

CASE REPORT

Challenging Therapy In Pregnant Woman With Systemic Lupus Erythematosus (SLE) and Chronic Hepatitis B

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ABSTRACT

Systemic Lupus Erythematosus (SLE) is an autoimmune disease that attacks various body systems, especially in women of reproductive age. Therefore, patients who are planning a pregnancy or are pregnant need to assess the risk and predicts of disease activity during pregnancy. The most common complications of SLE in pregnancy are SLE disease activity, preterm delivery, preeclampsia and pregnancy loss. Here, we report a pregnant SLE patient with co-infection hepatitis B. As the consequence of treated with immunosuppressant agent, both disease progression and immunosuppressant agent can lead to severe infection. Furthermore, perinatal transmission is the most common form of transmission of hepatitis B. Finally, proper management could save mother and newborn.

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Introduction

Systemic Lupus Erythematosus (SLE) is an autoimmune disease predominantly affects women of reproductive age. Gene and environmental factors are known to cause this disease.¹ SLE is characterized by the formation of pathogenic autoantibodies against nucleic acids and their binding proteins caused by intolerance to the body's own components. The highest incidence of SLE is found in the United States of 23.2 / 100,000 population each year with prevalence 241 / 100,000 population. Rheumatology as outpatient clinic in several hospitals in Indonesia showed an increase in SLE patient visits by 17.9-27.2% (in 2015); 18.7-31.5% (in 2016); and 30.3-58% (in 2017). The ratio of women and men is 15: 1 to 22: 1. With a good initial approach, survival rate has increased globally over the past five decades, around 74.8 and 63.3% (in 1950) to 94.8 and 91.4%.²

A well-prepared pregnancy in SLE women has a favorable prognosis.^{1,3} However, we should aware of complications of SLE during pregnancy. Disease flares can occur during pregnancy. Preeclampsia and lupus nephritis are two conditions that can occur. Both conditions can be distinguished thorough careful examination.⁴

Hepatitis B virus (HBV) infection is a major health problem in the world in general, including Indonesia. It is estimated that more than 2 billion people has been exposed

to HBV. Approximately, prevalence HBV in Indonesia 4-20.3%. Reactivation of HBV replication complicated liver decompensation in immunosuppressed patients is reported to occur around 20-50% in patients with hepatitis B infection undergoing chemotherapy or immunosuppression. Pregnant hepatitis B patients whose treatment decisions must be adjusted according to their conditions and benefits. Due to the close relationship between the immune system and the hepatitis B virus (HBV) replication, it is essential to monitor patients with current or past HBV infection under any type of immunosuppression.⁵

Case report

A 30-year-old pregnant woman came to emergency department due to general weakness 3 days prior to admission. She felt weakness, headache, epigastric pain, nausea and blurred vision. There was no rash at her face, shortness of breath, joint pain and hair loss. She also did not feel increase of appetite or loss of weight. There was no history of diabetes mellitus, hypertension, cardiovascular disease, hyperthyroidism, nor abortion. She confessed had previous history of muscle ache, weakness, and hair fall on 2016. She was diagnosed with SLE, anemia and hepatitis B since 2016. Her disease progression was controlled with medication cyclosporine 2x25 mg tablet, methylprednisolon (MP) 8-8-0 mg tablet daily and lamivudin 1x100 mg tablet. Physical examination showed lethargic, blood pressure 180/100

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mm Hg, pulse 109 beats per minute, respiratory rate 20 times per minute, axillary temperature 36,70C, weighed approximately 65 kgs, and consciousness level was alert. Inspection from sclera was anemia. From abdominal examination, uterine fundal height at umbilicus, there was ballottement, fetal beats 12-12-13 and no uterine contraction detected. Peripheral perfusion was warm and dry, minimal oedema in both legs and capillary refill time <2 seconds.

Her ultrasound showed placental fundal grade I with biparietal diameter 4,95 mm and fetal weight 349 grams as seen on 24 weeks pregnancy. She was diagnosed with SLE in pregnancy, G3 P2002 24-week with severe preeclampsia, anemia, chronic hepatitis B and intrauterine growth retardation (IUGR; estimated fetal weight 500 grams).

Patient then treated with 20% magnesium sulfate 1 gr/h

intravenous injection, nifedipine 3x10 mg tablet (BP<160mmHg), methyldopa 3x500 mg tablet, cyclosporine 2x100 mg tablet, tenofovir 1x300 mg tablet, calcium 2x500 mg, erythrocyte washed transfusion 2 bags/day until hemoglobin reached ≥ 9 gr/dl. After one day evaluation, patient was planned for normal delivery. However, the baby was stillborn. At this time, intravenous methylprednisolone 1 mg/kgBW was given due to stress condition of delivery. She showed sign of improvement with supportive therapy.

Methylprednisolone was tapered to 0,5 mg/kgBW i.v. Then patient was discharged after 5 days. Signs and symptoms of preeclampsia has been completely resolved during follow-up visit.

Table 1. Parameter Basic Laboratory of Patient

Variable	2017 (1st time diagnosis)	June 1st ,2018 (24week pregnancy)
Blood		
Hemoglobin	8.4 gr/dl	7.7 gr/dl
Leucocyte	6070/ μ L	6380 / μ L
Platelet	34.000 / μ L	116.000 / μ L
Erythrocyte Sedimentation Rate		22 mm/h
Ureum		12 mg/dl
Creatinin serum		0.86 mg/dl
Albumin		3.62 gr/dl
Sodium		134 mmol/L
Potassium		3.7 mmol/L
Chloride		98 mmol/L
SGOT		117 U/L
SGPT		11 U/L
Uric acid		8.2 mg/dl
Blood sugar		69 mg/dl
Immunology Analysis		
ANA	9.62 (positive)	
C3	63.1 (↓)	116 (N)
C4	24.4 (↓)	36 (↓)
Anti ds-DNA		5.6 (N)
HBV DNA		1.78 x 10 ⁷ copies/mL.
Coombs test		Negative for direct and indirect
Treatment	Pulse dose methyl prednisolone 500 mg 3 days	
Urine analysis		
SG		1.015
pH		6.5
Glucose		Negative
Ketone		+2
Bilirubine		+2
Protein		+4
Nitrite		Negative
Urobilinogen		+2
Leucocyte		0-1/ lpf
Erythrocyte		5-10/ lpf
Bacteria		Positive

Discussion

Disease flares can occur during pregnancy, as well as in the several months prior delivery.⁶ Score of disease activity is needed to assess of SLE activity during pregnancy. According to the Lupus Activity Index in Pregnancy (LAI-P) score, clinical data were divided into 4 groups. Group 1 consist mild clinical symptoms, group 2 is internal organs involvement, group 3 includes modifications of treatment and group 4 to laboratory parameters.⁷ In this report, patient was diagnosed SLE since 2016. From anamnesis, clinical and laboratory examination, LAI-P Score of this patient (hematology 1 and immunosuppressive drug 3) was 1. According to the score, she did not show any sign of lupus flares.

Preeclampsia defines blood pressure >140/90 mmHg and proteinuria >300 mg/24-h in urine after 20 weeks of pregnancy. To distinguish preeclampsia and active lupus nephritis is often subtle, since both condition may present with increasing proteinuria, hypertension, lower extremity oedema, and disruption in renal function.¹ This patient had no history of hypertension before pregnancy nor before 20 weeks gestation. To distinguish lupus nephritis and preeclampsia, there were several symptoms from patients. Preeclampsia usually happens after 20 weeks of gestation, proteinuria ≥ 300 mg/dl, no urine sediment, uric acid level $\geq 5,5$ mg/dl, stable ds DNA, and normal complement level. Thus we concluded that patient had sign of preeclampsia. Preterm birth may be the most common complication that can be encountered from mothers with SLE, because of prematurity lead to long-term medical complications and cause die soon after birth. Its disease activity it self during pregnancy increases the probability of preterm birth. Risk of having miscarriage and stillbirth are 3-16%, IUGR 12,7%, maternal lupus flare 25,6% and neonatal lupus syndrome 2%.⁸

Prevention of increasing SLE activity is important given its complications for both mother and baby. Medical drugs used in pregnancy should be in the safe category and should not need stopped.⁸ Glucocorticoids, mainly in the form of prednisolone, is usually safe for pregnancy. Azathioprine and hydroxychloroquine are immunosuppressant agents classified as safe for pregnancy.

Reactivation of HBV replication could be mediated by suppression of immune by glucocorticoid element. Its reactivation by liver decompensation in immunosuppressed patients is reported in 20-50% of patients with chronic HBV infection undergoing chemotherapy or immunosuppression. Although the incidence of reactivation in HBV patients receiving immunosuppressant therapy is unclear, a study reported that HBV reactivation occurred in about 72% of patients receiving prednisolone compared to 38% who did not ($p = 0.02$).⁹

A woman in reproductive age without advanced fibrosis who plans a pregnancy may delay antiviral until delivery. Pregnant women with hepatitis B chronic and advanced fibrosis or cirrhosis, therapy with tenofovir is recommended. Pregnant women whom already on nucleoside analogue treatment, tenofovir could be continued yet entecavir or other nucleosides analogue must be switched to tenofovir. All pregnant women with high HBV DNA levels (200,000 IU/ml) or HBsAg levels 4 log₁₀ IU/ml, antiviral prophylaxis

with tenofovir disoproxil fumarate (TDF) should start at 24–28 week of gestation and continue for up to 12 weeks after delivery.^{10,11} In our case, patient was switched from lamivudine to tenofovir due to failure of viral suppression.

Conclusion

Pregnancy and SLE is a never ending loop both. Pregnancy in SLE should be well planned so that any complication can be prevented. Awareness of disease activities and initial management could save lives. The use of antiviral is the right step to prevent the reactivation of viral replication in hepatitis B patients with immunosuppressants. Immunoglobulin is highly recommended for newborn from mothers with HBV infection.

Conflict of Interest

The author stated there is no conflict of interest

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