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Systemic Lupus Erythematosus with Severe Renal Dysfunction and Severe Hematological Manifestation Lead to Septic Shock: A Case Report

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ABSTRACT

Background Systemic Lupus Erythematous (SLE) is an autoimmune disease that can cause major mortality and morbidity if untreated well. Various clinical manifestations and adverse events may affect the patient condition. **Case Report** We reported a case of a 31 years old female patient with systemic lupus erythematosus who presented with lupus nephritis and a hematological manifestation lead to septic condition and septic shock. This is a case where initially the patient is well controlled for 1.5 years but due to 6 months of absence treatment, the SLE flare up and she suffers an end-stage renal disease (ESRD). This patient was treated with mycophenolate acid in combination with high dose steroids, antibiotics, granulocyte-colony stimulating factor and underwent hemodialysis. Because of the ESRD and a manifestation of severe neutropenia and lymphopenia, the patient experienced urinary tract infection. She suffered from severe septic with shock condition and passed away later on. **Conclusion** A SLE patient with a severe manifestation of neutropenia and lymphopenia accompanied with end-stage renal failure can cause an opportunistic infection that leads to severe septic shock condition and multi-organ failure.

1. Introduction

The systemic lupus erythematosus (SLE) is an autoimmune disease that affects multiple organ systems. This disease is commonly found in females of the reproductive age group. Lupus nephritis is one of the most severe manifestations of SLE and can lead to end-stage renal disease which had a bad prognosis. It is also a major cause of mortality and morbidity in the young SLE population. Hematological manifestations of SLE can be detected in various conditions such as leucopenia, lymphopenia, thrombocytopenia, anemia, thrombotic thrombocytopenic purpura (TTP) and myelofibrosis. We report a case of 31 years old female with lupus nephritis that suffered an end-stage renal disease and severe hematological manifestations. This patient hospitalized in the High Care Unit of Ulin General hospital and passed away after 14 days of treatment.

2.Case Report

A 31 years old female who came to Ulin

General Hospital of Banjarmasin with chief complained worsening shortness of breath since 3 days before admission. She was previously diagnosed with Systemic Lupus Erythematosus (according to SLICC 2012 criteria, namely malar rash/acute cutaneous lupus, discoid and is given mycophenolate sodium 360 mg twice daily, methylpredniolone 4 mg once a day and calcium supplementation 500 mg three times a day for 1.5 years, but in the past 6 months she stopped his medication himself because he felt there were no complaints anymore. One month before admission, she felt a general weakness and looked pale. She visited the nearby hospital and was diagnosed with anemia. She got a transfusion of 4 packs of red blood cells. No history of bleeding at that time.

On physical examination, she had patchy alopecia, palmar pallor, and plantar edema. Respiratory rate was 28 breaths/minute and the trachea was central. Rhonchi's sound was found on all of her lungs. Pulse rate was 114 beats/minute, blood pressure was 190/100 mmHg. There was a lateral and inferior displacement of the apex beat and heart sounds were muffled (the pericadial effusion cannot be ruled out). The patient had hyper-pigmented lesions on the abdominal skin and ascites.

Urinalysis revealed proteinuria +4 and serum albumin was 2.4 g/L. Serum creatinine was 4.82 mg/dL, serum urea was 216 mg/dL, glomerular filtration rate was estimated to be 11.24 ml/min/1.73m^2. Serum electrolytes were normal. Hemoglobin level was 9.3 g/dL with mean corpuscular volume and mean corpuscular hemoglobin 80.1 fL and 26.9 pg respectively. Direct Coombs test was negative, serum iron and ferritin was normal. Leukocyte count was only 300/µL with an absolute neutrophil count of 103/µL and a total lymphocyte count of 196/µL. The platelet count was 71.000/µL. Blood gas analysis revealed metabolic acidosis. HIV, hepatitis B, and C tests were negative. The anti-nuclear antibody (ANA) was positive and anti-double-stranded DNA (anti-dsDNA) was 479,4 WHO units/mL. A chest x-ray revealed cardiomegaly and pulmonary edema (chest radiograph is not displayed). The electrocardiogram showed sinus tachycardia. The diagnose of acute pulmonary edema was made based on clinical features.

Hemodialysis was performed 2 times and she felt better after that. Ten days later she suffered from high-grade fever and reduced consciousness. The laboratory showed diminished white blood cells and thrombocytes. Leukocyte count was only 270/µL and platelet count was 23.000/µL. Hemoglobin level was also decreased to 7.2 g/dL. Repeated urinalysis showed that there were many leukocytes, bacteria, and yeast (urine culture has not been done). The patient was treated as a septic condition suspected due to a urinary tract infection. She received moxifloxacin 400 mg in combination with fluconazole 200 mg, antihypertension drugs, Ramipril 5 mg daily, and the treatment for SLE was continued with the administration of mycophenolic acid 360 mg twice daily, hydroxychloroquine 200 mg daily, and a high dose of methylprednisolone 500mg/day for 3 days. She also got Granulocyte Colony Stimulating Factor and blood transfusion because there was a bleeding manifestation. Repeated blood urea test result was 327 mg/dL

and creatinine 6.40 mg/dL with eGFR 7.98 ml/min/1.73m^2. Urine output was only 500cc/24 hour. The third hemodialysis was performed but her condition was worsening and she went to a septic shock. Later on patient passed away after 2 weeks of treatment at the HCU Ulin General Hospital.

3.Discussion

Systemic lupus erythematosus is a complex autoimmune condition with various clinical features in which immune complexes play an important role in causing tissue injury, involving multiple organs and systems.[1] SLE manifestations are associated with multiple autoantibodies, ensuing immune complex formation and deposition, and other immune processes.[2] The diagnoses of SLE is usually made clinically with the presence of at least four of the 11 American College of Rheumatology Classification criteria; malar rash, discoid rash, photosensitivity, oral ulcers, arthritis, serositis (pleural effusion, pericardial effusion), renal disorder, neurological disorder, hematological disorder, immunologic disorder, and antinuclear antibodies.[3] The SLICC criteria emphasized that SLE is primarily an autoantibody disease, requiring at least one immunologic criterion to be present, and categorized histology-proven nephritis compatible with SLE as sufficient for classification if antinuclear antibodies (ANAs) or antibodies to double-stranded DNA (dsDNA) were present. While achieving their goal of increasing sensitivity, the SLICC criteria have lower specificity than the 1997 ACR criteria.[4] Our patient fulfilled the above criteria and the diagnosis of SLE with lupus nephritis was made.

Management of lupus nephritis requires a biopsy to histologically classify the condition based on the extensity, activity, and chronicity. The extent of renal involvement is also assessed and provides a baseline subsequent follow.[5] Lupus nephritis is histologically classified into six classes based on the International Society of Nephrology/Renal Pathology Society classification.[6] The six classes have been well described by Seshan & Jennete (2009), Bihl *et al.* (2006) and Weening *et al.* (2004). Our patient refused to perform renal biopsy but from clinical and laboratory finding she had been categorized as an end-stage renal disease that needs renal replacement therapy.

Hematologic abnormalities in SLE are often found. The manifestation including anemia, thrombocytopenia, leukopenia, bisitopenia, and pancytopenia from mild to the severe form. Hematological manifestations are found in 83-85% of SLE patients and the most common is anemia.[7] This patient had anemia chronic disease because the direct coombs test was negative and normal level in serum iron and ferritin. Anemia is thought to be caused by changes in iron homeostasis, inadequate erythropoietin (EPO) responses or erythropoiesis disorders. Low EPO and suppression of erythropoiesis are due to chronic inflammation and anti-erythropoietin autoantibodies. The treatment for anemia in chronic disease is based on the underlying disease and considered blood transfusion if there is a sign of bleeding.[8]

Leukopenia is defined as leukocyte count < 4000/µL in two examinations respectively (ACR criteria) and leukocyte count < 4000/µL in one examination (SLICC criteria). Leukopenia in SLE caused by neutropenia, lymphopenia or both of them.[9] Neutropenia is defined as neutrophils <1000/µL and autoimmune neutropenia are associated with circulatory antineutrophil antibodies, peripheral sequestration, bone marrow inhibition, and neutrophil apoptosis.

Specific therapy is administered of human recombinant G-CSF for 5 days and methylprednisolone pulse 1 gram/day for 3 days can be considered in severe neutropenia, life-threatening, or accompanied by opportunistic infections.[10]

Lymphopenia is defined as a lymphocyte count <1000/μL on ≥ 2 examinations based on ACR and SLICC criteria. Lymphopenia in SLE is associated with the presence of lymphocytic IgG antibodies, decreased expression of the regulatory protein surface complement CD55 and CD59 that causes lysis and increased the production of endogenous alpha interferon. Specific therapy by correcting the underlying disease and prophylactic antibiotics against *Pneumocystis jiroveci* can be considered in severe lymphopenia (<350/μL) with a good safety profile.[9,10]

Thrombocytopenia is defined as a platelet count <100,000/μL and it is found in 10.9-17% of SLE patients. Three important mechanisms that cause this abnormality are due to disruption of production in the bone marrow, sequestration in the spleen, and accelerated the destruction of platelets affected by antiplatelet antibodies. Specific therapy for SLE immune thrombocytopenia is similar to primary immune thrombocytopenic purpura and it is indicated for symptomatic thrombocytopenia with platelets <30,000/uL. First-line therapy is high-dose corticosteroids and when there are no response immunosuppressants can be given.[11]

The manifestation of severe neutropenia and lymphopenia could trigger opportunistic infection (in this case there is insufficient evidence of opportunistic infections) and our patient had also end-stage renal disease. In this condition, the patient is very susceptible to suffer from opportunistic infections and become severe septic with septic shock. Multi-organ damage due to septic shock carries a poor prognosis, later on, the patient passed away after 14 days of treatment of HCU Ulin General Hospital.

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Author's Contribution

INS in study design, data collection, and revision. ACA in writing and editing the main manuscript.

Availability of data and material

All data will be available on request

Ethics approval and consent to participate

Not applicable

Consent for publication

Written informed consent was obtained from the patient's relative for publication. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing Interest

The authors declare that there are no competing interests.

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