



Secondary Trimester Pregnancy in Systemic Lupus Erythematosus Patients with Pneumonia: A Case Report

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ABSTRACT

Background. Systemic lupus erythematosus (SLE) is an autoimmune disease that can attack multiple organs and has a high prevalence in women. Due to its treatment and resulting pathological conditions, SLE makes the patient susceptible to infections. Furthermore, physiological changes in the body that occur during pregnancy renders pregnant women with SLE vulnerable to disease exacerbation. Therefore, the management of such cases necessitates the evaluation and intervention of a multidisciplinary medical team. **Case Presentation.** We present the case of a female patient in her second trimester of pregnancy who complained of shortness of breath. The patient has a history of SLE diagnosed five years ago. Within 7 days of treatment, the patient experienced an improvement in symptoms. **Conclusion.** This is a rare case, and we report on the outcomes of treatment and our limitations to ensure better future treatment for pregnant women with SLE to prevent maternal and fetal death.

1. Introduction

SLE is a complex autoimmune condition that can affect various body systems. A combination of genetic and environmental factors contribute to the pathogenesis of SLE, characterized by the development of pathogenic autoantibodies against body proteins and nucleic acids of self-intolerance.¹ SLE was reported to have a global incidence and prevalence of 5.14 per 100,000 and 43.7 per 100,000 people, respectively, from 1997 to May 2022.² In Indonesia, the female-to-male ratio has increased from 13:1 to 22:1 from 2015 to 2017.¹

Nosocomial pneumonia or hospital-acquired pneumonia (HAP) is defined as pneumonia that develops more than 48 hours after hospital admission and is not in the incubation period at the time of

admission. Ventilator-associated pneumonia (VAP) is a substantial subset of HAP that develops in the intensive care unit (ICU).^{3,4} Meanwhile, community-acquired pneumonia (CAP) is a severe lung infection affecting the alveoli and people with no recent hospital admissions or healthcare exposures.⁵ Hospital-acquired pneumonia is a global concern, with the World Health Organization (WHO) reporting approximately 450 million cases per year, with 4 million deaths,^{3,4} while 23% of patients receiving care in intensive care unit die from CAP.⁵ Pregnancy with SLE carries substantial risks for both the mother and the fetus.⁶ This can result in prematurity, spontaneous miscarriage, fetal death, preeclampsia, and disruption of fetal growth, leading to placental malfunction.⁷ Maintaining pregnancy, promoting

maternal and fetal health, and enhancing the quality of life for both parties might be difficult when treating pregnant SLE patients complicated with pneumonia (both CAP dan HAP). Hereby, we present a case of 28-week pregnant patient with SLE and CAP/HAP that was treated at the Haji Adam Malik General Hospital in Medan, North Sumatra, Indonesia.

2. Case Presentation

Mrs. T, a 22-year-old woman, G2P0A0, presented to the emergency room with a chief complaint of shortness of breath since 4 days prior to admission which had gotten progressively worse in the last few hours. Her shortness of breath had not been triggered by changes in weather, dust exposure, or strenuous activity. Additionally, she also experienced a cough accompanied by difficult-to-expectorate phlegm and pain upon inspiration over the last 4 days. The patient reported weakness which had been ongoing since the onset of her pregnancy, which had gotten worse in the last few days. There was a history of joint pain, hair loss, mouth sores, and red rashes since the beginning of pregnancy. History of urination and defecation were within normal limits. There was a history of intermittent fever. Weight loss, night sweats, and decreased appetite were found in the past few months. Notably, she had a history of SLE 5 years prior. The patient had not been routinely controlled for treatment since the COVID-19 pandemic, during which she took mycophenolate sodium for SLE 1 year ago. Currently, she was only taking 4 mg of methylprednisolone twice daily. There was no history of other disease. The first day of the last menstruation was June 4, 2022. She had previously undergone caesarean section in 2020, but unfortunately, the baby did not survive (intrauterine fetal death) and the cause of the death is undetermined due to lack of data. Anti-Ro and ACA tests had not been conducted due to limited testing resources.

Upon examination, her vital signs revealed a blood pressure of 155/90 mmHg, a heart rate of 88 beats/minute, a respiratory rate of 24 beats/minute, a body temperature of 36.1°C, and an oxygen

saturation (SpO₂) of 96% on room air. The fetal heart rate ranged between 164 to 173 beats per minute.

Physical examination findings include alopecia on the head (Figure 1) and a dry rash on the forehead. Stomatitis was found in the oral cavity. Examination of the chest and abdomen was within normal limits. Examination of both upper and lower extremities (Figure 1) revealed rashes that had dried up and pain in the joints, such as the fingers, wrists, feet, and shoulders.

Laboratory examination yielded the following results: hemoglobin (Hb) 10.2 g/dL; leukocytes 9,960 / μ L; hematocrit (Ht) 29.4%, platelets 346,000 / μ L, mean corpuscular volume (MCV) 92 fL, mean corpuscular hemoglobin (MCH) 31.8 pg, mean corpuscular hemoglobin concentration (MCHC) 34.7 g/dL, neutrophils 80.50%, lymphocytes 16.40%, monocytes 2%, eosinophils 1%, and basophils 0.1%. Hemostatic physiologic examination results were as follows: APTT 43.9 seconds (control: 34.1 seconds), PT 12.2 seconds (control: 13.5 seconds), INR 0.82 seconds, TT 23.8 seconds (control: 22.3 seconds), fibrinogen 394.0 mg/dL, D-dimer 320 ng/mL, SGOT 35 U/L, SGPT 13 U/L, albumin 2.3 g/dL, ureum 9 mg/dL, creatinine 0,38 mg/dL. Immunoserological examination revealed the following results: C3 levels 66 mg/dL (N: 82-193 mg/dL), C4 levels 19 mg/dL (N: 15-57 mg/dL), ANA test 27.3 UI/mL (N: <20 UI/mL), anti-dsDNA levels 157 IU/mL (N: 0-20 IU/mL).

Chest x-ray examination revealed a specific long active duplex process with left pleural effusion (Figure 2). An ultrasound examination found a live baby with an estimated gestational age of 28 weeks. Based on these findings, the patient was diagnosed with systemic lupus erythematosus with severe disease activity (SLEDAI 16) with musculoskeletal and mucocutaneous manifestation, concomitant with a 28-week gestation pregnancy and CAP. *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* were found in the sputum culture.

The patient came to the emergency department with SpO₂ of 96% in room air and received initial oxygenation at 6 liters per minute (LPM) through a

nasal cannula, resulting in an increase of SpO₂ to 98%. However, the patient's symptoms did not improve. Subsequently, the patient was given an oxygenation at a rate of 15 LPM via a non-rebreather mask (NRM), leading to an improvement of SpO₂ to 100%. After that, the patient received intravenous fluid of NaCl 0.9% at 20 drops/minute and was given methylprednisolone 500 mg, ceftriaxone injection 1 gr/12 hours, and levofloxacin 500 mg/100 mL, ranitidine 50 mg/12 hours, hydroxychloroquine (HCQ)

1x200mg, N-Acetylcysteine (NAC) 3x200 mg, budesonide inhalation and folic acid 0.4 mg twice daily. Over the course of 7 days of treatment in the ward, the patient's symptoms such as fever, joint pain, and skin rash disappeared, and her shortness of breath gradually improved. The patient was finally discharged due to clinical improvement, with prescribed medication of oral methylprednisolone 0,5 mg/kg body weight (BW) tapering down, HCQ 1 x 200mg, NAC 3x200mg, and aspirin 1x80mg.



Figure 1. Clinical examination showing alopecia (left) and rashes on the patient's feet (right)



Figure 2. Pneumonia with pleural effusion was found on chest X-ray.

3. Discussion

This patient is a female patient, currently 22 years old, who previously had a history of SLE diagnosed 5 years ago. Systemic lupus erythematosus is more common in women than men with a ratio of 15:1 to 22:1. Generally, SLE symptoms will be seen in the age

range of 9-58 years with the highest incidence occurring between 21 to 30 years.¹ As the patient had a history of SLE 5 years prior, it can be inferred that she developed SLE at the age of 17 years. Patients with SLE who have not yet reached the age of 18 years can be diagnosed with juvenile-onset systemic lupus

erythematosus (JSLE).⁸ JLSE has higher mortality and morbidity than SLE in adults because it causes long-term organ damage, but in SLE patients both adults and children of Asian race are known to have clinical manifestations that are worse than in white races.⁹

In addition to the patient's history of SLE, we employed the EULAR/ACR 2018 classification criteria to make a diagnosis in this case, which have been validated and have sensitivity and specificity values of 96.12% and 93.38%, respectively. These criteria can be used if the ANA titration is positive above or equal to 1 in 80 or positive by other equivalent examination methods and there is no probable cause other than SLE. Patients are classified as having SLE if they scored above or equal to 10, with a minimum of 1 clinical criterion.¹

In this patient, we encountered several markers in various aspects. In the skin area, she exhibited acute cutaneous lupus. In the joints, we found synovitis in more than 2 joints with stiffness of more than 30 minutes. Low complement C3 and normal C4 were found in the immunological aspect, particularly complement proteins. Given the predominance of clinical signs affecting the skin and joints, it can be concluded that SLE in this patient has musculoskeletal and mucocutaneous manifestations.

Mucocutaneous manifestations include photosensitive rashes, malar rashes, non-scarring alopecia, or chronic discoid lesions. Additionally, less common mucocutaneous manifestations include mucosal ulcers, periorbital edema, bullous lupus, severe scarring alopecia, subacute cutaneous lupus, foot ulcers, panniculitis, and cutaneous vasculitis. The redness can be caused by environmental factors such as sunlight, stress, or infectious diseases which accelerate the process of cell death. The rash eventually becomes dry and black. The patient also experienced hair loss (alopecia) and joint pain.⁹

We performed an ANA test on this patient using the enzyme-linked immunosorbent assay (ELISA) method. In diagnosing SLE, two gold-standard methods can be used to assess ANA: the ELISA method and the indirect immunofluorescence (IFF) method with Hep-2

cell substrates.¹ In diagnosing connective tissue disease (CTD), ANA-IIF and ANA-ELISA have respective sensitivities of 63.3% vs 74.8%, with specificities of 86.72% and 89.5%, respectively.¹⁰ The sensitivity and specificity values of ANA-IIF examination can vary depending on the titer, with values of 98.4% at a titer of 1:40, 97.8% at 1:80, 95.8% at 1:160, and 86% at 1:320. Meanwhile, the specificity ranges from 66.9% at 1:40, 74.7% at 1:80, 86.2% at 1:160, and 96.6% at 1:320.¹ According to Martioso (2006), the comparison of ANA-IF to ANA-ELISA sensitivity is 97.5% to 95%; specificity 20% to 45%; positive predictive value (PPV) 70.9% to 77.5%; negative predictive value (NPV) 80% to 80.8%.¹¹ In this case, we were only able to perform the ANA-ELISA examination due to limitations in performing the ANA-IIF examination. However, it is recommended to use the ANA-IIF examination in similar cases.

In this case, an anti-double stranded deoxyribose acid (anti-ds-DNA) examination was also performed, which is usually carried out to confirm the diagnosis of SLE. This examination uses several methods such as ELISA, Farr assay, and Crithidia Luciliae Fluorescence Test (CLIFT). The Farr assay and CLIFT methods have better specifications.¹ In SLE, several antibodies such as anti-Sm, anti-Ro (SSA), and anti-La (SSB), as well as antiphospholipid (APL) antibodies could have also given positive results. In particular, it is important to assess anti-Ro, anti-La, and APL antibodies in this patient because they are associated with complications in SLE during pregnancy, such as fetal heart block in a fetus with positive anti-Ro and anti-La, which can potentially cause death. However, in this case, these specific antibodies were not examined due to facility limitations.

This patient received intravenous methylprednisolone at 500 mg/24 hours for 3 days, followed by an oral dose of 0.5 mg/kg BW, and HCQ 200 mg once daily. Disease activity was assessed using the SLEDAI 2000, and the patient was classified into severe disease activity based on the presence of alopecia, joint pain, oral ulcers, and low levels of complement C3.¹ Based on the guidelines for initial

therapy in severe SLE cases, treatment involves IV methylprednisolone 500-750 mg per day for 3 days and azathioprine (AZA) 2-3 mg/kg BW/day or mofetil mycophenolate (MMF) 2-3 g/day or mycophenolate (MPA) 1.44-2.16 g/day or cyclosporin \leq 2.5 mg/kg/day and HCQ 2.5 mg/kg/day. Meanwhile, regimen for maintenance therapy includes prednisolone \leq 7.5 mg/kg/day, AZA 50-100 mg/day, MMF 1.0-1.5 g/day, cyclosporin 50-100 mg/day, and HCQ 200 mg/day. In this case, we used MP 500 mg/day for 3 days followed by oral MP 0,5 mg/kg BW. Immunosuppressants were not given due to the concurrent pneumonia infection. Administration of corticosteroids is one of the main treatments given to patients with SLE.¹² Corticosteroids produce effects through various pathways, one of which is genomic action mediated by glucocorticoid receptors which results in anti-inflammatory and immunosuppressive effects. In addition, corticosteroids also have metabolic effects, especially on protein and carbohydrate metabolism. The glucocorticoid receptor is located in the cytoplasm. Upon binding with corticosteroids, it will translocate rapidly into the nucleus, affecting gene transcription and causing inhibition of gene expression and translation for inflammatory and structural leukocytes such as epithelium.¹³ In this case, the patient did not receive other immunosuppressants due to the pneumonia infection, and hydroxychloroquine was administered as an immunomodulator.

In pregnant SLE patients, as in the case of our patient, the use of HCQ has many proven benefits. Discontinuation of HCQ use will increase the risk of SLE recurrence during pregnancy. Other SLE drugs include azathioprine and calcineurin inhibitors, tacrolimus and cyclosporine. It is important to note that some SLE drugs can be teratogenic, such as cyclophosphamide, methotrexate, and mycophenolate.¹⁴

The interaction between SLE and pregnancy may have implications for the mother, the fetus, or both. This may give rise to adverse pregnancy outcomes (APO) which consists of several conditions such as

preeclampsia, premature birth, miscarriage, and intrauterine growth restriction (IUGR). Predictors of APO include active maternal disease, nephritis, proteinuria, hypertension, thrombocytopenia, and the presence of antiphospholipid (aPL) antibodies, especially lupus anticoagulant (LAC).¹⁴

In SLE patients with pregnancy, miscarriage may occur and higher rates of maternal death have been reported due to thrombosis, infection, and hematological complications. However, SLE patients who are not pregnant are also at risk of medical complications and death.⁴

Shortness of breath is caused by disturbances in the upper or lower respiratory tract. In the lower respiratory tract, it can be caused by tuberculosis or pneumonia, but after gene expert examination and culture analysis, no *Mycobacterium tuberculosis* was found, while *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* were found instead. Pneumonic infections affect as many as 15% of SLE patients, potentially influenced by factors such as race, hospitalization from long-term care of SLE patients, etc. The prevalence of SLE is high in Caucasians, and so is in Asia. A total of 158 SLE patients in Mexico experienced at least one episode of pneumonia infection.¹⁵

The mortality rate of SLE patients with pneumonia infection is 10-12%. In the United States, the prevalence of SLE patients with pulmonary involvement is 50-70%, 2% of them are found with lupus pneumonitis, and 3-9% of them are found with interstitial lung disease (ILD).¹⁶ Meanwhile, in Asia specifically in China, around 7.46% had pneumonia infections out of 11,533 patients with SLE.¹⁷ In Indonesia, specifically in Dr. Soetomo General Hospital Surabaya, out of a total of 273 patients with SLE, around 33.7% of patients had pneumonia infections.¹⁸ In general, HAP and VAP can be caused by aerobic gram-negative bacilli such as *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter* spp, *Acinetobacter* spp, and Gram-positive cocci such as *Staphylococcus aureus*, which includes methicillin-resistant *S. aureus*, and *Streptococcus* sp. Differences in host factors and

hospital's microbial flora can affect the pattern of pathogens that cause HAP and VAP.³ This is in line with the findings of sputum culture examinations conducted in this case. Levofloxacin and ceftriaxone were then administered. Additionally, inhalation of budesonide 0.5 mg/ml help relieve the patient's shortness of breath.

Antiphospholipid antibody syndrome frequently coexists with SLE, presenting a particular concern, especially in pregnant women with SLE.¹² This combination of conditions can cause recurrent miscarriage, preterm delivery, oligohydramnios, fetal growth restriction, fetal distress, fetal or neonatal thrombosis, preeclampsia, eclampsia, and HELLP syndrome.¹⁹

This case is a pregnant woman with SLE and pneumonia who is suspected of having antiphospholipid syndrome which may have contributed to the intrauterine fetal death. The results of the hemostatic physiologic examination found APTT 43.9 seconds (control: 34.1 seconds), PT 12.2 seconds (control: 13.5 seconds), INR 0.82 seconds, TT 23.8 seconds (control: 22.3 seconds), fibrinogen 394.0 mg/dL. D-dimer 320 ng/mL. It was concluded that the APTT ratio in patients was 1.28.

5. Conclusion

SLE complicated with pregnancy and respiratory tract infections represents a complex clinical scenario that affects various organ systems. The management should be carried out in a comprehensive approach, involving interprofessional collaboration from various disciplines. In this case, we have performed management for SLE and respiratory infection (pneumonia) in a pregnant woman experiencing her second pregnancy with prior history of intrauterine death. Nevertheless, we experienced limitations in making the diagnosis of antiphospholipid syndrome which can be found in pregnant women with SLE and has a high incidence rate as a cause of maternal and fetal death.

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