Treatment of Lupus Nephritic with Severe Preeclampsia: A Case Report

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Abstract

A 25 years-old pregnant woman with history of Systemic Lupus Erythematosus (SLE) complained shortness of breathing and swelling legs. Physical examination showed hypertension, tachycardia, tachypnea, anemic conjunctiva, and pitting edema in both legs. Workup examination found anemia, hypoglycemia, hypoalbuminemia, proteinuria, metabolic acidosis, strong positive dsDNA, trivial MR, mild TR, PR, dilated LV, decrease of LV systolic function, hypokinetic global LV, eccentric LVH, and severe oligohydramnios. The patient was diagnosed with severe preeclampsia, severe oligohydramnios, SLE, Lupus Nephritic (LN), stage II JNC VII hypertension, and peripartum cardiomyopathy.

An emergency caesarean section was planned as the main management to prevent infant and maternal morbidity and mortality. MgSO4 was given to prevent eclampsia. Methylprednisolone and azathioprine were given to control SLE and LN activity. Furosemide, spironolactone, ramipril, methyldopa and nifedipine were given to control blood pressure, help normalizing heart function, and prevent organ failure. The patient was suggested to postpone next pregnancy until 1 year after LV function turns to normal.

Keywords: *Lupus Nephritic, Pregnancy, Systemic Lupus Erythematosus, Severe Preeclampsia*

Introduction

LN developed during conception or pregnancy increases the risk of preterm birth (34%), pre-eclampsia (10-35%), maternal mortality, fetal death, neonatal death (12-38%), intrauterine growth delay (30%), chronic kidney disease (CKD) and end-stage renal disease (ESRD).[1]

Pre-eclampsia causes risk of stroke, premature birth and even death. Severe pre-eclampsia can develop into eclampsia with grand mal seizures.[2]

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Differentiating active lupus nephritis from pre-eclampsia becomes one of the biggest challenges in managing SLE patients with pregnancy. They both present with proteinuria, hypertension, leg edema and systemic effect, yet the treatment of these two diseases is different. Pre-eclampsia will improve once the pregnancy terminated and active SLE requires immunosuppression as treatment.[3]

Case Report

A pregnant woman, 25 years old housewife living in Gresik, Jawa Timur, Indonesia, visited Dr. Soetomo General Hospital with a chief complaint of shortness of breathing.

The patient suffered from shortness of breath starting from early pregnancy worsened 1 week before admission with exertion or while walking long distances and improved with rest. The patient also complained of

swelling in both legs since early pregnancy, worsened in the last week before admission.

It was her third pregnancy aged 39 weeks. There was no history of hypertension in the previous pregnancies. During the third pregnancy, the blood pressure was always normal, except 1 month before admission.

The patient was diagnosed with SLE in 2017 in other hospital due to malar rash, photosensitivity, joint pain, hair loss, mouth sores and positive result of ANA test and routinely consumed methylprednisolone 4 mg once per day, azathioprine 50 mg twice per day, and calcium lactate 1 tablet once per day. The therapy was continued during this pregnancy.

Physical examination found hypertension (170/100 mmHg), tachycardia (104 beats per minute), tachypnea (24 times per minute). The conjunctiva was anemic. There was pitting edema in both legs.

Laboratory tests resulted anemia (Hb 9.3 g/dL, Hct 28.1%). Complete urine examination showed proteinuria (3+). ANA profile test showed strong positive dsDNA. Echocardiography examination found trivial mitral regurgitation (MR), mild tricuspid regurgitation (TR), mild pulmonal regurgitation (PR), dilated left ventricle (LV), decrease of LV systolic function (EF by Teich 44%), hypokinetic global LV, eccentric LV hypertrophy (LVH). Obstetric USG showed severe oligohydramnios.

According to the history taking and examination, the patient was diagnosed with severe preeclampsia, severe oligohydramnios, SLE, LN, stage II JNC VII hypertension, and peripartum cardiomyopathy (PPCM).

A CITO caesarean section was planned due to severe preeclampsia and severe oligohydramnios. The patient was given MgSO4 40% intravenously 1 gram every hour up to 24 hours postpartum, nifedipine 10 mg every 8 hours orally if blood pressure ≥ 160/110 mmHg, methyldopa 500 mg every 8 hours orally, furosemide 20 mg every 8 hours intravenously, isosorbide dinitrate 5 mg every 8 hours orally, methylprednisolone 62,5 mg once 3 hours before C-section continued by methylprednisolone 62,5 mg 3-6 hours post C-section and calcium 500 mg per day. The patient was also given furosemide injection 20mg intravenously every 8 hours, spironolactone 25mg every 24 hours orally, and ramipril 2,5mg every 24 hours orally to help normalizing heart function. The dose of methylprednisolone was tapered down to 16 mg every 8 hours and azathioprine 50 mg twice per day was given.

The patient was discharged on the eight day of care and suggested to postpone next pregnancy until 1 year after LV function turns to normal. The patient was also planned to visit out-patient clinic after discharged, but she did not.

Discussion

Pregnancy and SLE influence each other. Hormonal and immunological changes in pregnancy can affect SLE activity in general, causing both short-term and long-term adverse effects on renal function. On the other hand, SLE leads to pregnancy complications such as preeclampsia, premature birth and fetal loss. Women with SLE are able to control their pregnancy if they choose the optimal time for conception and have proper management during their pregnancy.[1,4]

Distinguishing LN flare and pre-eclampsia is challenging due to similar symptoms and possibly simultaneous occurrence.[5]

Diagnosis criteria of SLE according to ACR are: (1) malar rash: (2) discoid rash (3) Photosensitivity (4) inflammation of the mouth or nose (5) non-erosive arthritis in two or more joints accompanied by tenderness, swelling or effusion, (6) heart-lung involvement (7) neurological disorders (8) kidney disorders (9) hematological disorders (10) immunological disorders (11) nuclear antibody (ANA) positive test if no known drugs can trigger.[6]

The patient had been diagnosed with SLE in 2017 in other hospital due to malar rash, photosensitivity, joint pain, hair loss, mouth sores and positive result of ANA test before admission.

Criteria of LN based on ACR are persistent proteinuria more than 0.5 mg per day or more than 3+ by dipstick, and/or cellular casts including red blood cells, white blood cells, hemoglobin, granular casts, tubular casts, or mixed casts.[7] According to the Italian Nephrology Society, renal flare-ups are defined as an increase in proteinuria of at least 2 g per 24 hours if the basal proteinuria is less than 3.5 g every 24 hours, or doubled if the basal proteinuria is more than 3.5 g per 24 hours, accompanied with concurrent microhematuria and cell cylinders in the urine sediment. Active LN is defined as the appearance of active urine sediment and/or proteinuria more than 0.5 g per day with or without an increase in serum creatinine.[8] Other results found are increase in ds-DNA antibodies and decrease in complement levels.[3] Meanwhile, inactive LN lupus was defined as proteinuria less than 0.5 g per day without urine sediment.

Complete urine examination in this patient resulted proteinuria (protein 3+). C3 and C4 examinations showed low values (C3 27.4 mg/L C4 7 mg/dl). And obtained high ds-DNA antibody results on the ANA profile examination. Therefore, this patient was categorized into active LN based on criteria mentioned.

SLE disease activeness in pregnancy is assessed by modifying the SELENA-SLEDAI score. The score of 3 or less is not counted as a flare, 2-12 is counted as mild to moderate flare, and more than 12 is counted as severe flare.[9] The score of this was 2, so that the patient did not undergo flare.

Diagnostic criteria of preeclampsia are persistent systolic blood pressure of 140 mmHg or higher, or a diastolic blood pressure of 90 mmHg or higher after 20 weeks of gestation in women with previously normal blood pressure, may accompanied by proteinuria 300 mg or more in a 24-hour urine collection. Proteinuria is not absolute criteria for preeclampsia. According to the criteria of the American College of Obstetricians and Gynecologists (ACOG), if preeclampsia is accompanied by systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 110 mmHg while resting, thrombocytopenia, elevated liver enzymes, severe right upper quadrant pain or epigastric pain that does not respond to treatment, progressive renal insufficiency, pulmonary edema, visual disturbances or brain disorders, it is classified into severe preeclampsia.[10] In this case, he patient was classified into severe preeclampsia due to blood pressure of 170/100 mmHg and edema in both legs.

Termination is the main therapy for preeclampsia. Those who have not reached term and have no severe manifestations are still evaluated with a non-stress test 2 times a week.[10] Therapy for severe preeclampsia includes corticosteroids for fetal lung maturation, MgSO4 for eclampsia prophylaxis, and anti-hypertension. The systolic blood pressure target is less than 160mmHg and diastolic less than 110mmHg. The first-line treatment for anti-hypertension in preeclampsia is nifedipine, hydralazine, and labetalol with alternative nitroglycerin and methyldopa.[11]

Patients with severe preeclampsia should be treated with expectative care. If there are contraindications to expectative care, delivery of the pregnancy should be prepared and carried out in stable condition. Contraindications for expansive treatment include eclampsia, pulmonary edema, dissemination of intravascular coagulation (DIC), severe and uncontrolled hypertension, fetal emergency, placental solution, and intrauterine fetal death. Complications of expected treatment include persistent symptoms, HELLP syndrome, IUGR, severe oligohydramnios, premature rupture of membranes, and severe kidney problems. If there are complications, corticosteroids should be given for lung maturation and delivery must be prepared.[11]

The patient was then planned for a caesarean section with indications of severe pre-eclampsia and severe oligohydramnios. Patients were also given injection therapy of 40% MgSO4 intravenously 1gram every hour up to 24 hours postpartum, nifedipine 10mg every 8 hours orally (if blood pressure ≥ 160/110 mmHg), methyldopa 500mg every 8 hours orally.

The treatment of LN consists of two phases: induction and maintenance. Induction therapy refers

is purposed to cure active disease while maintenance therapy to continuously maintain the remission and prevent organ damage.

Corticosteroids the main treatment of LN. They are effective in controlling kidney flares, but not to improve long-term results alone. However, steroid exposure should be limited to a minimum during pregnancy. High doses during pregnancy are associated with an increased risk of diabetes, hypertension, pre-eclampsia, premature rupture of membranes and congenital fetal abnormalities. Nevertheless, short doses and/or high doses of intravenous methylprednisolone can be used in the case of flares.[12]

Azathioprine may be the safest immunosuppressant drug to take during pregnancy. This drug is recommended especially if it has been consumed before pregnancy.[2] Apart from azathioprine, other immunosuppressants that can be used during pregnancy are cyclosporin A and hydroxychloroquine.[3]

The patient had taken 3x8mg Methylprednisolone orally, Azathioprine 2x50mg orally, 1x1 calcium lactate before admission. Then, the patient was then given methylprednisolone 1x62.5mg intravenous therapy 3 hours before cesarean section then followed by injection of methylprednisolone 62.5 mg intravenously every 3-6 hours postoperatively. Methylprednisolone therapy was continued and tapered down on the third day. Azathioprine 2x50mg was continued.

SLE in pregnancy should be monitored by an obstetrician and rheumatologist.[5] Pregnancy should be postponed until the disease is said to be inactive, at least 6 months before conception.[2] Basic laboratory tests should be repeated at the first prenatal visit and must be checked if no preconception counseling has been done. Monthly prenatal visits are necessary. The frequency of laboratory examinations depends on SLE or LN activity. Serial fetal ultrasound examination is planned to monitor fetal growth.[1]

A kidney biopsy is only indicated to rule out or classify LN if the results will affect management, due to risk of bleeding after biopsy in pregnancy.[5] A kidney biopsy is not recommended after 32 weeks of gestation.[1]

Conclusion

LN is often superimposed severe preeclampsia, which could end up with maternal and fetal mortality. This case showed early diagnosis and proper treatment. This kind of case commonly happens in pregnant women with LN.

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References

1. Stanhope TJ, White WM, Moder KG, Smyth A, Garovic VD. *Obstetric Nephrology : Lupus and Lupus Nephritis in Pregnancy*. 2012;**1**:2089–99.
2. Clowse MEB. *Lupus Activity in Pregnancy*. Rheum Dis Clin North Am. 2007;**33**:237–52.
3. Iozza I, Cianci S, Di Natale A, Garofalo G, Giacobbe AM, Giorgio E, et al. *Update on systemic lupus erythematosus pregnancy*. J Prenat Med. 2010;**4**:67–73.
4. Wu J, Ma J, Zhang W-H, Di W. *Management and outcomes of pregnancy with or without lupus nephritis : a systematic review and meta-analysis*. 2018;**14**:885–901.
5. Knight CL, Nelson-Piercy C. *Management of Systemic Lupus Erythematosus During Pregnancy*. Annu Rev Med [Internet]. 2017;**68**:271–85. Available from: http://www.annualreviews.org/doi/10.1146/annurev-med-042915-102658
6. Rekvig OP. *Systemic Lupus Erythematosus: Definitions, Contexts, Conflicts, Enigmas*. 2018;**9**:1–16.
7. Hahn BH, McMahon MA, Wilkinson A, Wallace WD, Daikh DI, Fitzgerald JD, et al. *American College of Rheumatology Guidelines for Screening , Treatment , and Management of Lupus Nephritis*.

2012;**64**:797–808.

8. Mecacci F, Simeone S, Cirami CL, Cozzolino M, Serena C, Rambaldi MP, et al. *Preeclampsia in pregnancies complicated by systemic lupus erythematosus (SLE) nephritis : prophylactic treatment with multidisciplinary approach are important keys to prevent adverse obstetric outcomes*. J Matern Neonatal Med [Internet]. 2017;**0**:1–7. Available from: https://doi.org/10.1080/14767058.2017.1404570
9. Buyon JP, Kalunian KC, Ramsey-Goldman R, Petri MA, Lockshin MD, Ruiz-Irastorza G, et al. *Assessing disease activity in SLE patients during pregnancy*. 1999;677–84.
10. American College of Obstetricians and Gynecologists. *Hypertension in Pregnancy*. Joseph Jr GF, O'Reilly N, Politzer A, Son S, Ngaiza K, editors. Washington, DC; 2013. 17–20 p.
11. Wibowo N, Frisiantiny E, Karkata M, Mose J, Chalid M, Siswishanto R, et al. *Pedoman Nasional Pelayanan Kedokteran Diagnosis dan Tatalaksana Pre-Eklamsia*. Jakarta: Perkumpulan Obstetri dan Ginekologi Indonesia; 2016.
12. Jaryal A, Vikrant S. *Current status of lupus nephritis.* Indian J Med Res. 2017;**145**:167–78.