Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2022 Aug 26; ; 10(C):267-271.
https://doi.org/10.3889/oamjms.2022.10386
eISSN: 1857-9655
Category: *C - Case Reports*
Section: *Case Report in Internal Medicine*

Daily Hemodialysis Helps Critical Nephritic Lupus Patient: A Case Report

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Edited by: Mirko Spiroski
Citation: Fitri L, Aditianingsih D. Daily Hemodialysis Helps Critical Nephritic Lupus Patient: A Case Report. Open-Access Maced J Med Sci. 2022 Aug 26; 10(C):267-271. https://doi.org/10.3889/oamjms.2022.10386
Keywords: Daily hemodialysis; critical nephritic lupus; SLED; SLEDD
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Received: 11-Jun-2022
Revised: 10-Aug-2022
Accepted: 16-Aug-2022

Funding: This research did not receive any financial support
Competing Interest: The authors have declared that no competing interest exists

Abstract

BACKGROUND: Nephritic lupus is the most common and serious complication of systemic lupus erythematosus (SLE) and is associated with a worse prognosis. Hemodialysis (HD) is effective in alleviating symptoms and renal involvement in a nephritic lupus patient.

CASE PRESENTATION: A 33-year-old female was diagnosed with SLE in September 2017. She was also diagnosed with diffuse membranous proliferative glomerulonephritis, as confirmed with a kidney biopsy. She complained of gradual onset limb weakness and peripheral edema 3 months before admission. She was treated with 6 cycles of cyclophosphamide and continued with methylprednisolone 16 mg once daily, hydroxychloroquine 200 mg once daily, and myfortic 360 mg twice daily. A day before ICU admission, her creatinine level was increased to 4.6 mg/dl with an estimated GFR of 12 ml/min and her symptoms then worsened into seizures and lung edema. Daily HD with heparin-free sustained low-efficiency daily diafiltration (SLEDD) was performed. About 2 L was extracted for the first 6 h with Qb 150 ml and Qd 300 ml and was continued until the day after. For the next 4 days, 3 L was extracted per day with Qb 200 ml and Qd 500 ml. The patients' hemodynamic status was within normal limits during dialysis period. The condition improved and the patient was transferred to the ward. HD is a way to solve kidney problems in nephritic lupus and SLE patients in general. It should not only be employed for mainly kidney problems but could be beneficial in autoimmune patients with conditions such as nephritic lupus. Slowly extracted dialysis type would be a good and inexpensive option to resolve nephritic lupus in compromising lupus patients. Filtration is ensured and solute removal is achieved relatively equivalent to continuous renal replacement therapy.

CONCLUSION: Daily HD could increase renal salvation by providing less creatinine serum and removing accumulated fluids. The SLEDD type could be used for critical nephritic lupus patients with reduced hemodynamic perturbations, minimal anticoagulant, and lower cost.

Introduction

Systemic lupus erythematosus (SLE) is a multisystem disease associated with many immunological disorders, including autoantibody formation, hypergammaglobulinemia, suppressed T-cell disorders, decreased serum complement levels, and elevated levels of immune complexes in the blood. SLE is a disease of unknown causes, where tissue and cell damage occur through autoantibodies and pathogenic immune complexes [1]. This disease is more common in women of childbearing age and affects several organs such as the joints, kidneys, skin, brain, and other organs. The incidence in the United States is 15–50 per 100,000 population [2]. Studies have shown that up to 60% of lupus patients will develop lupus nephritis, including more than half of children with lupus. Lupus nephritis is more common in women than men, and there are an even higher prevalence and severity among African-American, Asian, and Hispanic women between the ages of 15 and 44, who tend to develop the disease earlier and experience more serious complications [1], [2].

Lupus nephritis is one of the most serious complications of SLE and causes an increased mortality rate [3]. This occurs when the immune system mistakenly attacks the kidneys, causing inflammation and possible organ damage. Inflammation of the kidneys can compromise the overall ability of the kidney system to properly remove wastes from the blood, maintain proper amounts of bodily fluids, and regulate hormone levels to control blood pressure and blood volume. Lupus nephritis requires special attention to preserve kidney function and avoid serious kidney complications, such as kidney failure that may require dialysis or a kidney transplant [2], [4].

Case Presentation

A 33-year-old female was diagnosed with SLE and confirmed diffuse membranous proliferative glomerulonephritis from a kidney biopsy. The

patient entered the Emergency Unit (ER) at Cipto Mangunkusumo Hospital, Jakarta, Indonesia, with the complaints of swelling throughout the body and joint pain. The patient has regularly visited the internal medicine outpatient clinic and received hydroxychloroquine therapy and chemotherapy with cyclophosphamide for 6 cycles from the rheumatology division of the Cipto Mangunkusumo Hospital, and the complaints of swelling disappeared. On arrival in the ER, the patient had a blood pressure of 135/87 mmHg, pulse 88 ×/min, respiration 22 ×/min, ascites, pitting edema in all extremities, and weakened vesicular breath sounds at bilateral bases. Some remarkable laboratory parameters were as follows: White blood cell count of 787 μ/L; hemoglobin of 8.8 g/dl; hematocrit of 24.7%; platelet count of 304,000 μ/L; serum sodium of 136 mmol/L; potassium of 3.7 mmol/L; urea of 71 mg/dL; creatinine of 3.2 mg/dl; GFR of 18.2; C4 of 26; C3 of 53; Ca of 7.4; anti dsDNA of 52.8; ALT of 16 U/L; AST of 11 U/L; and serum albumin of 1.83 g/dL. The chest X-ray showed an enlarged heart (CTR >50%), pleural effusion, infiltrates in the lower right lung with suspected pneumonia, and calcification in the upper lung. During treatment in the ward, a thoracentesis was performed on the left pleura and 160 mL of fluid was obtained. Echocardiography results showed LA, dilated RA, hypokinetic global contractility LVH, mild MR, moderate TR and PR, decreased LV systolic function, Grade II diastolic dysfunction, good RA systolic function, minimal right pleural effusion, and 34% EF.

A day before ICU admission, her urea increased to 154.4 mg/dL, creatinine level to 4.6 mg/dl, monitored urine output of 0.1 ml/kg/h with estimated GFR of 12 ml/min, CRP of 216.32, and PCT of 126.5 ng/mL. Before ICU admission, the patient complained of shortness of breath, with a respiratory rate of 40–45 ×/min and blood pressure of 199/101 mmHg, a pulse of 131 ×/min, and oxygen saturation of 77%. Her symptoms then worsened into seizures and lung edema. The patient was transferred to the ICU and connected to a ventilator. In the ICU, daily hemodialysis (HD) with heparin-free SLEDD was performed. About 2 L of fluid was extracted for the first 6 h with Qb 150 ml and Qd 300 ml and was continued until the day after. For the next 4 days, 3 L of fluid was extracted per day with Qb 200 ml and Qd 500 ml. The hemodynamic status was within normal limits during the dialysis period. The patient's condition was resolved and she was transferred to the ward.

Discussion

Lupus nephritis is the most common manifestation in patients with severe SLE. This condition has high morbidity and mortality related to the worsening kidney function due to treatment with immunosuppressive drugs. The goal of treatment for lupus nephritis is to normalize kidney function or slow the progression of kidney damage [5], [6].

In critically ill patients, excess fluid causes several complications such as pulmonary edema, heart failure, delayed wound healing, tissue damage, impaired bowel function, and even death. Therefore, evaluation of volume status is very important in the initial management of critically ill patients. Various strategies are used to prevent fluid overload and protect kidney function in the ICU, including fluid therapy strategies, the use of diuretics, and extracorporeal renal replacement therapy. There is an association between positive fluid balance and mortality in critically ill patients, where fluid accumulation can lead to renal congestion, pulmonary congestion, and peripheral edema. A positive fluid balance in the ICU has been shown to be dangerous. Positive fluid balance and venous congestion are associated with poor outcomes in critically ill patients and may lead to dysfunction of various organs such as the lungs, kidneys, liver, and gastrointestinal tract. Critically ill patients experience acute inflammation that releases a cascade of inflammatory mediators causing microcirculatory dysfunction, capillary leakage, and distributive shock occurs [7]. Active fluid removal using diuretics or ultrafiltration is part of the treatment for organ congestion and fluid overload. The purpose of fluid removal is to treat interstitial edema and compartment pressure [7].

In patients with edema or fluid overload, pressure on the renal veins results in decreased renal perfusion and glomerular filtration. Creatinine is one of the parameters to identify kidney dysfunction. Changes in serum creatinine values of >0.3 mg/dL from the basal values indicate impaired kidney function in patients who have accumulated fluid [8].

Acute kidney injury (AKI) is an acute condition of decreased kidney function associated with increased mortality. AKI is diagnosed according to the kidney disease: Improving global outcome (KDIGO) criteria, which were based on changes in the creatinine levels and urine production [9] (Table 1).

Table 1: KDIGO's criteria for acute kidney injury [9]

Stage	Increase in serum creatinine	Urine output
1	≤0.3 mg/dL (26.5 pmol/L) within 48 h or 1.5–1.9 times baseline within 7 days	<0.5 mL/kglh for 6–12h
2	2.0–2.9 times baseline within 7 days	<0.5 mL/kglh for ≤12 h
3	≤3.0 times baseline, or ≤4.0 mg/d L (354 pmol/L) increase within 7 days or initiation of RRT or initiation of RRT or in estimated GFR to <35 mL/min/1.73 m^2	<0.3 mL/kglh for ≤24h or Anuria ≤12 h

In critically ill patients, restoration of cardiac output, systemic blood pressure, and renal perfusion require volume management, evaluation of volume status, as well as maintenance and modulation of tissue perfusion. Recent studies have established a correlation between fluid overload and mortality in critically ill patients [7], [10].

Accurate evaluation of volume status is essential for appropriate therapy because misevaluation

of volume can result in lack of essential medication or unnecessary fluid administration, and both scenarios are associated with increased mortality. There are several methods for evaluating fluid status; however, most of the tests currently in use are relatively inaccurate. Diuretics, especially loop diuretics, remain a valid therapeutic alternative. Diuretics are often used as initial therapy; however, due to their limited effectiveness, the use of continuous renal replacement techniques is often necessary for the treatment of fluid overload. Successful treatment of fluid overload depends on a proper assessment of the individual's volume status, understanding of the principles of fluid management by ultrafiltration, and clear treatment goals [7], [10].

HD as a modality for cytokine removal

Refractory fluid overload necessitates the use of continuous renal replacement therapy (CRRT) because critically ill patients often exhibit hemodynamic instability and/or multiple organ dysfunction. Accurate management of fluid balance aims to improve pulmonary gas exchange and organ perfusion while maintaining stable hemodynamic parameters. The choice of initial modality needs to be based on the availability of resources, local expertise, the individual needs of the patient, and ultimately on the patient's hemodynamic status [10].

Treatment of patients with lupus nephritis can be challenging. The disease presents problems that can lead to a poor prognosis, such as infection, lupus reactivation, vascular access thrombosis, and cardiovascular complications. Regular dialysis is highly recommended in lupus nephritis patients who have fluid retention problems [11]. Mojcik reported that the survival of lupus patients on HD was comparable to or even better than that of non-lupus patients or patients with other systemic autoimmune diseases. However, lupus patients on dialysis tend to be younger and predominantly female, which have a beneficial impact on survival. In the general course of the disease, clinical and serological decline during dialysis, although the degree of immunosuppression can be reduced [6], [12]. An analysis performed in 55 lupus patients undergoing dialysis treatment, only 8% of patients, disease activity increased, and in >50% disease activity decreased or disappeared ($p < 0.001$). The percentage of patients using high dose of prednisone decreased from 69% to 15% and the use of cytotoxic drugs from 72% to 7%. The percentage of patients taking high-dose prednisone decreased from 69% to 15% and the use of cytotoxic drugs from 72% to 7%. In 10–20% of patients, renal function may (partially) recover within a 4-month period, which allows for discontinuation of HD [6]. Early death of lupus patients undergoing HD is more often due to infection than active lupus [6], [12].

Figure 1 shows the relationship between fluid balance, cumulative fluid balance, and urine output. It can be seen that in this patient, there was an increase in cumulative fluid balance and an increase in urine output. The urea and creatinine values tended to decrease (Figure 2). In this patient, positive fluid balance caused organ dysfunction, especially acute kidney injury and disorders of the respiratory system, which will aggravate pulmonary edema which eventually results in impaired gas exchange, reduced lung complaints, and increased breathing efforts.

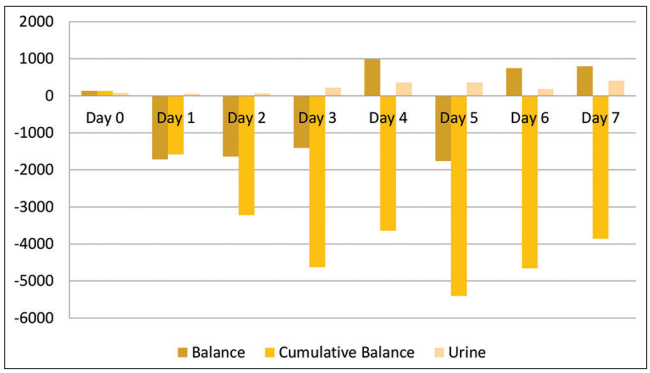

Figure 1: Fluid balance, cumulative fluid balance, and urine output

HD is still an option that is often used in the management of AKI and chronic renal failure in addition to peritoneal dialysis and kidney transplantation. Hybrid dialysis is a combination or graft (hybrid) between intermittent hemodialysis (IHD) and CRRT techniques. Hybrid dialysis or now referred to as prolonged intermittent renal replacement therapy (PIRRT) aims to provide renal replacement therapy or RRT at the same dose as the recommended dose for IHD and CRRT without compromising the utility or patient safety [13]. In 1988, Kudoh developed a hybrid therapy that combines the efficiency of IHD and the hemodynamic stability of CRRT through solute separation and ultrafiltration [13], [14]. This technique is called slow continuous HD. PIRRT is primarily used as a substitute for CRRT in hemodynamically unstable critically ill patients. The choice of performing PIRRT over CRRT has been influenced by various factors such as reduced cost compared to expensive CRRT, unavailability of CRRT machines, and the ability to provide adequate RRT in hemodynamically unstable patients [13].

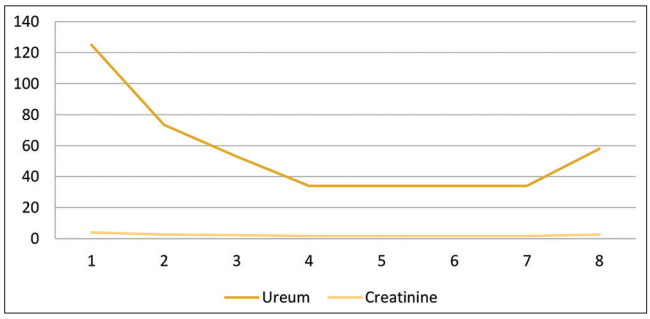

Figure 2: Urea and creatinine level

Intermittent renal replacement therapy is a conventional dialysis that is performed intermittently for 4–5 h for each dialysis at intervals of 2–3 times

per week. Sustained low-efficiency dialysis (SLED) is almost the same as conventional IHD. The basic principle of SLED is to slow down the flow of Qb blood and slow down the flow of dialysis Qd so that the risk of hemodynamic instability can be reduced but with the length of HD being extended to 6–12 h so that sufficient HD efficiency is achieved [15]. The SLED technique was first introduced in 1998 by Marshall *et al*. in the United States by performing dialysis using a hybrid technique on a dialysis machine by slowing blood flow and dialysate flow by prolonging the dialysis time. SLEDD refers to a SLED that is performed daily, while SLEDD-f uses a dialysis process and prioritizes filtration in it [15].

Hybrid dialysis modalities, including SLED, have good efficacy and tolerability in the correction of acidosis, electrolytes, and fluid overload in AKI conditions with septic shock [16]. In critically ill patients with AKI, mortality at 90 days and 1 year did not differ between SLED versus CRRT [17].

If the hemodynamics is unstable, the smaller the ultrafiltration that can be done every hour, the longer the dialysis time needed. Flieser and Kielstein reported that SLED performed for 12 h every day was as efficient as CVVH performed for 24 h 28 [18]. SLED is a technique that can be used as a modality to eliminate cytokines circulating in the systemic circulation in addition to being more effective and stable in reducing fluid. It can also facilitate parenteral nutrition, intravenous treatment, as well as improve and stabilize acid-base and electrolyte balance [15], [16], [17]. A meta-analysis and systematic review on AKI patients found no difference between SLED and CRRT in the recovery of renal function, days required for recovery, and the incidence of hypotension in ICU patients. SLED shows almost the same results as CRRT performed continuously for 24 h in hemodynamically unstable patients, but at a more affordable cost [19].

Conclusion

SLED is dialysis that combines the IHD technique with CRRT. SLED provides an advantage in hemodynamically unstable patients with unavailable or limited equipment and human resources to perform CRRT, but provides almost the same outcomes as CRRT at a more affordable cost. Daily hemodialysis can improve renal safety by providing less serum creatinine and removing accumulated fluid. The SLEDD type can be used for critically ill lupus nephritic patients with reduced hemodynamic compromise, minimal anticoagulation, and lower costs. In our patients, SLEDD can provide excellent clinical and metabolic outcomes at reduced costs.

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