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Pregnancy with Systemic Lupus Erythematosus: A Case Report

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Abstract: ***Systemic Lupus Erythematosus (SLE) is a rare idiopathic autoimmune disease that was usually found in women of reproductive age. Pregnant women with SLE may have a higher risk of flares and pregnancy complications, including preterm birth, cesarean delivery, preeclampsia, low birth weight, intrauterine growth retardation (IUGR), congenital heart block (CHB), and intrauterine and neonatal mortality. Here we report a 33-year-old Balinese woman with a second pregnancy, controlled SLE, and history of retinal detachment. The patient was managed by a multidisciplinary team involving an obstetrician, rheumatologist, ophthalmologist, and pediatrician. The patient had methylprednisolone 4 mg once per day to control the SLE during pregnancies. Then, the drug was switched to dexamethasone 0.5 mg orally twice daily at 2 weeks before the due date. The patient routinely visited the Obstetrician and Rheumatology Polyclinic every 2 weeks. Later, the patient came to Emergency Ward and was diagnosed with premature rupture of membranes for more than 12 hours. Therefore, the cesarean section was chosen as the delivery method followed by bilateral tubectomy. The outcomes of pregnancy with SLE are very much affected by the activity of the disease. Our patient had controlled SLE before and during her pregnancy. Therefore, this patient had good pregnancy outcomes and the baby was also born healthy.***

Keywords: Autoimmune, Pregnancy, Systemic Lupus Erythematosus, SLE

1. Introduction

Systemic Lupus Erythematosus (SLE) is an idiopathic autoimmune disease that may involve multiple organs. The diagnosis is based on clinical manifestations and laboratory examination. The course of the disease can be sporadic and unpredictable but is usually followed by periods of relapse and remission.[1] SLE predominantly affects women of reproductive age, occurring in about 1/1000 of women between 15 and 45 years of age. The exact prevalence of SLE in Indonesia is unknown, but it is estimated that the prevalence is similar in America which is about 1,500,000 people per year.[2]

SLE is a progressive disease. Previous data suggest that if a woman becomes pregnant during the period of SLE disease, she will minimize the risk of flares in pregnancy, but will not eliminate them. The flare rates in pregnant women with SLE is ranged from 20% to 40% during the remission period.[1,2] Pregnancies with SLE are considered high-risk pregnancies, due to the association with higher maternal and fetal morbidity. Although most pregnancies with SLE had live births, active disease and involvement of major organs can affect both the mother and the fetus. Ultimately, there may be silent flares, such as renal flare or thrombocytopenia, that requiring further monitoring during pregnancy because these silent flares may increase the risk of obstetric complications.[2]

All pregnant women with SLE should be informed about possible problems during their pregnancy, including the risk of flares, a higher pregnancy complication rate, suboptimal obstetric outcomes, and a higher risk of neonatal lupus syndrome. The need for optimal disease control with safe therapy during pregnancy should also be explained.[3]

Compared with the non-SLE population, pregnant women with SLE have an increased risk of preterm birth, cesarean delivery, preeclampsia, low birth weight, intrauterine growth retardation (IUGR), congenital heart block (CHB), and intrauterine and neonatal mortality.[2]

Many factors affect the pregnancy outcome in pregnant women with SLE. These include the state of the disease in early pregnancy, age and parity, the presence of other medical or obstetric disorders, and the antiphospholipid antibodies status. SLE may improve in one-third of women during pregnancy, one-third may remain unchanged, and one-third may get worse. Major morbidity during pregnancy with an estimated 1 in 20 life-threatening conditions has been reported. This is life-threatening conditions may occur due to renal impairment, myocarditis, or serositis, but the complications associated with preeclampsia and the antiphospholipid antibody syndrome are dangerous.[4]

2. Case Report

A 33-year-old Balinese female patient came to the Obstetric Polyclinic for routine antenatal care. This was her second pregnancy. The first pregnancy was 10 years ago and she did not have any complications during the pregnancy nor labor. The patient had SLE since 5 years ago with the main complaint of pain and swollen joints all over her body. The patient had a positive ANA test with a titer of ≥1/1000. Before the pregnancy, the SLE in our patient has controlled with methylprednisolone 4 mg daily and azathioprine 50 mg daily orally. The patient never had any single flare for one and half year before this pregnancy. The patient also had a history of retinal detachment and had undergone vitrectomy surgery 2 years ago. The patient was managed by a multidisciplinary team involving an obstetrician, ophthalmologist, and rheumatologist. The patient has regularly visited the Obstetric Polyclinic for antenatal care

every 2 weeks and Rheumatology Polyclinic for SLE monitoring and treatment.

The rheumatologist also changed the SLE treatment into only 4 mg of methylprednisolone daily orally due to the pregnancy. The SLE treatment in this patient was planned to be switched to dexamethasone 0.5 mg orally twice daily at 2 weeks before the due date. The patient had no flare during pregnancy and was controlled with pharmacological therapy given by the rheumatologist.

The patient had fetal scanning at 39 weeks of gestational age because the patient was first found to be pregnant at 28 weeks of gestational age. Based on the fetal scanning result, there was no major abnormality found in fetal organs and fetal echo seems normal. Based on the multidisciplinary team meeting, there were no absolute contraindications for vaginal delivery in this patient. However, the ophthalmologist suggests that the patient should have an instrumental assisted vaginal delivery or even cesarean section to minimalize the risk of retinal detachment because the patient had a history of retinal detachment 2 years ago. The patient also did not plan to have more children. Therefore, an elective cesarean section was planned on the due date which would be followed by bilateral tubectomy as a method of female sterilization.

Two days before the due date, the patient came to the Obstetric Emergency Ward with a complaint of sudden leakage of fluid from the vagina 19 hours ago. There was active fetal movement felt by the mother. The patient weighs 60 kg and height 156 cm. Based on the physical examination, it was found that the patient's vital signs and general condition were within normal limits. There was no sign of flares. On the obstetric examination, fundal height was 30 cm, fetal heartbeat was 148 beats per minute, and no uterine contraction was found. Based on vaginal inspection using a vaginal speculum, there was clear fluid that is positive when tested with litmus paper, indicating it was amniotic fluid. According to the vaginal toucher examination, the cervical opening was 1 cm, cervical effacement was 25%, the head was palpable, and no amniotic membrane was palpable. The patient also had a reactive non-stress test result that indicates there was no fetal distress. The complete blood count result was also within the normal limit. Thus, the patient was diagnosed with term pregnancy (39 weeks gestational age), premature rupture of membranes more than 12 hours, and controlled SLE. Later, the patient had an emergency cesarean section followed by bilateral tubectomy. A baby girl was born healthy with a birth weight of 2900 grams and an APGAR score of 8-9.

Two days later, the patient was discharged with take-home medicine as follows: Cefixime 100 mg twice daily, Paracetamol 500 mg three times daily, ferrous sulfate 300 mg once daily, and methylprednisolone 4 mg once daily orally. Then, the patient also had to regularly visit the Obstetric and Rheumatology Polyclinic for follow-up and routine examination.

3. Discussion

Systemic Lupus Erythematosus (SLE) is an idiopathic chronic inflammatory disease in which tissues and cells are damaged by autoantibodies and immune complexes that directly attack one or more components of the cell nucleus.[4] SLE mainly affects young women of childbearing age that may involve multiple organs, such as the skin, muscle, bone, blood, nerve, brain, and kidney.[5] The clinical manifestations of this disease may vary, including rashes, arthritis, anemia, thrombocytopenia, serositis, nephritis, seizures, and/or psychosis. Usually shows clinical symptoms that increase or decrease in weight, but in some patients, the disease activity can be sustained.[6]

SLE is the most common autoimmune rheumatic disease found in pregnancy.[6] Not all pregnant women with SLE are considered a high-risk pregnancy. Only pregnant women with active SLE, lupus nephritis or anti-Ro/ La/ antiphospholipid antibodies should be considered as a high-risk pregnancy and should be managed in a more experienced center. SLE may cause maternal and fetal complications during pregnancy (See Table 1). Patients with the more active disease need to be monitored more closely and require hospitalization. For individuals with stable disease, monitoring for active SLE symptoms, fetal growth, blood pressure, and proteinuria should be done every 4 weeks. For patients with certain risks, such as fetal growth restriction and/ or preeclampsia due to active SLE or other previous histories, more frequent examinations are required. In women who are anti-Ro/ La positive, the fetal heart rate should be monitored and recorded at each visit, and fetal echocardiographic examinations should be performed at 18-20 weeks to 28 weeks of gestation age.

Table 1. The Effect of SLE on Pregnancy.[4,5]

Complication	Description
Maternal	
SLE flare	Increased risk of flare during pregnancy. Flare may be life-threatening (1 out of 20 cases) Flare is associated with poor perinatal outcomes. Poorer prognosis is found when antiphospholipid antibodies are present. The incidence of flare is increased in pregnancies with lupus nephritis.
Pre-eclampsia	It is controversial whether the incidence is increasing or not
Premature birth	Increased risk in pregnancies with SLE
Perinatal	
Intrauterine growth retardation	Increased risk in pregnancies with SLE
Stillbirth	Increased risk in pregnancies with SLE, particularly when antiphospholipid antibodies are present.
Neonatal lupus	The incidence was about 10% in pregnancies with SLE

Pregnancies with a history of active SLE 3-6 months before conception had an increased risk of flares, and most flares occur in the second trimester of pregnancy. Patients with SLE who have experienced remission more than 6 months before becoming pregnant have a 25% risk of flares during

pregnancy and 90% of pregnancy had good outcomes. On the other hand, if the SLE remission period before pregnancy is less than 6 months, the risk of flare during pregnancy becomes 50% with a poor pregnancy outcome. If pregnancy occurs when the SLE is in an active state, the risk of fetal death is 50-75% with the maternal mortality rate being 10%. As the gestational age increases, the risk of flares also increases, which is 13% in the first trimester, 14% in the second trimester, 53% in the third trimester, and 23% during the puerperium.[5,6,7] Fortunately, most flares during pregnancy tend to be mild flare and can be managed only with pharmacological therapy. The blood pressure and urine protein should be monitored closely to detect hypertension or preeclampsia. The urine protein should be measured by the urine protein:creatinine ratio (PCR) or 24-hour urine collection.[1]

Our patient had a history of SLE since 5 years ago and has been on treatment. The patient had an ANA test examination 4 years ago with a positive result with a titer ≥1/1000. She has been on treatment and routinely visited Rheumatology Polyclinic in our hospital since 5 years ago. The patient never had any single flare since one and half years before her pregnancy.

SLE treatment is gonadotoxic so it can cause premature gonadal failure. As a result, it is difficult for SLE patients to conceive. Therefore, the preservation of gonadal function and fertility is very important for many SLE patients who are mostly young women of childbearing age. Some fertility preservation methods are well known, while others are still applied with caution. In particular, ovarian tissue cryopreservation is a chosen fertility preservation method for SLE patients at (before) childbearing age.[1,2,8]

Since diagnosed with SLE, our patient consumed methylprednisolone 4 mg and azathioprine 50 mg every day as the SLE treatment. The treatment was changed to only 4 mg methylprednisolone daily since her pregnancy. The patient stopped consumed azathioprine since she was pregnant because the azathioprine had side effects of lowering the body's immunity (see Table 2).[5] In our patient it is suspected that premature gonadal failure has not occurred and the patient is still of reproductive age, 33 years, so there was no disturbance in hormonal function or reproductive function in our patient. Thus, our patient can conceive despite receiving the SLE treatment. This pregnancy was unplanned and the patient first found out that she was pregnant at 29-30 weeks of gestation.

More than half of the pregnancies in women with SLE result in adverse outcomes for the mother or the fetus. To reduce the frequency of untimely pregnancies and treatment non-compliance, women with SLE need counseling about pregnancy planning. Also, pregnancy with SLE should be managed by a multidisciplinary clinician involving obstetricians, pediatrician, and rheumatologist.[9] During her pregnancy, our patient was managed by an obstetrician, a rheumatologist, a pediatrician (for anticipation of neonatal SLE), an ophthalmologist (because our patient had a history of retinal detachment), and an anesthesiologist (for preparation of cesarean section). All clinicians agree that there were no absolute contraindications for vaginal delivery in our patient. However, a cesarean section was the first choice in this case because the patient did not plan to have more children and willingly did the female sterilization procedures. Besides, our patient also had premature rupture of membranes for more than 12 hours.

Table 2: The Adverse Effect of SLE Therapy in Pregnancy.[9]

Drug	Toxicity in Pregnancy
Prednisolone	Increased risk of cleft lip, cleft palate, premature rupture of membranes, hypertension, preeclampsia, DM
Azathioprine	Relatively safe at therapeutic doses in some different studies. However, some clinicians believe that this drug may cause bone marrow suppression in both the mother and the fetus. It has a teratogenic effect in pregnant mice and rabbits.
Cyclosporine	Relatively safe at therapeutic doses in some different studies. However, some studies also found this drug may cause severe intrauterine growth retardation.
Cyclophosphamide	May crosses the placenta and causes fetal toxicity when administered to pregnant women. Abnormalities (loss of fingers and/ or toes, heart defects, hernias) may occur in babies born to mothers treated with the drug during pregnancy. Other maternal complications that may occur due to the use of this drug are hemorrhagic cystitis, spinal cord suppression, and infection.
Methotrexate	Has teratogenic potential. May cause neural tube defect.

4. Conclusion

Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by the production of antibodies against the cell nucleus. The outcomes of pregnancy with SLE are very much affected by the activity of the disease. Our patient never had a flare since one and half years before her pregnancy and had good pregnancy outcomes.

Counseling and education for pregnant women with SLE is a must because of the increased risk of flares during pregnancy and possible complications of neonatal SLE. Even after the delivery process, the mother and baby still need to be closely monitored for possible complications.

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