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Systemic lupus erythematosus and preconception care

Abstract

Systemic lupus erythematosus (SLE) is an autoimmune disease that predominately affects women of reproductive age group. Pregnancy and its outcome are a major concern to most of the SLE patients. Concerns of the risk of disease flare during pregnancy and chances of fetal loss, adverse outcome to fetus and safety of the drugs used are to be addressed. The article emphasis the requirement and importance of pre pregnancy counseling in optimizing the maternal and fetal outcome in lupus pregnancy.

Keywords: systemic lupus erythematosus, SLE, pregnancy in SLE, flare

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Abbreviations: SLE, systemic lupus erythematosus; APS, anti-phospholipid syndrome; NSAIIDs, non steroid anti-inflammatory drugs

Introduction

SLE or sometimes referred to lupus, is a multisystem rheumatologic disease. Lupus is considered a chronic autoimmune disease that is distinguished by auto antibodies with certain clinical manifestations to the skin, joints, heart, kidney, lungs and /or nervous system. The diagnosis is aided by the use of classification criteria. The diagnostic criteria currently in use are 2. The first being American College of Rheumatology (ACR) Classification Criteria That require a patient meet at least 4 of the 11 criteria. The second being (SLICC) or Systemic Lupus International Collaborating Clinics Classification Criteria. This requires at least 4 of the 17 criteria with at least 1 of the 11 clinical criteria and 1 of the 6 immunologic criteria , or patient has biopsy –proven lupus nephritis along with antinuclear antibodies (ANA) or anti –double stranded (ds DNA) antibodies.[1–3] Table 1 shows the summary of diagnostic criteria for SLE.

Table 1 Diagnostic criteria for systemic lupus erythematosus[1–3]

ACR diagnostic criteria	SLCC diagnostic criteria	Immunologic criteria
Malar Flush	Acute Cutaneous Lupus	Positive ANA result
Discoid rash	Chronic Cutaneous lupus	Elevated ds DNA antibody
Photosensitivity	Non scarring Alopecia	Elevated anti –Sm antibody
Oral or nasal ulcers	Oral or Nasal Ulcers	Elevated antiphospholipid antibodies
Pleuritis or pericarditis	Joint Disease (e.g Synovitis)	Low complement (C3, C4, CH50)
Persistent Proteinuria > 0.5 g/d or ≥3 on urine dipstic test or cellular casts	Serositis (e.g Pleurisy or pleural effusion)	Direct Coombs test (in the absence of haemolytic anemia)
Seizures or Psychosis	Renal (e.g red blood cell casts)	
Nonerosive arthritis involving ≥2 joints	Neurologic (e.g seizures or psychosis)	
Haemolytic Anemia, Leukopenia, lymphopenia, thrombocytopenia	Hemolytic anaemia	
Positive ANA test	Leukopenia or Lymphopenia	
Elevated anti- dsDNA, anti –Sm or antiphospholipid antibodies	Thrombocytopenia	

Pregnancy and flares of SLE

Whether there is an increased risk of lupus flare during pregnancy when compared with those who are non pregnant is a subject of controversy. While some study[4–6] claim increase incidence of flares during pregnancy other studies refute[7–9] this. The cause for the discrepancy of results from these studies is multifactorial and

probably related to the differences in the definition of lupus flares, assessment of disease activity, selection of the control group. Certain physiological changes that occur during pregnancy may be misinterpreted as flares for example palmar erythema , transient facial blush , increase in proteinuria due to increase in glomerular filtration rate, and postpartum alopecia. This may result in overestimation of the frequency of lupus flares during pregnancy. Therefore, modification of the commonly used disease activity indices has been proposed for the assessment of lupus activity during pregnancy.[10] However, every SLE patient should be followed up during pregnancy under the assumption that there is a risk of flare.

Prediction of the time of flare during pregnancy is also difficult. However, studies have reported equal frequency of flares during the second and third trimester but no patients flared in the postpartum period.[4] Probably the use of prophylactic steroid treatment in late pregnancy explains less or absence of postpartum flares.Overall, the result from several studies do not suggest lupus flares during pregnancy are exceedingly more severe than those occurring outside pregnancy.[11,12] However, the high frequency of flares during pregnancy makes pregnant women with SLE to be at high risk and close monitoring for disease is mandatory throughout the pregnancy and puerperium.

Preconceptional counseling

Optimal timing for conception

A number of studies have demonstrated that active lupus at the time of conception was associated with a higher risk of disease flares during pregnancy. In SLE patients, pregnancy is best undertaken during periods of quiescent disease or remission for at least six months before conception.[13] It has been proposed patients who have stabilization of renal function , resolution of urine sediment abnormalities, proteinuria of less than 1g per day, normalization of the C3 level for at least six months be regarded as having renal remission. As a general rule, the longer the patient is in the remission at the time of conception, higher is the chance that the pregnancy will have less chances of exacerbation.[13]

Baseline investigations

The baseline laboratory evaluation should be done before pregnancy which include complete blood count with platelet, creatinine, blood urea nitrogen, liver function tests, anti Ro/SSA, anti-La/SSB, anti-dsDNA, C3, C4,CH50, 24 hour urine protein, creatinine clearance or spot urine protein –to – creatinine ratio. Both complement and anti-dsDNA levels can help differentiate preeclampsia from lupus flare in pregnancy if a baseline is established.

Renal insufficiency

In the presence of moderate to severe renal insufficiency (creatinine >1.4 mg/dl) before pregnancy, the patient has a 43 % chance of worsening renal function and/or 10 % chance of irreversible renal decline.[14,15] Renal function is not altered significantly with normal or mild renal insufficiency (creatinine <1.4 mg/dl).

Assessment of antiphospholipid antibodies

The panel of antibodies includes lupus anticoagulant, anticardiolipin immunoglobulin M/ immunoglobulin G (IgM/ Ig G) and anti β2 –glycoprotein –I IgM/IgG, should be repeated in 12 weeks. Approximately 30% to 40 % of patients with SLE have antiphospholoipidantibodies.[16] The presence of antiphospholipid antibodies however does not establish the diagnosis of anti-phospholipid syndrome (APS). Regardless of the diagnosis, the patient with SLE should be started on low dose aspirin at the end of the first trimester, around 12 to 13 weeks gestation to reduce the risk of preeclampsia.

Teratogenic medication

Methotrexate and mycophenolate mofetil are absolutely contraindicated in pregnancy. Cyclophosphamide is avoided in pregnancy, especially because it is associated with not only first trimester miscarriage but also fetal demise.[17] Hydroxychloroquine is the safest and most effective medication for pregnant women with SLE. It is recommended to continue Hydroxychloroquine during pregnancy because there is some evidence that lupus activity and flares increase with its discontinuation.[11,12] If patients are in remission on Azathioprine before pregnancy, then the medication should be continued during pregnancy. However, it should not be started right before pregnancy, as it has been associated with cardiac malformation.[18] Corticosteroids are considered safe in pregnancy if necessary, for suppression of disease activity. Non steroid anti-inflammatory drugs (NSAIIDs) are typically avoided in pregnancy, but continued if beneficial for the patient. Patients should be monitored for oligohydroamnios with the administration of NSAIDs, and should be continued at 30 -32 weeks to avoid premature closure of the ductus arteriosus.[19]

Prenatal multivitamins

Multivitamins are recommended to start in thepreconception period. Vitamin E, Zinc, Vitamin A and Vitamin B are all beneficial in a lupus diet. Vitamin C can increase ability to absorb iron and is a goodsource of antioxidants. Vitamin D is especially important for patients with Lupus because they tend to avoid the sun and can result in lower absorption of Vitamin D. Calcium and vitamin D are known to reduce the risk of osteoporosis which is common in patients with lupus. Current studies are exploring onuse of Vitamin D to help relieve lupus symptoms. Furtherit has been seen, that patients are often on medicines like predisone which may lead to significant weight gain and predispose to osteoporosis. Regular, low impact exercise may off set weight gain and also improve health in general.

Multidisciplinary approach

Clear communication between the obstetrician and the rheumatologist is essential for optimal care of both mother and baby. Table 2 outlines the approach.

Neonatal lupus erythematous syndrome

NLE is a syndrome comprising of Congenital heartblock, transient photosensitive cutaneous lupus lesions, cytopenia, hepatic, and other systemic manifestation in children born to mother with SLE, Sjogren syndrome, or other rheumatic disease with a positive anti-Ro or anti –La antibodies.[11,20] The pathogenesis is controversial. But circumstantial evidence has shown that placental transfer of these anti bodies occur during the second trimester and mediates immunological injuries to the fetalheart and the conduction system Once complete heart block is established, it is irreversible.[21,22]

Table 2 Outline of pregnancy management for the patient with SLE

Preconception	Complete blood count
	Creatinine, Blood urea Nitrogen
	Anti RO/SSA, Anti La/SSB
	Antiphospholipid antibodies
	24 Hr urine protein or spot protein creatinine ratio
	Complement levels
	Start prenatal Vitamins
	Discontinue Teratogenic medications
	Continue Hydroxychloroquine
	Recommend trying for pregnancy after 6 months of remission
	Refer to maternal fetal medicine
First trimester	Obtain baseline laboratory evaluation
	Offer Genetic testing/screening
	Initial aspirin at the end of first trimester
Second trimester	Begin Surveillance for Congenital heart block at 16 weeks in patients with positive SSA/SSB antibodies
	Anatomy Ultrasound 18- 22 weeks
	Fetal echocardiography to look for CHB, fetal myocarditis, pericardial effusion, valvular regurgitation
	Interval Growth Ultrasound
	Screen for gestational diabetes
Third trimester	Continue Ultrasound Growth Scans
	Begin antenatal testing at 32 weeks, or sooner if indicated
	Monitor for signs and symptoms of Preeclampsia
	To consider corticosteroids if preterm delivery indicated
Delivery	Delivery at 39+week, or sooner if clinically indicated
	Cesarean Section reserved for usual obstetric indications
	Give Stress –dose corticosterids, if indicated
	Neonatal evaluation at the time of delivery[15]
Postpartum/Contraception	Breast feeding encouraged
	To continue Corticosteroids/Hydroxychloroquin in postpartum period to avoid flare
	Combined hormonal contraceptives are contraindicated in those with positive or unknown antiphospholipid antibodies

Conclusion

Early Preconceptional counseling and antepartum surveillance are fundamental for a healthy pregnancy outcome. SLE being chronic inflammatory conditions which has implications for both mother and fetus. Appropriate management of the mothers' illness andpreventing the ill effects to the fetus is to be addressed.Preconceptional planning forms the mainstay of the management.

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Conflicts of interest

None

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