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Research Article

The Severe Varicella Zoster Infection with Kidney Transplant Patient Using Immunosuppressant

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ABSTRACT

Varicella zoster infection is a self-limiting disease with good outcome. We report an unusual case of varicella zoster infection in kidney transplant patient treated with immunosuppressant. A 44-year-old male patient was admitted to emergency room with complaints of fever, nausea and vomiting. Later on, he presented some blisters, diagnosed as chickenpox and treated with acyclovir. His condition was worsening at the 5th day of treatment and admitted to intensive-care unit. He was passed away at the 8th day of treatment. This case illustrates that immunodeficiency kidney transplant patient had a risk of severe varicella infection.

Keywords: Varicella-zoster, kidney transplant, chronic kidney disease, immunosuppressant

INTRODUCTION

Varicella-zoster virus (VZV) infection is rare in kidney transplant recipients with an incidence of 1% to 11% but is more serious in transplant patients than in the general population. In adults, reactivation in the form of shingles is more common than primary infections because of the incidence of infection everywhere in childhood.[1,2] Chickenpox, due to primary infection or re-infection, is very rare in adults and can be associated with very high morbidity and mortality.[1]

Impaired immunity in immunosuppression-kidney transplant patients may increase the risk of varicella-zoster infection. The incidence of the infection in solid organ transplant patients (SOT) is 10 to 100 times higher than the general population, with lung and heart recipients appearing to be at the highest risk. The most common manifestation is cutaneous.[3]

CASE REPORT

A 44-year-old male patient came to the Emergency Room (ER) of Suaka Insan Hospital (Secondary Hospital) in Banjarmasin with complaints of fever, nausea and vomiting. Patients complained of fever accompanied by nausea and vomiting for 2 days before hospital admission.

He was diagnosed with the end-stage renal disease with hemodialysis for 6 months and since 2 years ago he had undergone a kidney transplant at a hospital in Guangzhou, China. He got immunosuppresants for his kidney transplant (mycophenolate mofetil, steroid and tacrolimus). He had history of chickenpox at young age, no history of diabetes, varicella or urinary stone symptoms. He never had varicella vaccination. His child had varicella zoster virus infection for couple of weeks before admission.

At the ER, he was fully alert, moderate pain, adequate nutrition, with vital signs: blood pressure (BP) 140/100 mmHg, pulse 72 times per minute (tpm), respiration rate (RR) 18 tpm, temperature 37.4 °C. There was no anemic conjunctiva, non-jaundice sclera, nasal lobe breathing (-), oral peri cyanosis (-), pupils were equal. Jugular venous pressure did not increase, lymph nodes are not palpable, no tenderness and no neck stiffness. Chest examination within

normal limit, no rales or wheezing. Abdomen had normal bowel sounds, liver and spleen not palpable. Limb examination showed adequate turgor and no edema, inguinal lymph nodes were not palpable.

Blood test: hemoglobin (Hb) 14.7 g/dl, hematocrite (Ht) 46.7%, leukocyte 10,300/mm3, platelet 151,000/mm3, MCV 80 fl, MCH 26.1 pg, MCHC 31.4%, PPT 17.6 seconds, APTT 38.9 seconds, blood urea nitrogen (BUN) 19 mg/dl, creatinine 1.3 mg/dl, random blood glucose (RBS) 109 mg/dl, Sodium 136 mEq/l, potassium 3.1 mEq/l

Urine: cloudy yellow, blood (-), leukocytes (-), specific gravity 1.015, pH 6.0, Nitrite (-), Albumin (+3), Urobilinogen (+), Bilirubin (-), Leukocytes 2- 5.

Ultrasonography: right and left kidney appeared smaller. There was no other organ abnormality (Figure 1).

He was diagnosed with end-stage renal disease on kidney transplant, observation of fever day 2 caused by Viral (differential diagnose Bacterial) and acute dyspepsia. At the emergency room, he got some therapy: diet 2100 kcal/24 hours, protein 1.6 g/kg/24 hours, IVFD D5% 1500 cc/24 hours, Injection Omeprazole 40 mg/24 hours, per oral Sucralfate 3x5 cc, per oral paracetamol 3x500mg (if necessary), per oral Amlodipine 5 mg. He was admitted to the ward.

On the second day of treatment, he had no fever but abdominal discomfort and bloating. On the 3rd day of treatment, he got some red spots and blisters that appeared on the face and body. He was fully alert with moderate pain, BP: 140/90 mmHg, temperature: 37.0 °C, RR 20 tpm, pulse: 88 tpm, other physical examination did not change. He was consulted with dermatovenerology department and diagnosed with varicella infection. He got a lotion, per oral Acyclovir 5x800 mg, and Injection Ceftriaxone 1 gr/12 hours.

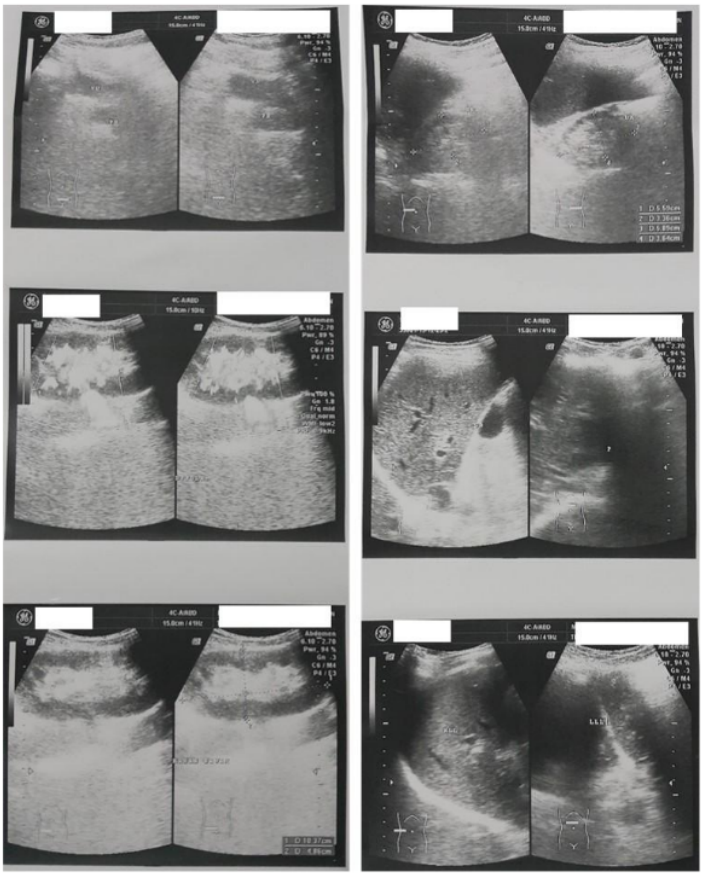

Fig.1. Abdominal ultrasound: right and left kidney appeared smaller, there was no apparent abnormality in the kidney in the lower right abdomen. Other organs had no abnormalities.

On the 5th day, he complained that red spots increased on the face and body. He began to weaken and delirium. Vital signs: BP 90/64 mmHg, pulse 90 tpm, RR 28 tpm, temperature 38.7 °C. Then he was admitted to intensive care unit (ICU). Blood test results Hb 15.5 g/dl, Ht 43%, L 40,040/mm^3, T 28,000/mm^3, MCV 74 fl, MCH 27.41 pg, MCHC 37%. CT scan results showed no abnormality (Figure 2).

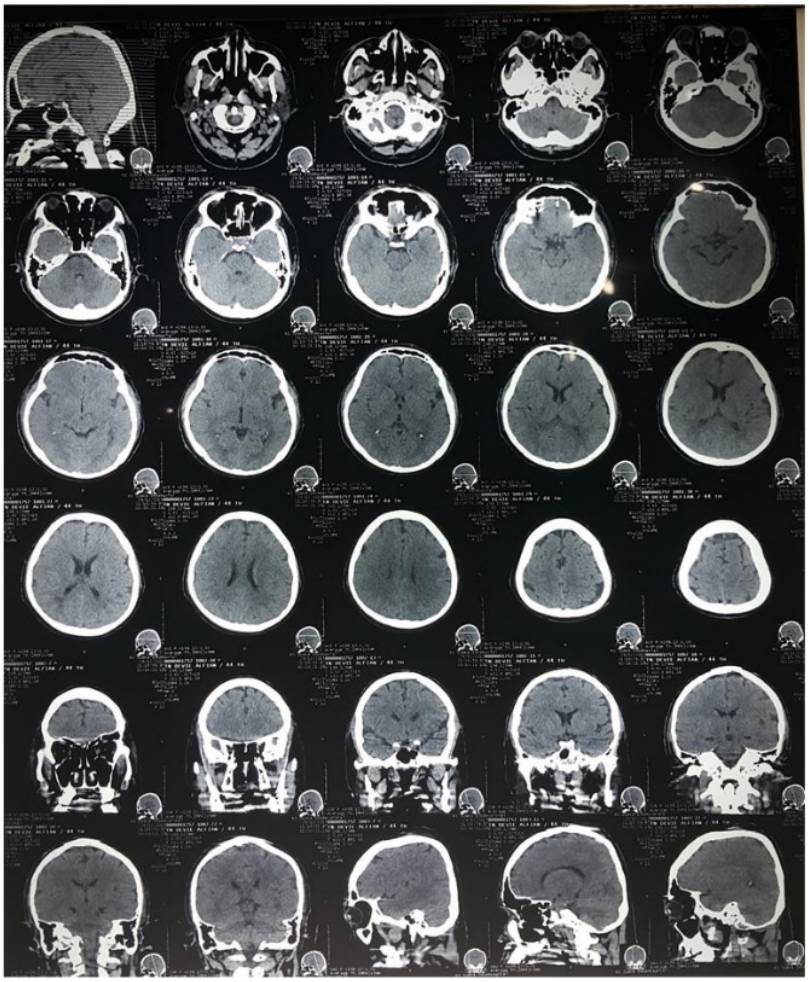

Fig.2: Head CT Scan within normal limits. No intracerebral hemorrhage was seen.

On the 6th day of treatment, he was somnolence and anxiety. BP 70/52 mmHg, pulse 100 tpm, RR 28 tpm, temperature 38.9 °C. The rashes were followed by bloody papules and pustules throughout the face and body (Figure 3). He was consulted to the neurology department with GCS 4-4-6, neck stiffness and diagnosed as meningoencephalitis caused by viral infection. He got acyclovir and piracetam from the neurologist.

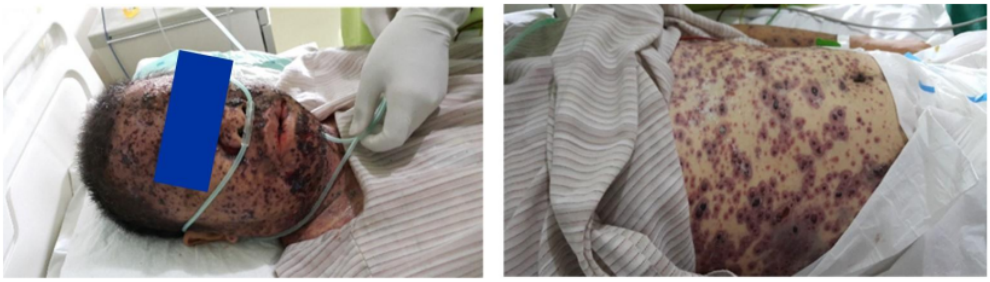

Fig.3: Patient's clinical condition

Laboratory follow-up showed that he had Hb 10.7 g/dl, Ht 28.7%, Leukocyte 25,710/mm^3, T 25,000/mm^3, MCV 73.2 fl, MCH 27.3 pg, MCHC 37.3% , PT 19.9 seconds and APTT 67.3 seconds. RBS 79 mg/dl, Ureum 90 mg/dl, Creatinine 2.1 mg/dl, AST 1,908 IU/L, ALT 980 IU/L.

Diagnosis: septic shock, severe sepsis caused by varicella, meningoencephalitis, with multi-organ dysfunction syndrome (MODS), acute hepatic failure, acute kidney injury on CKD in kidney transplants, thrombocytopenia, suspect DIC. He got fluid resuscitation 1000 cc ringer lactate in 2 hours, and 2500 cc for the next 24 hours, Injection Meropenem 1 gr/12 hours (stop Injection Ceftriaxone).

On the 7th day of care, his condition was worsened. He suffered a decrease of consciousness, fever, nausea, face and foot edema. BP 70/50 mmHg, pulse 112 tpm, RR 28 tpm, temperature 39.3 °C. Laboratory evaluation showed that Hb 8.0 g/dl, Ht 21.8%, Leukocyte 18.200/mm^3, platelet count 21,000/mm^3, MCV 73 fl, MCH 26.8 pg, MCHC 36.8 %. Diagnosis: septic shock, severe sepsis with MODS, (encephalopathy, thrombocytopenia, acute hepatic failure, acute superimposed on CKD), anemia, varicella meningoencephalitis, CKD on a transplant. He got 1000 cc ringer lactate loading in 2 hours follow 2500 cc for the next 24 hours, Injection Meropenem 1 gr/12 hours, norepinephrine infusion starting from 0.1 meq/kg/minute (titration dose) and paracetamol infusion 3x1000 mg. Immunosuppressant drugs were stopped temporarily.

On the next day, his condition was worsening. BP 60/40 mmHg, pulse 116 tpm, respiration rate 28 tpm and temperature 39.3 °C. He got rales from both lungs. Diagnosis: Septic Shock, Severe Sepsis with MODS (Encephalopathy, thrombocytopenia, acute hepatic failure, acute superimposed on CKD), anemia, varicella meningoencephalitis, CKD on a transplant. He was still on norepinephrine. He was passed away on the 8th day of treatment.

DISCUSSION

Kidney transplantation is a therapeutic choice for end-stage renal disease. Kidney transplantation offers patients a better quality of life. They are free from fluid and potassium restriction, free to work and travel, better metabolic function and normal hemoglobin as normal kidney function return. Many factors have contributed to the development of transplants over the past 25 years, one of which is the use of better immunosuppressive agents.[4]

The patient had been undergoing kidney transplants for the past 2 years and during this time there were no complaints. He got 3 immunosuppressants: corticosteroids, mycophenolate mofetil, and tacrolimus. Immunosuppressants are the key to the success of the allograft function. These agents work by suppressing the allograft rejection reaction. Immunosuppressants are used for induction (intense immunosuppressants in the early days after transplantation), maintenance, and handling rejection reactions. However, the use of immunosuppressants also creates its problems. Along with the suppression of the body's immune system, the body will be susceptible to various opportunistic infections which can disrupt the success of kidney transplants but can also cause mortality.[5,6]

The patient had a fever 2 days, the cause of fever in the transplanted patient is still possible due to opportunistic infections. As a result of using drugs that suppress T-cell function, kidney transplant recipients show an increased risk of infection by various intracellular pathogens such as viruses, protozoa, bacteria, and fungi. Post-kidney transplant infections in recipient patients occur in up to 44.9-82% of patients including urinary tract infections, pneumonia, urinary infections and viral infections such as cytomegalovirus and varicella. Overall infections caused by viruses, bacteria,

and fungi are respectively around 50%, 30%, 5% of cases, and in 15% of cases, the infection is caused by polymicrobial.[2,7]

This patient had a varicella virus infection. Viral infections can directly cause invasive diseases while indirectly can support other opportunistic infections and oncogenesis. Rapid and sensitive microbiological testing for various post-transplantation viral infections has been replaced by serological and in vitro culture tests. The progress of this diagnosis has unfortunately not been accompanied by the development of specific and non-toxic antiviral agents and specific vaccines. Any vaccine if possible should be given as early as possible to optimize the immune response. [2,8,9]

The clinical manifestation of viral infections is fever and, pneumonia, enteritis, meningitis or encephalitis and indirect effects such as responses to viral infections in the form of cytokine, chemokine or growth factor release. This results in suppression of the immune system and an increased risk of opportunistic infections. Viral infection can cause surface antigen expression that causes graft rejection reaction or cause dysregulation of cellular proliferation.[8,10,11]

The patient suffered papules and pustules throughout the body that bleed (Figure 3). The patient was diagnosed with varicella virus infection even though no culture or diagnostic examination, but based on the symptoms and clinical signs that there was very clear varicella virus infection which is a group of VZV.

VZV is an alpha herpes virus family, double-chain DNA. This virus is very sensitive to temperature and depends on the protein sheath for its infectivity. Viral infections are transmitted through direct skin contact with skin lesions and respiratory droplets.[12] In this patient, transmission occurred in direct contact with her child who was infected with varicella several days before the patient complained of fever.

Varicella is rarely seen in organ transplant recipients but zoster appears in 11% of organ transplant recipients in the first 4 years after transplantation due to the use of immunosuppressant regimens.[13,14] Some studies even report the use of mycophenolate mofetil, a drug that is often used for immunosuppressants after transplantation, can increase the incidence of zoster in organ transplant recipients and may induce necrotizing herpetic retinopathy.[15] Shingles appear more and more as time goes by after transplantation due to the termination of antiviral prophylaxis accompanied by increased immunosuppressant therapy.[8,12]

At the time of acute VZV infection, prompt diagnosis is needed to choose the right antiviral therapy in immunocompromised patients. VZV can be isolated from tissue culture. However, this method is not fast enough to influence decision making in determining therapy. The fastest test is the virological test to detect VZV antigens using monoclonal antibodies. In this patient, the diagnosis was not made using culture isolation or other methods because of the limitations of resources. The clinical manifestation was very clearly varicella infection (chickenpox).

The patient had been given acyclovir 10 mg/kg orally. Some guidelines recommended it should be given parenterally. Giving antiviral sought as early as possible, especially in the first 24 hours after the rash appears to achieve optimal benefits. If clinical improvement occurs, then antiviral can be replaced orally. Dose adjustment of immunosuppressants should be considered, especially in patients with severe varicella infection. Late parenteral (after 3 days of oral administration) may worsen the condition of the disease. Patients with extensive or invasive skin infections such as these patients who cause pneumonia, hepatitis, encephalitis should be given acyclovir 10 mg/kg/8 hours parenterally. Antivirals are given for a minimum of 7 days or until the lesions turn into crusting. In kidney transplant recipient therapy can be prolonged because the process of changing skin lesions into crusting also usually takes longer. In patients who have resistance to acyclovir, the alternative treatment is phosphonomethanoic acid 40 mg/kg/IV every 8 hours for 10 days. However, phosphonomethanoic acid therapy has a disadvantage because it has the potential to cause metabolic and renal toxicity. Intravenous immunoglobulin can also be used in patients with severe infections, but there are no studies that prove the benefits of this therapy. [8,12]

This patient had never been done vaccination before. Some guidelines recommend that for every organ transplant patient for vaccine administration. Pre-transplant vaccination is indicated in seronegative patients to prevent severe infection, where 2 doses of vaccine are given 4 weeks apart. The selected vaccine must be safe for people with CKD.[16]

CONCLUSION

Kidney transplant patients tend to be immunocompromised due to immunosuppressants so they are vulnerable to infection. Varicella-zoster virus vaccine is needed to prevent infection in the kidney-transplant patient. In case of severe varicella infection in

kidney-transplant patients, antiviral treatment should be considered.

CONFLICT OF INTEREST

The authors denied any conflict of interest.

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