The Management of Systemic Lupus with Multi Organ Involvement

Ihsanil Husna, Ari F. Syam,** Djumhana Atmakusuma****

ABSTRACT

Systemic lupus erythematosus (SLE) as a chronic autoimmune disease with multi-organ involvement often occurs in women of childbearing age. We report a case of active SLE in a-23 year old woman who presented with multi-organ involvement, including pericardial effusion, severe anemia that caused congestive heart failure, and kidney involvement. ANA and anti ds DNA were positive. The patient was treated with intravenous digoxin followed by a daily dose of oral digoxin, 80mg/day of furosemide, 600 ml packed red cell transfusion, and 1.5 mg/kg bodyweight/day of prednison. The patient was discharged in good condition on the 15th day of hospitalization.

INTRODUCTION

Systemic lupus Erythematosus is a chronic autoimmune disorder characterised by clinical features of multiple organ involvement and alternate periods of remission and exacerbation. The cause of this chronic systemic inflammatory autoimmune disorder is unknown. Genetic, environmental, and hormonal factors are involved in the pathogenesis, as are characteristic abnormal immune responses that lead to tissue damage. Great variability exists in its clinical presentation, depending on the nature of organ involvement. It is likely that the development of SLE depends on environmental factors and their interplay with susceptibility genes. Females appear to be more susceptible than males.[1,2,3,4] The onset usually occurs during 2nd to 3rd decade of life or during reproductive age. The interval between the onset of the symptoms and the diagnosis varies from a few weeks to several months, and may even be as long as 5 years. The variability in clinical presentation makes it difficult and may delay the diagnosis.[1,2]

The diagnosis of SLE should be established from the presence of 4 out of the following 11 criteria from the American Rheumatism Association (Revised Criteria for the Classification of SLE): malar rash, discoid rash, photosensitivity, oral ulcers, arthritis, serositis, renal disorder, neurological disorder, haematological disorder, immunological abnormalities (Anti Ds DNA, Anti-Sm) and positive ANA.[1,2,5,6,7]

The incidence rate of SLE varies for all races. In Asia, it is estimated that there are 48.8 cases per 100,000 population, while in the United States, it is estimated that there are 14.6–50.87 cases per 100,000 populations, most commonly among African Americans.[1,2]

Early symptoms such as fever, fatigue, and weight loss as non-specific systemic clinical manifestations are often attributed to other diseases. The most common initial manifestation that may cause suspicion of SLE are hair loss, photosensitivity, arthralgia, and chronic anaemia. Anaemia occur in 70% of SLE patients, most of that as autoimmune haemolytic anaemia (AIHA).[6] Severe anaemia can cause heart failure that require blood transfusion.[7]

Cardiac involvement can manifest as pericarditis, myocarditis, pericardial effusion, tamponade, endocardial and valvular lesions (Libman Sach endocarditis, mitral regurgitation), pulmonary hypertension, and anti-phospholipid antibody syndrome. These manifestations can be detected from chest x-rays and echocardiography.[5,7,8] Pericarditis usually occurs during flare ups of the disease. It is clinically detected in about 20-45% of patients during the course of their disease. Pericarditis should be suspected when SLE patients have pleuritic pain, pericardial friction rub or an enlargement of the cardiac sil-

* *Department of Internal Medicine, Faculty of Medicine of The University of Indonesia/Dr.Cipto Mangunkusumo General Central National Hospital, Jakarta, Indonesia*

** *Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine of The University of Indonesia/Dr.Cipto Mangunkusumo General Central National Hospital, Jakarta, Indonesia*

*** *Division of Hematology-Medical Oncology, Department of Internal Medicine, Faculty of Medicine of The University of Indonesia/Dr.Cipto Mangunkusumo General Central National Hospital, Jakarta, Indonesia*

houette on the chest x-ray. Pericarditis due to SLE may be accompanied by other cardiac lesions including veruccous endocarditis, inflammation, and necrosis involving the conduction system and coronary arterial system, frequently in association with nephritis. Cardiac tamponade occurs in less than 10 percent of SLE.[1,2,5,9,10,11]

Kidney involvement occurs in 33-67% of patients and seems to be the most serious complication of SLE[1]. Lupus nephritis has been identified as a predictor outcome of the SLE course. The WHO classification for glomerular disease from renal biopsy is used as guidelines for the treatment. Diffuse, proliferative, and progressive forms of focal proliferative nephritis are associated with poor prognosis than the membranous and mesangial form of the disease.[1,2]

Anti-phospolipid antibody syndrome (APS) is a special problem in SLE. It may occur with coexisting systemic lupus erythematosus (secondary APS) or occur alone (as primary APS). It occurs in one-third of patients, and is characterised by arterial and venous thrombosis, recurrent foetal loss, thrombocytopenia, and lupus anticoagulant and/or anticardiolipin antibody. Livedo reticularis may develop as a skin marker for APS.[1,2]

The main problem in the management of SLE patient is how to make an early diagnosis. The periods of remission and exacerbations make it difficult to choose between a conservative approach and an aggressive approach. In general, conservative treatment is indicated for non life-threatening manifestations, while life threatening disease with major organ involvement and high risk of irreversible organ damage need aggressive intervention.

Conservative treatment is administered for systemic lupus erythematosus with non-specific symptoms such as low grade fever, myalgia, weight loss, fatigue, and musculoscletal complaints. In cutaneous lesions, the use of analgesics, NSAIDS, salisylates, local steroids, antimalarials (cloroquine, hydroxychloroquine), and sunscreen may be adequate.[1,2,5,6,12]

CASE REPORT

The patient, a twenty-year-old woman, was admitted to the hospital with breathlessness since 1 day before admission.

Two years prior to admission, the patient had a spot rash that itched on her cheek. She consulted a dermatologist that treated it as an allergy with pills and creams. After this treatment, she still suffered from this skin problem, come and goes for about 8 months. A couple months later, she had other problems such as hair loss, pale, fatigue, headache, arthralgia, and rash in her face especially after exposure to sunlight. She also started to feel breathless and this condition became worse up to the point when she came to the hospital. She felt that even with minimal activities, she suffered from difficulty in breathing. She needed two pillows to sleep, and often suddenly awoke at night. The patient also suffered from swelling of her lower extremities. There was no history of other chronic illness, drug reaction nor allergy, oral ulcers or abnormality of the menstrual cycle. None of her family members suffered from this kind of disease. There was no history of hypertension from her parents.

During physical examination, she was found to be severely ill, fully alert, with a blood pressure of 130/80 mmHg, a heart rate of 140 beats/m, a respiratory rate of 24 x/m, a temperature of 37,3° C. Her conjunctiva were pale, and her sclera were not icteric. There were no oral ulcers. There was erythema on the skin of her face. The jugular venous pressure was 5+2 cm H_2O. From the heart examination, we found gallop and systolic murmur grade III at all ostia. Lung examination revealed high-pitched crackles. The abdomen showed no enlargement of the liver. There was shifting dullness. There were bipedal edemas in both of the extremities.

The initial laboratory findings revealed a haemoglobin level of 5.5 g/dl, a white blood cell count of 6000/mm^3, a platelet count of 378,000 /mm^3, and an ESR of 135/1 hr. The patient's reticulocyte count was 14%. The patient's MCV was 68, MCH 22, and MCHC 32. Morphological examination of erythrocytes showed microcytic hipochrome anemia and anisopoikilsitosis. The coombs test examination was negative. The electrolytes were within normal limit. Proteinuria was +++. ANA was positive 1/40 and Anti Ds DNA was positive 2670 (N<200), C3 was 52.9 (N: 15-39), and C4 was 3.0 (49-94). Liver enzyme and creatinine levels were within normal limits. ECG showed low voltage, sinus rhythm, QRS rate 140 x/m, no hypertrophy, and normal ST-T waves. Chest X-ray showed CTR 60% and cardiac silhouette.

The problems in this patient were congestive heart failure functional class III-IV, pericardial effusion, severe anemia, systemic lupus erythematosus (SLE), and.nephritic lupus. The congestive heart failure functional class III-IV was treated with 1 cc/6 hour of digoxin until the heart rate was below 100 beats/m, followed by oral digoxin, 80 mg/day of intravenous furosemide, and potassium supplementation. Transfusion of packed red cells was given to this patient due to the severity of the anemia. After 2 days and 600 cc of blood transfusion,

the patient's haemoglobin level was increased to 10.0 g/dl.

For her systemic lupus erythematosus, she was treated with 75 mg/day of prednisone and ranitidine 150mg twice daily.

During treatment, the patient's breathlessness gradually decreased followed by a reduction in bipedal edema and jugular venous pressure. The congestive heart failure was compensated on the fifteenth day of hospitalisation. Echocardiography showed moderate pericardial effusion, with left ventricle systolic and diastolic function within normal limits, and there was no hypokinesia of the valves. On follow up echocardiography examination two weeks later, there was reduced pericardial effusion. The treatment was continued with 0.25 mg of oral digoxin once daily, 40 mg/day of furosemide, and a single daily dose of oral potassium.

On the 14th day of hospitalisation the patient developed tonsilopharingitis, with leukocytosis. The patient received 500 mg of Cefadroxyl twice daily for seven days.

Laboratory findings showed a slightly elevated anticardiolipin IgG (26.3) and IgM (38.3), with absence of antiphospolipid anti body syndrome.

For the kidney involvement, the protein was reduced to 1+, after 7 days of treatment. The proteinuria quantitative value was 690 mg/24 hours. The proteinuria remain 1+ until the 15th day of hospitalization.

The patient was discharged after 16 days of hospitalisation under good condition. She was advised to come for regularly control visits and take her medicine regularly and continuously.

DISCUSSION

Systemic Lupus Erythematosus is defined by its clinical features. ARA has established criteria to distinguished SLE from other connective tissue diseases. In this patient, SLE was diagnosed based on the criteria from the American Rheumatism Association. There were malar rash, photosensitivity, serositis (evidence of pericardial effusion), hematologic disorder (anaemia), renal disorder (proteinuria greater than 0.5 g/d), and an abnormal titer of ANA and positive anti ds DNA. Alopecia and anemia indicated active disease that had commenced for more than 1 year.

Laboratory tests such as complete blood count, erythrocyte sedimentation rate, C3 and C4 testing can be used to evaluate the activity of the disease. In active disease, normochromic normocityc anemia is often found. However, leukopenia or lymphocytopenia are used to differentiate it from rheumatoid arthritis.[1,2,5]

In 70-80% of SLE patients, anemia due to chronic disease is present, which may be aggravated by poor iron intake and malnutrition in some Asian patients.[1] In this patient, we found chronic severe anemia that made the patient seek medical attention. From the laboratory findings there were severe anaemia with elevated of blood sedimentation rate, increased of C3, and positive ANA as well as anti ds DNA. There was no leucopenia nor lymphocytopenia and trombocytophenia. Anemia as the first manifestation occurs in 60-80% cases. Severe anemia can cause congestive heart failure needing blood transfusion.[4,11] For the problem of anemia, we gave blood transfusion until the hemoglobin was increased to 10.0g/dl.

Actually, polyarthitis and dermatitis are the most common first clinical manifestation of SLE, and the most common present symptoms.[2] In this patient, we found anemia as the first manifestation of SLE. The other report from Jakarta also reported anemia as the first manifestation of SLE.[4]

Renal disease occurs in 20-50% of all SLE patients, but end stage of renal failure is rare (<5%).[2] Renal biopsy should be performed to guide the treatment. WHO classification of glomerular diseases classifies renal involvement in 5 classes. In this patient, a proteinuria of 690mg/24 hours makes nephritis lupus as one of the major target organ of this disease. We had planned to make a renal biopsy for the further treatment, but since the protein level was less than 1 gram/24 hours, while hematuria was absent and the creatinine level was normal, the biopsy was cancelled.

As to cardiovascular involvement, several clinical studies have shown a high incidence of cardiovascular involvement such as pericardial effusion, tamponade, presence of murmur, particularly with heart valve involvement (Libman-Sacks endocarditis) associated with antiphospolipid antibody syndrome, and heart failure.[1] Pericardial involvement was observed in more than half of patients and suggest active diseases.[9] Pericarditis is the most frequent manifestation of cardiac lupus, and pericardial effusion can lead to tamponade.[8] Myocarditis can cause arryithmia, sudden death, and heart failure. Endocarditis Libman sach is associated with anti-phospholipid antibodies syndrome and is also an uncommon complication, but could cause cardiac emboly. These symptoms are usually associated with anti-phopholipid antibodies syndrome. Myocardial infarct usually results from degenerative disease, although it can be caused of vasculitis.[6,7] The increase in IgM and IgG of anticardiolipin antibodies may be correlated to the cardiac involvement in SLE.

In this patient, echocardiography showed moderate pericardial effusion as a part of serositis. Such condition was also aggravated by dyspnoea due to severe anemia. Congestive heart failure in this patient was due to prolonged severe anemia aggravated by moderately pericardial effusion.

The lupus anticoagulant and anticardiolipin antibody are manifestations of APS, with clinical manifestations of thrombocytopenia, recurrent fetal loss, recurrent thrombosis and valvular heart disease.[9] Evaluation of APS in this patient showed slightly elevated IgM and IgG anticardioplipin antibodies without clinical manifestations of APS.

Aggressive therapy is required in CNS, renal, cardiac and hematological involvement in SLE. High doses of prednisone is indicated for SLE with life-threatening manifestations such as moderate to severe pericardial effusion, hemolytic anemia.[1,2] After the disease is controlled, therapy should be consolidated to one morning dose; thereafter, the daily dose should be tapered as rapidly as the clinical disease permits. In this patient, 1.5mg/kg/day of prednisone was useful in treating multi-organ involvement in SLE.

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