 14 after admission, the necrotic tissues of the lower extremity were amputated.

Respiratory function was supported by tracheal intubation. On day 5, spontaneous breathing was successful, but weaning failed, so the trachea was opened on day 10. On day 10 of anti-infective therapy, the anti-infection combination of imipenem and Cilastatin sodium and Vancomycin was replaced by Cefoperazone sodium and Sulbactam sodium.

Beside physical rehabilitation was started, she was weaned from the ventilator on day 20 after admission. The tracheotomy tube was sealed on day 25.

The patient was discharged successfully on day 32, although she continued intermittent hemodialysis. At the 6-month follow-up, the patient declared that she could take care of herself, although she still required intermittent hemodialysis.

Discussion

Sepsis due to infection is characterized by dysregulation of the body's reactions, leading to life-threatening organ dysfunction. The diagnostic criteria are the presence of infection and a sequential organ failure assessment score of ≥ 2 .⁶ Although our knowledge of sepsis pathophysiology is deepening, sepsis is still one of the problems threatening human life, resulting in high cost and death of ICU patients.⁷ Sepsis often causes dynamic disorder of the circulation, generally manifesting as high output/low resistance—i.e. cold shock. Dynamic monitoring mostly shows high cardiac output and low resistance, although some septic patients show low output and high resistance—mainly cardiac function inhibition but without myocardial structural change. Hemodynamic studies show reduced cardiac output, and echocardiography reveals a reduced cardiac ejection fraction and an enlarged double chamber, called “sepsis-induced cardiomyopathy”.⁸ Sepsis-induced cardiomyopathy occurs at an incidence of 40%–60%, and the risk of death is high, up to 70%.⁹

The pathogenesis, however, remains unclear. It is possibly caused by an inflammatory disorder, in which nitric oxide (NO) plays an important role.¹⁰ Elevated myocardial enzyme creatine kinase isoenzyme (CK-MB) and troponin may be the markers for septic myocardial necrosis and damaged cardiac function, and troponin with the highest diagnostic value.¹¹ The urosepsis in this study was caused by HLL and simultaneously involved the

respiratory organs, circulation, platelets, coagulation, and kidney function. The sequential organ failure assessment score was 8, and myocardial troponin I and CK-MB levels were increased. Ultrasonography proved that the LVEF was only 20.3%, and the oxygenation index was <100 . The elevated creatinine was three-fold higher than the upper limit, and the urine volume was <0.3 mL for a continuous 12 h. All these values suggested a diagnosis of sepsis-induced cardiomyopathy, acute renal failure, and ARDS.

As traditional treatment for sepsis failed, VA-ECMO combined with CRRT was instituted. ECMO is basically an extracorporeal circulation machine, with the core composed of a membrane lung and a centrifugal pump, which gains the time to treat reversible cardiopulmonary diseases.¹² As the technique has matured, the application range has gradually extended, from supporting post-operative cardiopulmonary function following major cardiac surgery, to patients with end-stage structural lung disease who are awaiting lung transplantation, to its current applications in patients with various critical illness, such as cardiopulmonary resuscitation, acute myocardial infarction, severe fulminant myocarditis, and poisoning. Thus, ECMO plays an increasingly important role in quite drastic medical situations.

ECMO is currently being applied as sepsis therapy in newborns and children, and has been considered a feasible treatment measure to improve the survival rate. Maclaren and Butt¹³ reported that ECMO could provide enough tissue oxygen transport for children and newborns with damaged cardiopulmonary function caused by sepsis. In 2002, the society of critical care medicine suggested that ECMO is an appropriate method for treating newborns and children with refractory septic shock.¹⁴ For adult septic patients, however, the results are often contradictory. Reports of ECMO successfully curing refractory septic patients describe only individual cases or are studies with small sample size. For example, a study enrolling 14 septic shock patients combined with severe myocardial inhibition reported by Bréchet et al.¹⁵ indicated that LVEF <0.25 , cardiac index <2.2 $\text{L}\cdot\text{min}^{-1}\cdot\text{m}^{-2}$ could be used as a reference standard for ECMO support in sepsis-induced cardiomyopathy. Nevertheless, the control group generally showed negative results. For example, Ro et al.¹⁶ reported that, in a single-center study of 71 septic patients, only 15.5% were successfully weaned from ECMO support, and the proportion of those successfully discharged was even lower (7%). No statistical difference was found in the therapy outcome between those undergoing ECMO and those who did not.

The patient in the current report developed refractory urosepsis after HLL and met the indications for initiating ECMO. Because cardiopulmonary function was also involved, VA-ECMO support was initiated as well. With ECMO support, the patient's circulation became more stable than it was before, which created conditions under which other treatments could be applied and allowed sufficient time for recovery from the sepsis-induced cardiomyopathy. Although the use of ECMO for sepsis, especially adult refractory sepsis, is controversial, the pathogen in this case was confirmed. For septic shock patients in whom the source of the sepsis can be removed, ECMO may be the last treatment opportunity.

The purpose of CRRT is to scavenge water and solute. It can be used not only for patients with nephropathy, but also for those with pathology of the liver, lung, heart, and pancreas. Sepsis is also an indication for CRRT because it scavenges solute via diffusion, convection, and adsorption and maintains dynamic equilibrium of the internal environment via its ultrafiltration managing capacity. One of the derivations of sepsis is an inflammatory disorder, such as systemic inflammatory response syndrome or the compensatory anti-inflammatory response syndrome, leading to multiple organ functional damage. Thus, CRRT can alleviate the early systemic inflammatory response of sepsis by scavenging cytokines.¹⁷ Although

a single-center study indicated that CRRT, especially with its high-capacity filtration, can improve the outcome of sepsis,¹⁸ a randomized controlled study is still lacking. Furthermore, it has been reported that CRRT does not improve the prognosis of septic patients.¹⁹

In this study, first, after ECMO, the urine volume was <0.3 mL/kg/>24 h, and the creatinine level was elevated to three-fold that of the upper limit of normal. In addition, abundant rales were detected in the lung, with a central venous pressure of 20 cmH₂O and the NT-BNP >35,000 pg/mL. Second, the lactic acid level was >10 mmol/L, so the patient suffered from lactic acidosis. Thus, the indications for CRRT treatment were indeed present. CRRT scavenges excessive water and inflammatory mediators are scavenged simultaneously, thereby adjusting the internal environment to gain time for anti-infection drug use and for it to take effect.

Sepsis-induced cardiomyopathy can appear as myocardial damage caused by various cytokines due to infection. Myocardial inhibitors and NO play important roles. They are small molecular substances with molecular weights of <5000 Da. Thus, it is believed that CRRT could scavenge them, thereby improving and accelerating cardiac functional recovery.

The case of refractory urosepsis reported here was successfully cured using a combination of ECMO and CRRT. ECMO replaces cardiac and lung function, improves circulation dynamics and oxygenation, increases oxygen delivery, and improves tissue perfusion. CRRT not only replaces renal function and scavenges water and creatinine, it simultaneously scavenges the inflammatory factors caused by sepsis, buying time for anti-infection drugs to play their role and for recovery of the affected organs (e.g. heart, lung, kidney). Thus, for adult patients with refractory septic shock, we suggest using a combination of ECMO and CRRT to improve their prognosis.

Finally, the limitation of the study is the amputation made necessary by the ischemic necrosis of both upper and lower extremities. The possible reason is prolonged hypoxia and ischemia of the fingertips. The necrosis of the right upper extremity may be related to failure of an invasive arterial pressure puncture and failure to frequently monitor the patient using noninvasive blood pressure measurements, as well as recognizing the severity of the patient's condition. Above all, refractory septic shock patients undergoing ECMO combined with CRRT are difficult to manage. It requires cooperation between the ECMO and CRRT teams and should be performed at a center that is familiar with the ECMO protocol.

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Ethical Statement

This study was conducted ethically in respect of the principles of World Medical Association Declaration of Helsinki and was approved by the Ethics Review Committee of the First Affiliated Hospital of USTC, written informed consent was obtained from guardian.

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Declaration of Competing Interest

The authors have no conflicts of interest to declare.

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