

A Near Fatal Puerperal Flare of Systemic Lupus Erythematosus: Case Report and Review

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Abstract

Background: Systemic lupus erythematosus (SLE) is a chronic, multisystem autoimmune disease predominantly affecting women, particularly those of childbearing age. It is characterized by fluctuations of disease activity, with periods of high disease activity (i.e., flares) followed by periods of low activity. SLE provides significant challenges in the pre-pregnancy, antenatal, intrapartum, and postpartum periods for these women, and for the medical, obstetric, and midwifery teams who provide care for these women. History: A 28-year-old woman with SLE, diagnosed two years ago, compliant with medications and medical care and in remission, embarked on a planned pregnancy. Shortly after becoming pregnant, she started losing the hair with the recurrence of skin rash. She developed preeclampsia. She was managed on hydroxychloroquine together with antihypertensives (Nifedipine 30mg BD, Methyldopa 500mgTDS, and Angiotensin Receptor Blocker (Losartan) 100mg daily.

Index terms— puerperium, systemic lupus erythematosus, flare, hydroxychloroquine.

1 Introduction

he systemic lupus erythematosus (SLE) is a chronic, multisystem autoimmune disease predominantly affecting women, particularly those of childbearing age. The clinical manifestation and management of SLE provide challenges in the prepregnancy, antenatal, intrapartum, and postpartum periods for the woman and the medical, obstetric, and midwifery teams who provide care for these women. The manifestation of SLE is characterized by fluctuations of disease activity, with periods of high disease activity (i.e., flares) followed by periods of low activity.

There are conflicting results about the effect pregnancy has on the health of SLE women. Some studies report an increased rate of flares during pregnancy, while others report no difference in disease activity. [1,2,3,4] A study by Lockshin et al. [5] analyzed the flare characteristics of pregnant and non-pregnant SLE patients and did not find a difference between women who were and were not pregnant. In contrast, Petri et al. [1] found the rate of a flare was greater during pregnancy than in non-pregnant controls, and subsequent analysis by Ruiz-Irastorza et al. [2] found the flare rates during pregnancy and, 6-weeks postpartum were increased compared to non-pregnant, age-matched controls.

Understanding the effect pregnancy has on disease activity is clinically significant as high disease activity during pregnancy is associated with maternal and fetal complications in the antenatal and intrapartum periods and the puerperium. Additionally, examining the rate of flares during the postpartum period is important in determining if patients need to be more closely monitored in the months following pregnancy.

We present a case of a life-threatening flare of SLE in the puerperium and review the literature on the multidisciplinary care of these women during prepregnancy, antenatal, and postpartum periods.

2 II.

3 Case Summary a) Medical history

Two years before the index presentation, a 28-year-old woman presented to the Medical team with a month's history of having a malar rash associated with non-scarring alopecia. She was a carrier of the sickle cell gene (genotype AS). Skin examination revealed hyperpigmented rash in her ears, and erythematous rash on the hands and trunk. She had low-grade fever with weight loss. Her laboratory investigation results revealed a moderate anaemia [Hb: 9.3g/dl MCV: 82%, MCH 28.8], normal WBC: 4.5×10^9 /L, urine: RBCs 8-10, urine protein: negative, Anti-ds DNA: positive (>1000). A diagnosis of Systemic Lupus Erythematosus (SLE) was made. She was commenced on the following treatment regimen: Tablets hydroxychloroquine 200mg daily, Tablets Prednisolone 40mg daily, Tablets Azathioprine 100mg daily, sunscreen, and Betnovate ointment. The Prednisolone tablet was later tapered to 10mg daily. She was advised to continue with the hydroxychloroquine, Azathioprine, and low dose prednisolone for a year before becoming pregnant. She was compliant with her medications and this advice. She practiced the natural method of contraception. She had no side effects from the medications. Three months into this treatment, the alopecia, and all the rashes resolved. She continued reviews with the medical team. Two years after her diagnosis of SLE, she achieved a spontaneous pregnancy and was referred for obstetric care. fetal growth, liquor volume measurements, and Doppler velocimetry.

At 35weeks + 3days, she had an elevated blood pressure of 150/90mmHg and 2+ proteinuria and frontal headaches. She was grossly oedematous. She was admitted for blood pressure control and maternal antenatal administration of steroids to enhance fetal lung maturation.

At 35 weeks + 6 days of gestation, she had an induction of labor on account of preeclampsia with mild features. She had normal progress of labor resulting in spontaneous vaginal delivery to a healthy male baby with a birth weight of 2.5kg and normal APGAR Scores of 6 and 9 at 5 and 10 minutes, respectively. The immediate postpartum period was uneventful, and she was discharged home on the third post-delivery day with a blood pressure of 140/90mmHg.

4 c) Post-partum events

Three weeks postpartum, she was admitted for emergency obstetric care on account of gradual onset of bipedal swelling, abdominal distension, easy fatigability, and breathlessness over a week. There was no headache, dizziness, epigastric pain, or blurred vision. She had no urinary symptoms such as frequency, dysuria, or nocturia. There was no yellowish discoloration of the sclera. Physical examination revealed a young woman who was grossly oedematous -anasarca. She looked ill. She was afebrile, anicteric, but pale. She had a grossly distended abdomen and bipedal pitting edema of the whole lower limbs. There was non-scarring alopecia with papular lesions on the body.

5 b) Obstetric history

Her past obstetric history revealed that she had her first pregnancy five years ago. This pregnancy was unplanned and unwanted, so she had a medical termination of pregnancy at one month. There were no post-termination complications. Her second pregnancy, two years after the first, was a wanted one, which unfortunately ended in a missed miscarriage at 12 weeks gestation. She had surgical evacuation of the uterus with no complications. There is no known history of antecedent flare.

She was a Customer care worker married to a banker. She neither smoked cigarettes nor drank alcohol. She had no significant gynecological history.

For the index pregnancy, she booked in early at seven weeks + 3 days. She had a normal booking blood pressure (BP= 120/80mmHg) and a trace of proteinuria. All her booking investigations were normal. She had a total of 11 antenatal visits with a multidisciplinary team of Obstetricians and Physicians. She was compliant with all her antenatal medications. For the SLE, she was managed on hydroxychloroquine.

She was found to have elevated blood pressure at 17 weeks (150/100mmHg) with insignificant proteinuria and bipedal edema. She had no headaches, epigastric pains, or visual disturbances. She was started on antihypertensives (Nifedipine 30mg BD, Methyl dopa 500mgTDS, and Angiotensin Receptor Blocker (Losartan) 100mg daily. The blood pressure stabilized between 120 -140 systolic and 80 -90 diastolic. At 33 weeks + 6 days, her blood pressure was 140/100mmHg, urine dipstick showed 2+ proteinuria, but she was asymptomatic of preeclampsia. She continued with the antihypertensives. Throughout the pregnancy, she had normal serial ultrasound scans for She could not lie down in the supine position for a thorough examination as she was breathless with a respiratory rate of 30 cycles per minute. She had decreased chest expansion, stony dull percussion note with diminished breath sounds all on the left side. She had a blood pressure of 118/95mmHg but a tachycardia of 120beats/minute. Heart sounds were normal. Her central nervous system was grossly intact with a Glasgow Coma Score (GCS) of 15/15. Her abdomen was grossly distended. Her liver, spleen, and kidneys were not palpable. There were significant as cites preventing proper evaluation of the postpartum uterus.

A diagnosis of a known SLE patient with pleural effusion suspected to be due to pneumonia and hypoalbuminemia in the puerperium was made. She was admitted to the postnatal ward, stabilized, propped up in bed, and given intranasal oxygen as her SPO₂ was < 92%. Hematological, biochemical, and radiological investigations were

done. She was started on intravenous cefuroxime 1.5g stat, 750mg TDS for 48 hours, intravenous metronidazole 500mg TDS for 48 hours, Tabs Folic acid 5mg daily and iron and multivitamin supplements. In the course of her admission, she was started on antipyretics and antimalarials due to the development of pyrexia of 39.0 Celsius and the presence of malaria parasitemia. She had nutritional supplementation and intravenous albumin due to the hypoproteinemia with anasarca and enoxaparin for thromboprophylaxis. The cardiothoracic team was involved in the draining of the pleural effusion. She also developed elevated blood pressure that raised the suspicion of postpartum preeclampsia, and she was managed with antihypertensives. She subsequently developed hemoptysis and so pulmonary tuberculosis was suspected, but sputum for AFBs was negative. She additionally developed an ulcer of the right popliteal and posterior thigh with 2 x 2cm infected floor -infected decubitus ulcers. The ulcer was managed with daily dressing, high protein-rich diet, and change in position of the leg. Due to her history of SLE, her Medical team was promptly involved in her care. There was a reintroduction of the initial therapy for SLE. She was started on Tab azathioprine 100mg, Tab prednisolone 10mg, Tab hydroxychloroquine, iron and multivitamin supplements, and Tab Folic acid 5mg daily. The anasarca and chest symptoms gradually subsided.

She was on admission for nine days with regular input from the dermatologist, and she was discharged subsequently when the anasarca and chest symptoms had resolved to have a follow-up with the dermatologist. This case report is a case of near-fatal puerperium flare of Systemic lupus erythematosus (SLE). SLE is the commonest autoimmune rheumatic disease encountered in pregnancy; knowledge of pregnancy management in such patients is thus important. [6] SLE typically shows a waxing and waning clinical course, but some patients have continuous disease activity. [7] SLE provides challenges in the pre-pregnancy, antenatal, intrapartum, and postpartum periods for these women. Undoubtedly, the medical, obstetric, and midwifery teams who provide care for these women are not spared of these challenges.

Complications during pregnancy may be maternal (lupus flares, worsening renal impairment, the onset of or worsening hypertension, development of preeclampsia, or venous thromboembolism) and fetal/neonatal (miscarriage, intrauterine growth restriction, preterm delivery, neonatal lupus syndrome [NLS]). [8] Pregnancy in a woman with SLE is associated with an increased risk of adverse maternal and fetal outcomes. This observation prompted physicians in the past to advise their lupus patients not to consider childbirth. With the improvement in outcomes due to better understanding and management of these women, many have been able to achieve successful pregnancies.

As with many medical conditions in pregnancy, the best maternal and fetal-neonatal outcomes are obtained with a cohesive multidisciplinary approach. For patients with SLE, the multidisciplinary team may ideally include a rheumatologist and dermatologist, nephrologist, (based on their predominant symptom), obstetrician, fetal cardiologist, fetal medicine specialist, neonatologist, and specialist midwife. The woman's care should include effective pre-pregnancy risk assessment and stratification, followed by individually tailored prepregnancy counseling. When she conceives, she should book early for pregnancy care with rheumatology/ physician and obstetric appointments in the first trimester and an individually tailored antenatal management plan. Early recognition and management of flares and complications (medical and obstetric) are important, with the involvement of practitioners experienced in managing pregnancy in patients with SLE. [6] The pre-pregnancy assessment is aimed at gathering detailed information to decide on a woman's risks related to pregnancy. This assessment should include past and current SLE disease activity (including most recent flare and frequency), preexisting organ damage (particularly cardiac, lung, and renal), medication history, and a recent serological profile (anti-dsDNA, anti-Ro/La antibodies, antiphospholipid antibodies [aPL], complement). The presence of any additional medical disorders should be elicited, in particular hypertension, diabetes, renal disease, and venous thromboembolism, along with any additional medications. [6] Additionally, an assessment of the outcomes of all her previous pregnancies is important. Particular attention must be paid to fetal and neonatal complications such as miscarriage, stillbirth, small-for-gestational-age, preterm birth, congenital heart block, and the rash of neonatal lupus erythematosus. Maternal complications such as preeclampsia, antenatal or postpartum flares, and venous thromboembolism are also important. This assessment must necessarily include blood pressure, urinalysis, full blood count, renal and liver function tests. Based on the outcome of these assessments, women with SLE can be stratified into the following groups: 1) current remission, or stable low disease activity, with stable treatment; 2) early-stage or currently active disease; or 3) severe impairment of organ function or preexisting severe organ damage. [11] Women in group 3 are prone to extremely high risk of complications, including worsening disease progression and end-organ failure. Additionally, serious maternal and fetal/neonatal morbidities and mortalities are associated with such a pregnancy. These women must be advised to avoid pregnancy and use effective contraception. For patients in remission, or stable low disease activity, planned pregnancies are safe, and they are advised to continue their medication. Therefore, SLE patients should be counseled on the risks of SLE with pregnancy, such as flares, progressive organ damage, preeclampsia, venous thrombo-embolism, miscarriage, intrauterine growth restriction, preterm birth, stillbirth, and neonatal lupus syndrome. pre-pregnancy advice, counseling on optimization of BMI, lifestyle modification, and compliance with medications for SLE are paramount. These measures will improve her health, her chance of conceiving, and the health of her fetus. Optimization of maternal SLE is a sine qua non in ensuring better maternal and fetal outcomes in pregnancy.

In this case, our patient had adequate care of the SLE pre-pregnancy with her Physician. She was in remission, and so she carried on with her fertility wishes.

Once pregnancy starts, that pregnancy is considered a high-risk pregnancy in the SLE patient. However, studies provide conflicting results as to whether flares are more common or of unchanged frequency. [10] Overall, the risk of flare (antenatal or postpartum) appears to be dependent on disease activity 6-12 months before conception. Women with quiescent SLE over this period have less risk of flare during pregnancy, whereas women with active SLE have a high risk of flare. [11] Most flares are non-severe, [8] with articular, dermatological, and mild hematological involvement. These are usually well controlled with a short-term introduction or increase of oral steroids. Nonetheless, severe flares with major organ involvement may occur. [11] The detection of flares in pregnancy is hampered by the fact that many of the typical signs and symptoms associated with flare are considered normal manifestations of pregnancy.

Apart from flares, the risk of complications such as renal complications, worsening of hypertension, or onset of new hypertension and preeclampsia and venous thromboembolism is increased. Medical complications such as stroke, pulmonary embolism (PE), deep vein thrombosis (DVT), major infections, bleeding, and thrombocytopenia are two to eight times more frequent among women with SLE. [12] To reduce these adverse outcomes, most studies recommend the continuation of hydroxychloroquine in pregnancy. A systematic review established the protective effect of hydroxychloroquine in terms of organ damage, flares, venous thromboembolism, bone mass loss, and long-term survival in the general SLE population, as well as the potential to prevent disease activity in pregnant women. [13] Another challenge of SLE in pregnancy is that some normal physiological symptoms of pregnancy may mimic some symptoms of SLE, thus making a clear distinction between pregnancy-associated signs and symptoms from those of SLE difficult. Therefore, the involvement of an experienced physicians is important. Fatigue, mild arthralgia, hair loss, dyspnea, headaches, malar and palmar erythema, edema, anemia, and thrombocytopenia represent common ambiguous manifestations. [8] Monitoring of disease status and identification of flares should be done antenatally using full blood count, serum urea, creatinine and electrolytes, liver function tests, serological profile, and urinalysis with proteinuria quantification.

The risk of preeclampsia is noticeably increased in women with SLE. Twenty-three percent or more may develop pre-eclampsia: two-to four-fold higher than the general population. [12,14,15] One goal of antenatal visits in these patients is the detection of hypertension, and protein uria to institute early management of preeclampsia. Women with SLE also have a four-fold increased risk of developing eclampsia compared with the general population, although absolute numbers remain small (0.5% vs. 0.09%). [12] A particular challenge in pregnant patients with SLE is differentiating between preeclampsia, and lupus nephritis as these conditions have common symptoms, and they may also be coexistent.

A meta-analysis showed a 10% risk reduction in preeclampsia, preterm delivery <34 weeks, perinatal death, birth weight less than tenth centile, or serious pregnancy outcomes (maternal death, development of preeclampsia; preterm delivery, SGA fetus, stillbirth, or neonatal death) if women take aspirin from <16 weeks of gestation throughout pregnancy. Administration of aspirin is therefore, recommended for all women with SLE in pregnancy. [15, ??6] Fetal complications are also evident in women with SLE. Ongoing pregnancies in patients with SLE carry increased risks of small-for-gestational-age fetuses, intrauterine growth restriction, preterm labor, and preterm delivery. [6] These fetal complications are a result of the risk of uteroplacental insufficiency. As such fetal assessment using fetal ultrasonography for weight, amniotic fluid volume measurements, and Doppler velocimetry is required.

Due to these potential complications, care of these women must ideally be by a multidisciplinary team. Antenatal care of this woman was by a multidisciplinary team involving the obstetricians, maternal medicine specialist, Physicians, and fetal medicine specialist. She had about 11 antenatal care visits during which a full maternal and fetal assessments were done. The development of hypertension was detected with the prompt institution of a management plan. The prompt treatment of the hypertension ensured minimal complications of the pregnancy until at 35 weeks + 6 days that she developed pre-eclampsia, which was also managed appropriately, leading to a better outcome.

Women should be reassured that while pregnancy with SLE is generally considered a high-risk pregnancy, a tailored management approach with close multidisciplinary surveillance in pregnancy and the puerperium will result in high rates of successful pregnancies. [14] Labor is not free from the exacerbations of SLE. There may be the need for acute administration of steroids. Stress doses of steroids are required during labor to compensate for the anticipated adrenal insufficiency due to the chronic use of steroids. However, the management of obstetric complications during labor and delivery is not altered due to SLE.

The puerperium, the first six weeks postpartum, was thought to be a period of a high risk of lupus flares, [11] although some groups have found that disease activity decreases after pregnancy. [17] It is likely some patients stop taking their SLE medications due to fear of the adverse effects of these medications on their breastfeeding neonates leading to the flares. Women taking hydroxychloroquine, azathioprine, and steroids for immunosuppression in pregnancy should be reassured that these medications are safe for breastfeeding, and advised to continue.

Properly arranged multidisciplinary postnatal care is important to detect and manage any postpartum lupus complication, and ensure a smooth return to rheumatology outpatient services for ongoing care. A detailed history, clinical examination, and investigations (hematological, biochemical, and serological) is paramount to detect any complications and manage these accordingly. At the postnatal appointment, postpartum counseling and provision of contraception are particularly important in patients with SLE as planned pregnancy is associated

with fewer complications and higher pregnancy success rates. [11] This patient had a prolonged near-fatal flare in the puerperium. Prompt institution of emergency care with a multidisciplinary involvement of the Medical team resulted in the resolution of her condition and returned to normal life activity. Pregnant women with SLE present an increased risk for maternal and fetal complications. The identification of worsening disease activity in pregnancy and puerperium can be challenging. The best maternal and fetal/neonatal outcomes in SLE in pregnancy and puerperium are obtained with a cohesive multidisciplinary team approach. Maintaining disease remission and treating any flares rapidly is vital. Even in low resource settings, a concerted effort from all involved in the care of these women results in better outcomes.



Figure 1: A



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Figure 2: Figure 1 :



23

Figure 3: Figure 2 :Figure 3 :

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