Available online at **www.ijmrhs.com**

ISSN No: 2319-5886

International Journal of Medical Research & Health Sciences, 2018, 7(5): 58-69

Early Continuous Renal Replacement Therapy and Antibiotic Management in Shock Patients due to Urosepsis with Immunocompromised Post Renal Transplantation

Sandhi Prabowo* and Dita Aditianingsih

Department of Anesthesiology and Intensive Care, Cipto Mangunkusumo General Hospital, Universitas Indonesia, Jakarta, Indonesia

**Corresponding e-mail: yudaiswanto91@gmail.com*

ABSTRACT

Introduction: *Septic shock is still a major cause of morbidity and mortality in the intensive care unit (ICU), resulting in the death of more than 30% in the first 28 days of treatment. Mortality reaches 20-49% when accompanied by shock. Transplant recipients who receive immunosuppressive drugs are at high risk of septic shock due to nosocomial infections.* ***Case Report:*** *A 32-year-old man, who had a history of kidney transplantation, was admitted to the ICU due to shock and respiratory failure. The patient had undergone cystoscopy evaluation, ante grade pyelography, cystography, and renal allograft nephrostomy replacement a day before ICU admission. The patient was diagnosed with septic shock due to urosepsis, hospital-acquired pneumonia (HAP), and acute kidney injury (AKI) post renal transplantation. Prospective observational descriptive analysis was performed on the patient. The patient was intubated, given fluid resuscitation with crystalloid (ringer lactate) more than 20 ml/kg/hour with no response. Norepinephrine 1 mcg/kg/min and dobutamine 5 mcg/kg/min were given to reach mean arterial pressure (MAP)>65 mmHg. Due to unstable hemodynamics, continue renal replacement therapy (CRRT) was performed to remove inflammation mediator, which caused cytokine storm. Continuous venous-venous hemodiafiltration (CVVHDF) with dose 30-40 ml/kg/hour was run for 5 days. On day 5 the patient was stable with the minimal dose of vasopressor. The patient was extubated by day 8 and discharged from ICU 10 days later. The urine output was >0.5 ml/kg/hour and creatinine levels tend to decrease.* ***Conclusion:*** *Early CRRT could prevent organ failure and further complications caused by septic shock by removing inflammation mediators.*

Keywords: Urosepsis, Immunocompromised, Hemodynamics, Vasopressor

INTRODUCTION

Urosepsis is a systemic infection that comes from the focus of infection in the urinary tract causing bacteremia and septic shock. Bjerklund, et al., stated that the incidence of urosepsis is 20-30% of all occurrences of septicemia and more often comes from complications of infection in the urinary tract [1]. Mortality reaches 20-49% when accompanied by shock. Proper treatment should be quick and adequate to prevent organ failure and further complications (Table 1).

Table 1 Structural and functional abnormalities of the urinary tract associated with sepsis

Abnormalities	
Obstruction	Congenital: urethral stricture, phimosis, urethrocele, polycystic kidney disease Acquired: Calculi, prostatic hypertrophy, tumors of the urinary tract, trauma, pregnancy, radiation therapy
Instrumentation	Indwelling urethral catheter, ureteric stent, nephrostomy tube, urological procedures
Impaired voiding	Neurogenic bladder, cystocele, vesicoureteral reflux
Metabolic abnormalities	Nephrocalcinosis, diabetes, azotemia
Immunodeficiency	Patients on immunosuppressive drugs, neutropenics.

Etiology

Giessing, et al., in 2012 stated that because of the use of immunosuppressant, renal transplant recipients are susceptible

to infection where 75% of recipients are infected in the first year of post renal transplantation [2]. The risk of infection is influenced by immunosuppressive and environmental interactions. In the first month of renal transplantation, the infection is often caused by reactivation of recipient infections, especially urinary tract infections and tuberculosis, transmission of infection from donors, surgical wound infections, intravenous catheters and urine catheters. In the first six months, infection is often caused by viruses such as herpes, bacteria, and fungi. The cause of bacterial infections after renal transplantation is similar to the primary infection-causing bacteria in the urinary tract of gram-negative coliform germs such as *Escherichia coli* (50%), *Proteus spp* (15%), *Klebsiella* and *Enterobacter* (15%), and *Pseudomonas aeruginosa* (5%). Gram-positive bacteria are also involved but the frequency is smaller, which is around 15% (Figure 1).

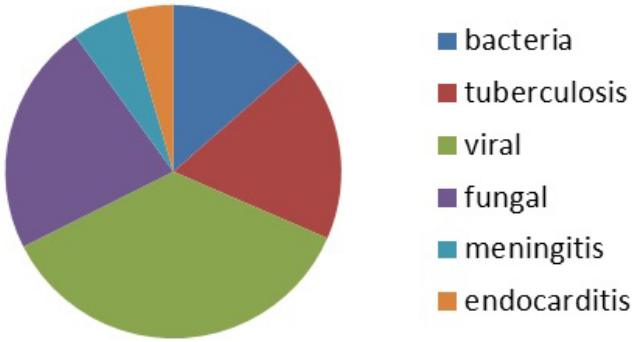

Figure 1 The incidence of the infection of post renal transplantation etiology

In the study of the European Study Group on Nosocomial Infections (ESGNI-004 study), by comparing patients using catheters and non-catheters, it was found that *E. coli* was 30.6% in patients with catheters and 40.5% in non-catheters, *Candida spp* 12.9% in patients with catheters and 6.6% in non-catheters, *P. aeruginosa* 8.2% in patients with catheters and 4.1% in non-catheters (Figure 2).

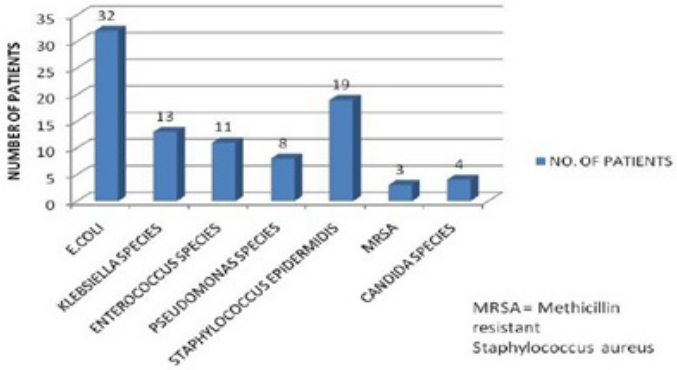

Figure 2 The bacteria that cause UTI (Urinary Tract Infection) post renal transplant

Diagnosis

Dellinger, et al., in survival sepsis campaign defined sepsis as a life-threatening organ dysfunction due to the dysregulation of the body's response to infection [3]. Organ dysfunction is defined as rapid change in the total score of the sequential organ failure assessment (SOFA), with a score greater than 2 points with the cause of the infection. Singer, et al., in 2017 defined septic shock by hypotension requiring a vasopressor to maintain an average arterial pressure of 65 mmHg or higher and a lactate serum level greater than 2 mmol/L (18 mg/dL) despite adequate volume resuscitation [4]. This new definition, also called sepsis 3, eliminates the presence of systemic inflammatory response syndrome (SIRS) to determine sepsis, and the definition of severe sepsis is removed. What was previously called severe sepsis is now a new definition of sepsis (Figures 3-8).

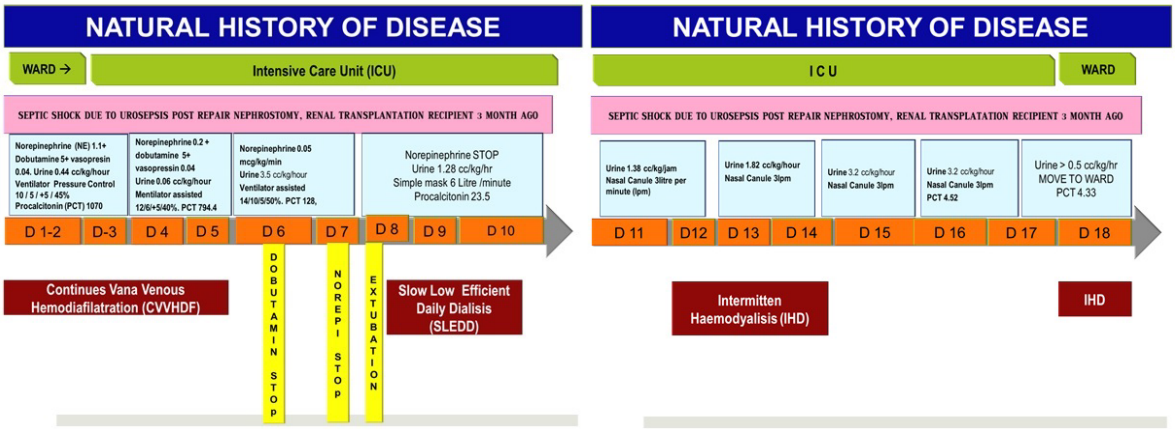

Figure 3 Natural history of disease

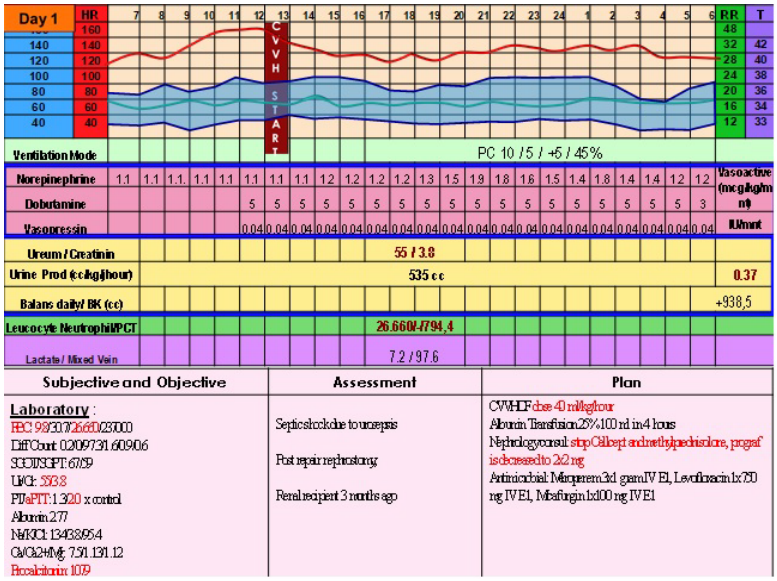

Figure 4 Day 1 observation chart and treatment in ICU

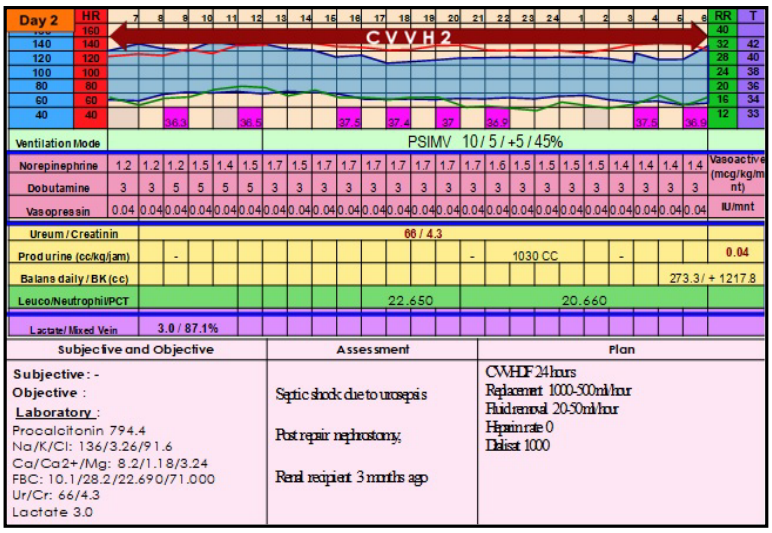

Figure 5 Day 2 observation chart and treatment in ICU

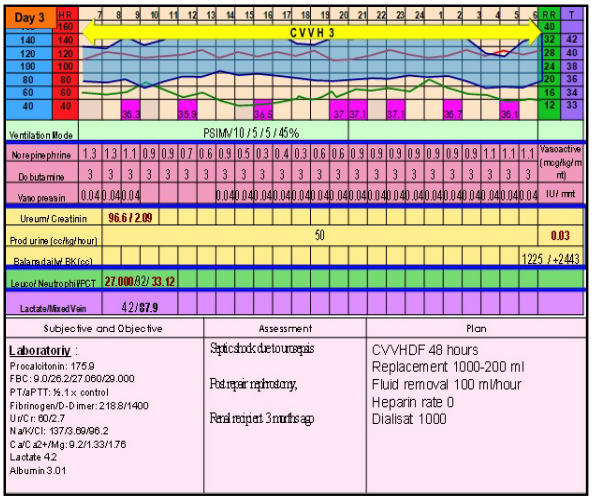

Figure 6 Day 3 observation chart and treatment in ICU

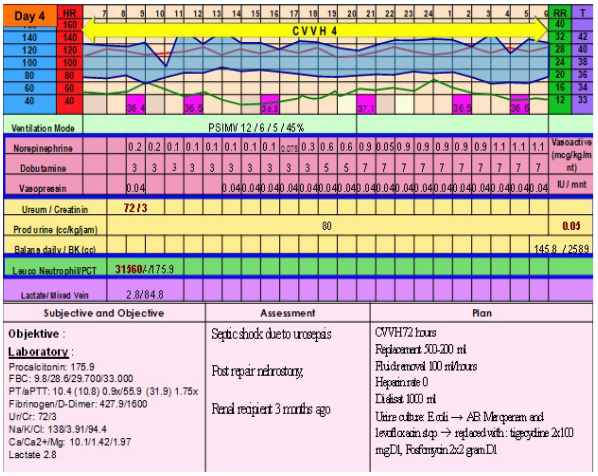

Figure 7 Day 4 observation chart and treatment in ICU

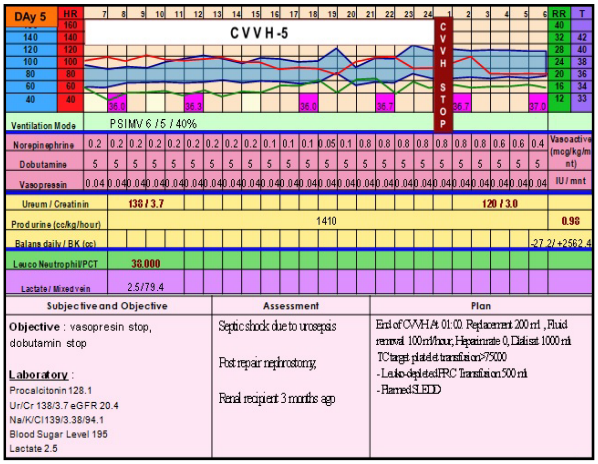

Figure 8 Day 5 observation chart and treatment in ICU

Urinary tract infection (UTI) can be established from anamnesis, physical examination, and imaging support (rontgen, CT scan abdomen, USG, MRI) and laboratory (urinalysis, urine culture). In immunocompromised post kidney

transplant patients, it is difficult if we rely solely on physical examination, as the symptoms of an inflammatory response from infection are collected by immunosuppressant drugs. Therefore a complete and comprehensive investigation is required to establish a diagnosis of UTI in post renal transplantation patients (Figures 9-15).

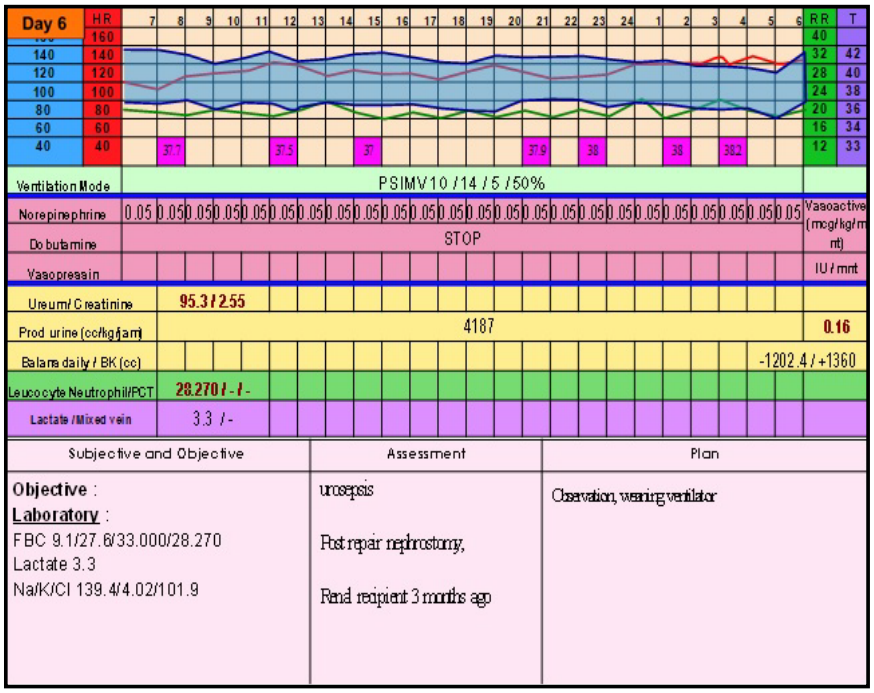

Figure 9 Day 6 observation chart and treatment in ICU

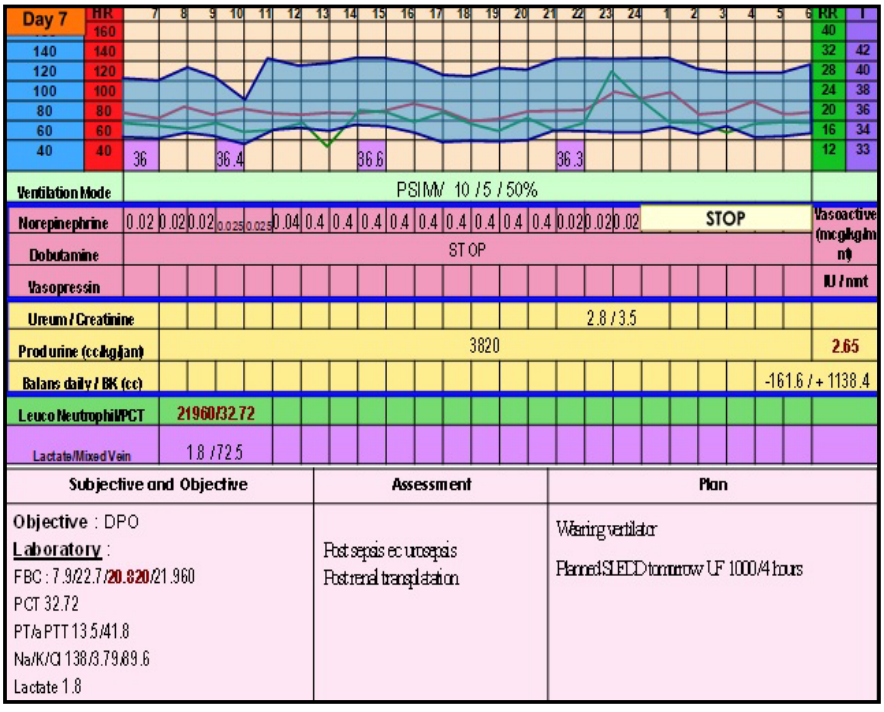

Figure 10 Day 7 observation chart and treatment in ICU

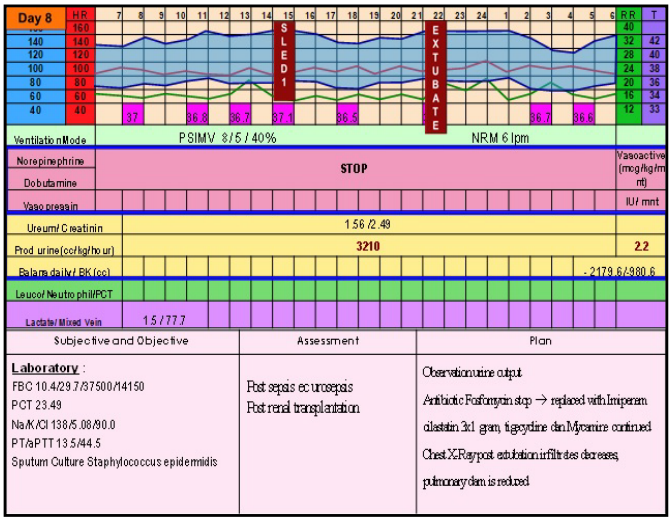

Figure 11 Day 8 observation chart and treatment in ICU

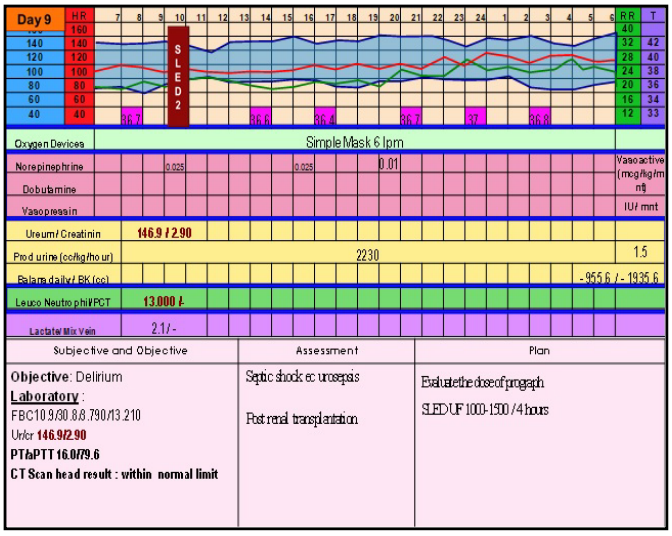

Figure 12 Day 9 observation chart and treatment in ICU

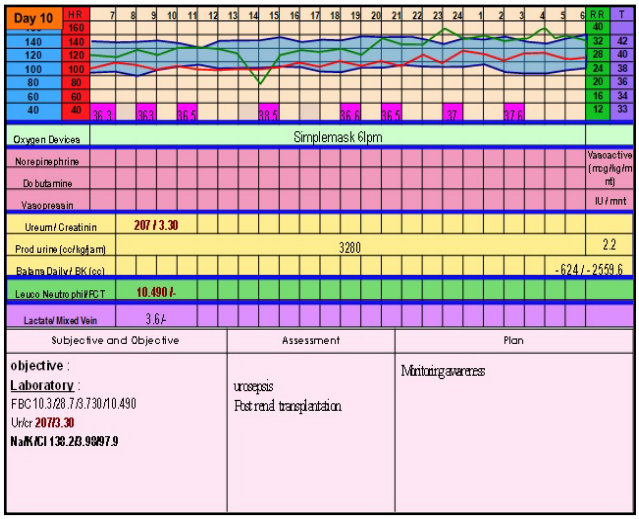

Figure 13 Day 10 observation chart and treatment in ICU

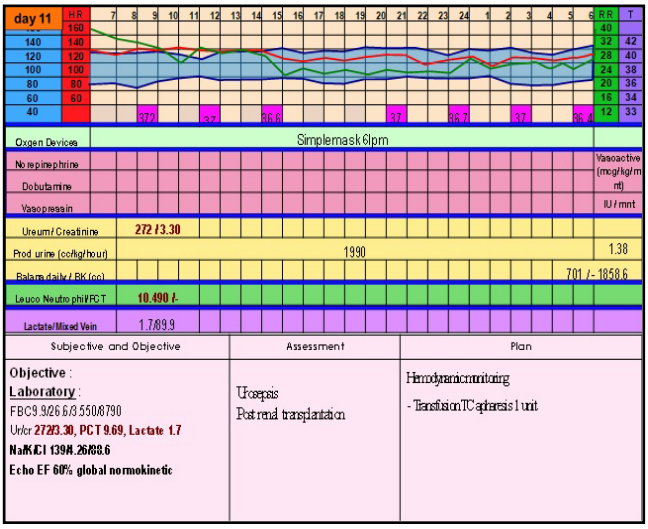

Figure 14 Day 11 observation chart and treatment in ICU

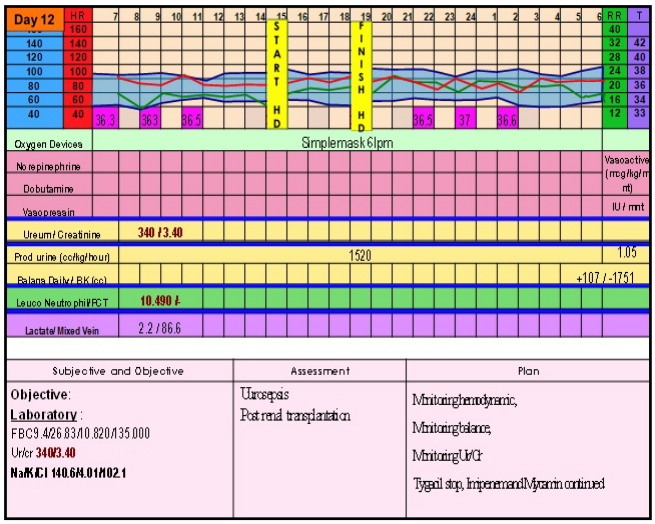

Figure 15 Day 12 observation chart and treatment in ICU

Management

The handling of urosepsis in post-transplant patients should be fast, adequate, and balanced between immunosuppressive status and epidemiological exposure. In principle, the handling consists of:

1. Handling of shock according to survival sepsis campaign (SSC) bundle.
2. Broad-spectrum antimicrobial administration, including anti-fungal or antiviral if necessary.
3. Liquid and electrolyte management.
4. Therapeutic drug monitoring (TDM) for immunosuppressant drugs.
5. Definitive action (urological causes).

Provision of antibiotics as a treatment of bacterial infections aimed at eradication of infectious bacteria and eliminates the source of infection. The study by Naber, et al., demonstrated that administration of fluoroquinolone and piperacillin/tazobactam injectable antibiotics was recommended for urosepsis therapy [5]. Administering antibiotics should be fast and effective so that the antibiotics given are broad-spectrum and includes all the germs that often cause urosepsis is a group of aminoglycosides (gentamicin, tobramycin or amikacin) group of ampicillin combined with clavulanic acid or sulbactam, 3rd generation cephalosporin or fluoroquinolone group (Figures 16-18).

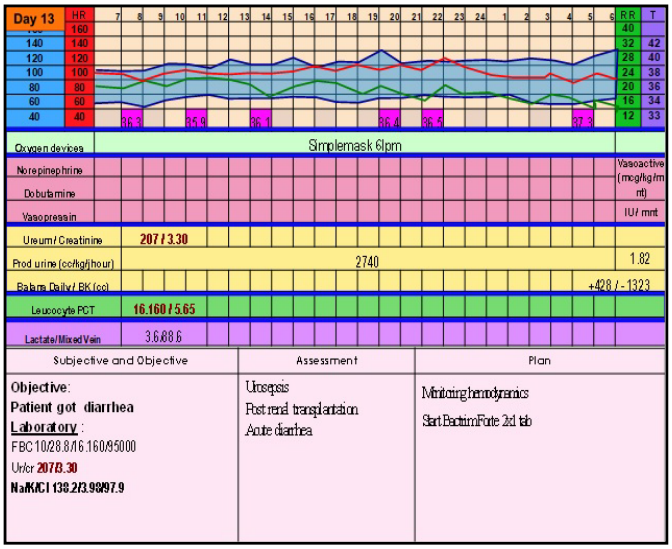

Figure 16 Day 13 observation chart and treatment in ICU

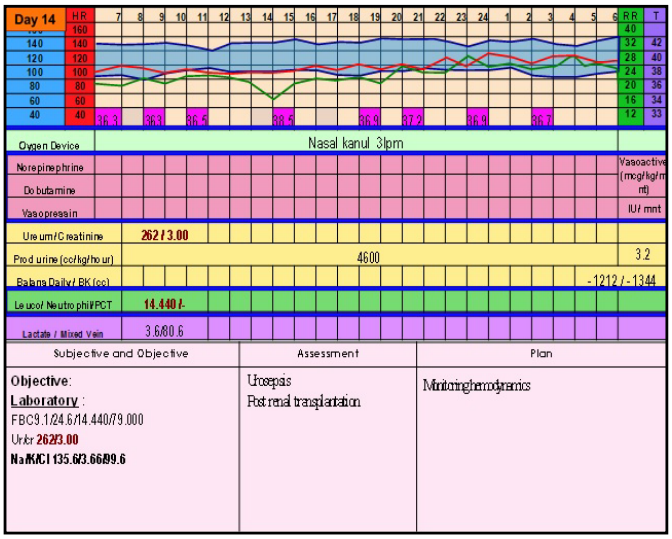

Figure 17 Day 14 observation chart and treatment in ICU

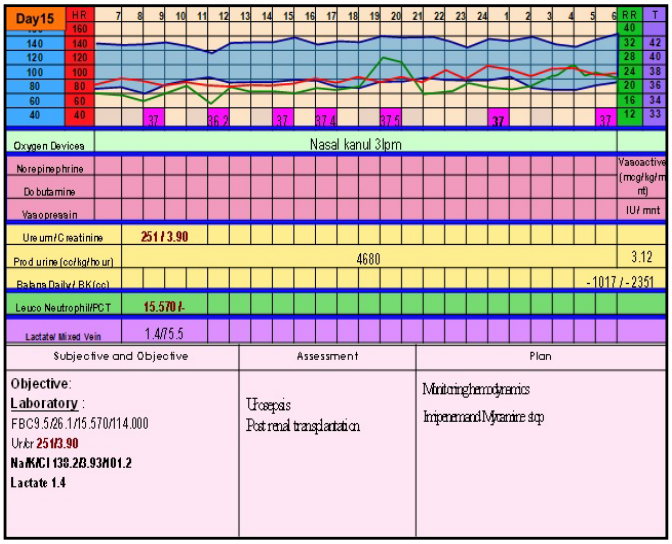

Figure 18 Day 15 observation chart and treatment in ICU

The 3rd generation cephalosporin is recommended to be given 2 grams at 6-8 hours intervals and for cefoperazone and ceftriaxone groups at 12-hour intervals. Subsequent research by Concia and Azzini on levofloxacin proves that levofloxacin as an adjunctive therapy has an effect on renal excretion and is available in the form of intravenous and oral injections [6]. Bjerklund, et al., in the Board of the European Society of Infections in Urology recommends the use of fluoroquinolone or aminoglycosides, combined with broad-spectrum cephalosporin or penicillin's, or carbapenem groups for the management of urosepsis [1].

Resuscitation of fluids, electrolytes, and acid-base is to restore the state to normal. Urosepsis is a fairly severe disease that usually causes decreased oral intake. The condition of fever/febris also requires extra fluid. The fluid and therapeutic requirements can be monitored from blood pressure, central venous pressure, and urine production. If there is electrolyte disturbance, it should also be corrected. When serum is 7 meq/L or more, renal replacement therapy (RRT) needs to be done. RRT is also required when serum creatinine is >10 mg%, BUN >100 mg%, or there is pulmonary edema, or even with patients with hemodynamic instability caused by cytokine storm. Bellomo, et al., in 2007 stated that continuous renal replacement therapy (CRRT) can be a choice of modalities in patients with unstable hemodynamics [7]. CRRT modes that can be used vary according to patient needs. CRRT in the form of continues vena venous hemodiafiltration (CVVHDF) in high volume hemofiltration (HVHF) mode is one method that can be used as blood purification therapy, in addition as renal replacement therapy in patients with catecholamine-resistant sepsis shock [8] (Figures 19-21).

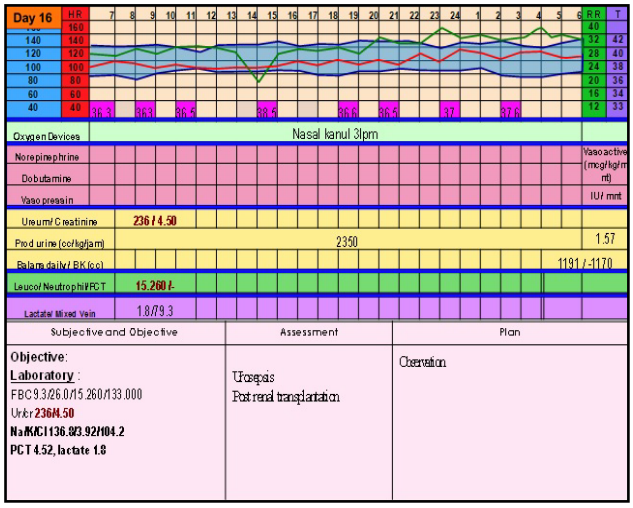

Figure 19 Day 16 observation chart and treatment in ICU

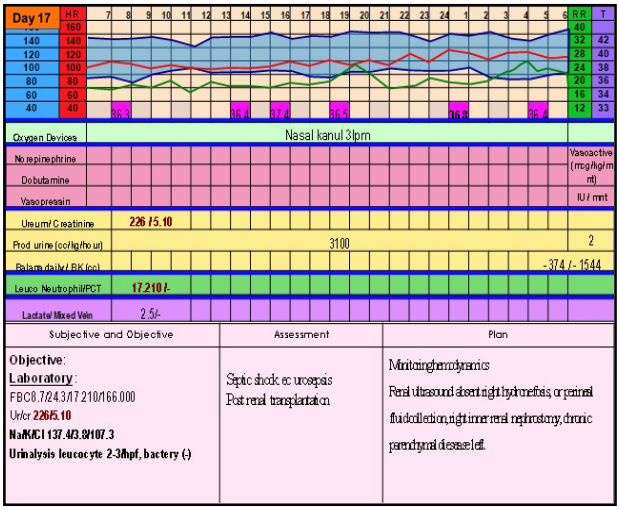

Figure 20 Day 17 observation chart and treatment in ICU

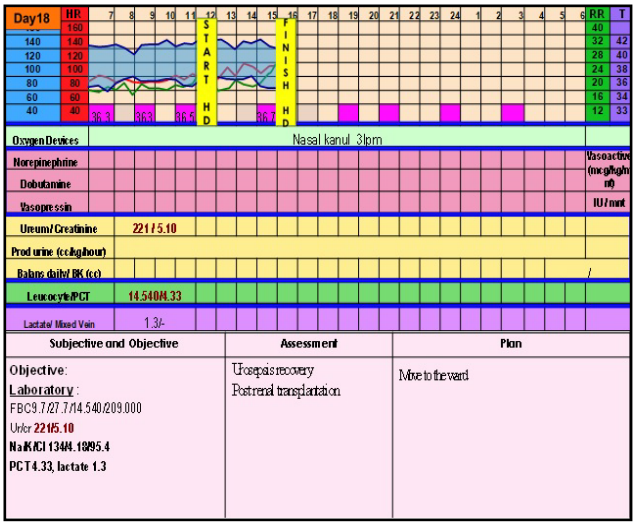

Figure 21 Day 18 observation chart and treatment in ICU

Immediate drainage needs to be done if there is a pile of pus like pyonephrosis or severe hydronephrosis (degree IV). Severe pyonephrosis and hydronephrosis lead to ischemia, thereby reducing the penetration of antibiotics. Drainage can be done percutaneously or with regular surgery (lumbotomy). Patients who have passed the critical period of septicemia should immediately be undertaken definitive measures for their primary urological abnormalities.

CASE REPORT

A 32-year-old man admitted to the ICU with a major complaint of decreased consciousness, shock and respiratory failure.

Preliminary Assessment

Patient post-operative cystoscopy evaluation, cystography, replace nephrostomy renal allograft H. Previously patient had a history as a renal transplant recipient 3 months ago. Patients reported code blue in the room due to decreased consciousness, shock, and respiratory failure.

When he was admitted to ICU, the patient was diagnosed with

- Septic shock urosepsis
- Hospital-acquired pneumonia (HAP)
- Chronic kidney diseases (CKD) post renal transplantation.

The patient was then given oxygen therapy with non-rebreathing mask (NRM) of 10 liters per minute, then fluid resuscitation with crystalloid (ringer lactate) 20 ml/kg/hour but did not respond. He was also given norepinephrine 0.5 mcg/kg/min to achieve 104/70 mmHg blood pressure, pulse 125 times per minute, and SpO_2 98%. However, due to unstable hemodynamics, it was decided to intubate and then perform central vena catheter (CVC) installation.

Supporting Investigations

FBC (Full Blood Count): 10.1/32.3/27.700/265000

Diff Count: 0.2/0/97.3/1.6/0.9/0.6

Blood (serum) glutamic-oxaloacetic transaminase (SGOT) test/serum glutamic pyruvic transaminase level (SGPT): 67/59

Ureum/Creatinine (Ur/Cr): 55/3.8

Protrombin time (PT) /activated protrombine time (aPTT): 1.3/2.0 x control

Albumin 2.77

Sodium/Kalium/Chloride (Na/K/Cl): 134/3.8/95.4

Calcium/Calcium^{2+}/Magnesium (Ca/Ca ion/Mg): 7.5/1.13/1.12

Procalcitonin (PCT): 1079

Blood gas analysis (BGA) artery: 7.460/40.1/103.5/5.2/28.8/97.6

BGA mixed vein: 7.337/27.8/58.4/15/15/74.4

Lactate: 7.2

Blood sugar level: 118

Chest X-ray: No apparent radiological abnormalities in the heart and lungs

Installed catheter double lumen (CDL) and Central vein catheter (CVC) with tip of the superior vena cava projection as high as Th5.

Installed endotracheal tube (ETT) with tip 6 centimeters above the carina.

DISCUSSION

At the time of ICU admission, the patient showed signs of sepsis shock. The diagnosis of septic shock was predicted by the rapid total score change in the sequential organ failure assessment (SOFA), with a score greater than 2 points [4]. The patient was with hypotension and requiring vasopressors to maintain an average arterial pressure of 65 mmHg or higher and lactate serum greater than 2 mmol/L (18 mg/dL) despite adequate volume resuscitation. The risk factor for septic shock in this patient was thought to be immunocompromised due to immunosuppressive drug consumption of celcept, prograph, and methylprednisolone.

After the patient was diagnosed with septic shock, sepsis bundle was immediately carried out. Previously the balance of delivery and oxygen consumption was maintained by intubation so that oxygen consumption can be reduced as much as possible. In addition to fluid resuscitation of 20 cc/kg, the broad spectrum antibiotic administration of meropenem and levofloxacin was immediately given within the first hour of patient admission to the ICU. The micafungin antifungal was also administered considering the patient was immunocompromised with a candida score 3. A culture resistance examination was taken to find the source of the infection and determine the definitive antibiotic. The vasopressor administration was started with norepinephrine to achieve MAP>65 mmHg. Because the norepinephrine dose was too high (reaching 1.1 mcg/kg/min), the combination with vasopressin was administered. The inotropic administration was also performed due to high lactate and suspected SIMD (sepsis-induced myocardial dysfunction). The monitoring during resuscitation and therapy used parameters $ScvO_2$ and lactate blood as a parameter of successful resuscitation and therapy in microcirculation level in addition to macro parameters such as blood pressure, CVP, and urine production that we had been using.

From the results of initial laboratory tests obtained ur/cr increased to 55/3.8, lactate 7.2, and procalcitonin (PCT) was very high, it was 1070. Even with 6 hours in ICU, the patient's condition decreased and urine did not come out. Because of suspected cytokine storm, it was decided to initiate CVVHDF with a dose of effluent rate of 40 ml/kg/h (blood flow rate 80-10ml/hour, fluid removal 60 ml/h, 1000 ml/hour replacement, 1000 ml/hour dialysate, heparin rate of 2ml/hour). CVVHDF was performed for 5 days non-stop, and then after urine started to come out, CVVHDF was carried out with SLEDD as needed.

Immunosuppressive drugs were suspended, but tacrolimus was only reduced to 2×2 mg. Therapeutic drug monitoring of tacrolimus was done so that the optimal dose (5.0-20 ng/ml) could be maintained in the plasma. After the 4th day, the resistance culture results were out. *E-coli* were found in urine, definitive antibiotics, like tigecycline and fosfomycin, were given. The doses administered were normal doses and no dose adjustments were given as the patient was undergoing CRRT. Inotropic dose and vasopressor were reduced each day until they successfully stopped on the 7th day. On the 8th day the sputum culture result came out with *Staphylococcus epidermidis* bacteria. This result was confirmed by pulmonary X-Ray result indicating an infiltrate in the right lung. Based on the result of resistance, it was

decided to replace fosfomycin with imipenem-cilastatin. Patients were extubated on day 8. On day 12, tigecycline was stopped and replaced with bactrim forte. On day 15, imipenem and micafungin were stopped. The PCT on the 18th day before patient moved room was 4.33 with lactate 1.3, urine output 2cc/kg/hour.

CONCLUSION

The balance of immunosuppressant and epidemiological exposure is important in the management of infections in post-transplant patients. A sharp diagnosis, early blood purification therapy, and good antibiotic management determine the success of therapy in these patients. Management of such patients should use the most updated survival sepsis campaign (SSC) guidelines adapted to the situation and conditions in the hospital where the patients are treated.

DECLARATIONS

Conflict of Interest

The authors have disclosed no conflict of interest, financial or otherwise.

REFERENCES

[1] Johansen, Truls E. Bjerklund, et al. "Prevalence of hospital-acquired urinary tract infections in urology departments." *European Urology,* Vol. 51, No. 4, 2007, pp. 1100-12.

[2] Giessing, Markus. "Urinary tract infection in renal transplantation." *Arab Journal of Urology,* Vol. 10, No. 2, 2012, pp. 162-68.

[3] Dellinger, R. Phillip, et al. "Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock." *Critical Care Medicine,* Vol. 41, No. 2, 2013, pp. 580-637.

[4] Singer, Mervyn, et al. "The third international consensus definitions for sepsis and septic shock (sepsis-3)." *JAMA,* Vol. 315, No. 8, 2016, pp. 801-10.

[5] Naber, K. G. "Urinary Tract Infection (UTI) Working Group of the Health Care Office (HCO) of the European Association of Urology (EAU): EAU guidelines for the management of urinary and male genital tract infections." *European Urology,* Vol. 40, 2001, pp. 576-88.

[6] Concia, Ercole, and Anna Maria Azzini. "Aetiology and antibiotic resistance issues regarding urological procedures." *Journal of Chemotherapy,* Vol. 26, No. 1, 2014, pp. 14-23.

[7] Uchino, Shigehiko, et al. "Continuous renal replacement therapy: a worldwide practice survey." *Intensive Care Medicine,* Vol. 33, No. 9, 2007, pp. 1563-70.

[8] Bouza, E., et al. "Co-operative Group of the European Study Group on Nosocomial Infections II: A European perspective on nosocomial urinary tract infections I." *Clinical Microbiological Infection,* Vol. 7, 2001, pp. 532-42.