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A Case Report of Successful Pregnancy Outcome in Women with Recurrent Miscarriage with Systemic Lupus Erythematosus

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Abstract: ***Background: Recurrent pregnancy loss defined as the loss of ≥2 pregnancies includingpregnancy losses either after spontaneous conception or by ART but excluding ectopic and molar pregnancies[8] according ESHRE 2018. Systemic Lupus erythematous in pregnancy is an idiopathic, chronic autoimmune disorder more common in reproductive age group affecting skin, joints, kidney, lungs, serous membranes, liver, and CNS[10]. Pregnancy and SLE affects the immune system thus increases the pregnancy associated complication like miscarriage, intrauterine fetal death, prematurity, pre eclampsia and fetal growth restriction. Materials & Methods: An 29 years female came to department of OBG with history of recurrent pregnancy loss for prepregnancy counselling and further evaluation. Case Report: 29 years old female came with history of recurrent pregnancy losses which was managed medically. Evaluated for recurrent pregnancy loss and diagnosed with SLE. Preconceptional counselling was given, again she conceived spontaneously and started on Aspirin and low molecular weight heparin. Close monitoring was done throughout the pregnancy. Elective cesarean section done in view of major degree CPD and delivered a healthy female baby. Conclusion: Here we report a rare case of Systemic Lupus Erythematous presented with recurrent miscarriages followed by successful delivery.***

Keywords: Recurrent pregnancy loss, Systemic lupus erythematous, LMWH, autoimmune antibodies.

1. Introduction

The etiology of recurrent pregnancy loss includes metabolic/endocrinological diseases, genetic factors, anatomical factors, immune disorders. Systemic autoimmune disorder like antiphospholipid syndrome and SLEhave been found to be major causes of RPL in recent decades.

Systemic Lupus Erythematous is a multiorgan autoimmune disorder thus affects various organs of the body. It is predominantly seen in childbearing age group with clinical manifestations like fever, arthralgia, myalgia, weight loss, skin rashes, lymphadenopathy, nephropathy effusion (pleural and pericardial) and seizures**.** Its course is characterized by phase of remission and relapse. SLE is known to have familial predisposition linked to alteration in HLA system[8].

Maternal Complication due to SLE includes Lupus flare (25%), hypertension (15%), nephritis (16%), pre eclampsia (7%), and eclampsia (<1%) and fetal complications are preterm delivery (39%), spontaneous miscarriage (16%), still birth (3.6%) and fetal growth restriction (12%) [3]. We are reporting this case because of the positive pregnancy outcome.

2. Methods

An 29 years female came to department of OBG in Sree Balaji medical college and hospital with history of recurrent pregnancy loss for pre pregnancy counselling and further evaluation. Patient was evaluated for recurrent pregnancy loss to rule out endocrine, genetic, immunological causes. Laboratory investigations done. Karyotyping of both parents was normal. Serological markers for Autoimmune diseases were done and found to have systemic lupus erythematosus and followed up closely.

3. Case Report

29 years old female married since 4 years came for pre-pregnancy counselling. She had five recurrent miscarriages all of which was in the first trimester and medically managed. Patient was evaluated for recurrent pregnancy loss to rule out endocrine, genetic, immunological causes. Laboratory investigations done. Karyotyping of both parents was normal. Serological markers for Autoimmune diseases were done which confirmed the presence of autoantibodies like ANA, dsDNA and anti smith antibodies, hence according EULAR criteria diagnosed to have SLE. Patient was counselled and explained in detail about risk of further abortions, antenatal care and management of SLE. She was started on folic acid tablet and asked to report immediately after missed periods. Again she conceived spontaneously which was confirmed by urine pregnancy test and T. ASPIRIN 75mg od started immediately Patient started on

Injection Low Molecular Weight Heparin (Enoxaparin) 40mg subcutaneously daily after confirming live intrauterine pregnancy in ultrasound continued up to 6weeks postpartum. Patient was followed up closely throughout antenatal period for flare up of SLE, maternal and fetal wellbeing. Aspirin was stopped at 36 weeks and LMWH was continued upto 12 hours before delivery. Elective lower segment cesarean section was done at 39 weeks after a short of prophylactic antenatal steroids in view of major degree CPD and delivered an healthy female baby of 2.9kg who cried immediately after birth. Heparin was restarted 12 hours postpartum and continued for 6weeks, Postoperatively patient was monitored for any evidence for thrombosis. Postoperative period was uneventful. Neonatal period was uneventful. Suture removal done on 8th postoperative day and discharged. Patient was kept under regular follow up under OG and rheumatology clinic.

4. Discussion

Recurrent miscarriage is defined as the loss of three or more consecutive pregnancies. According to ASRM, RPL as 2 or more clinical pregnancies as documented by ultrasonography or histopathological examination whereas RCOG and ACOG uses the definition of three or more clinical pregnancies[9]. It affects about 1 - 3 % of women.

Risk factors of RPL [8]:

1) Maternal age: risk of miscarriage least in women around 20 to 35 years whereas miscarriage rate drastically increased after 40 yeas of age.
2) Weight: Significant obstetric complications are encountered in obese womenand even in significantly underweight women too.
3) Alcohol: excessive alcohol intake is also a causative factor for abortion.

Etiology[9, 10, 11]:

1) **Idiopathic**
2) **Endocrinal** causes: accounts of about 20% thus includes like Diabetes, thyroid dysfunction, hyperprolactinemia, luteal phase defect and polycystic ovarian syndrome.
3) **Autoimmine Disease**: accounts of about 15%. High level of antiphospholipid antibodies (IgG, IgA or IgM isotopes), lupus anticoagulant and anticardiolipin antibodies can lead to repeated miscarriages.
4) **Anatomical:** accounts between 2 - 15%. It includes fibroids, synechiae, polyps, adenomyosis and cervical insufficiency.
5) **Chromosomal** anomalies about 3 - 5% like trisomes, balanced translocation
6) **Infections** rare causes.

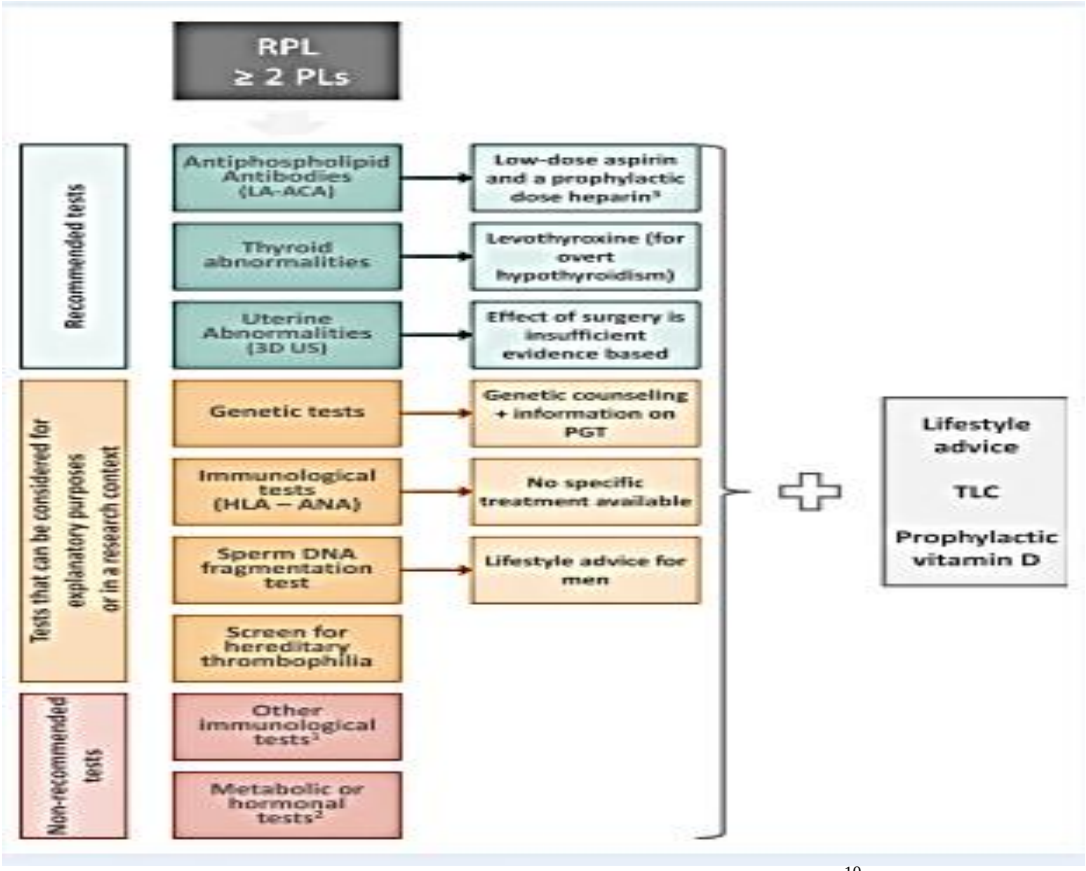

Figure 1: Test recommended for recurrent pregnancy loss[10]

Systemic Lupus Erythematosus is an autoimmune connective tissue disorder that affects various organs and system diagnosed between 20 and 40 years of age. Most commonly encountered during pregnancy and puerperium[6].

Types of antibody[5] involved in SLE are:

1) Antinuclear antibodies.
2) Antidouble stranded DNA antibodies.
3) Anti smith antibodies.
4) Anti Ro and Anti La antibodies.
5) Antiphospholipid antibodies.

Important immune changes that occurs in women with SLE are defect in immune system and tolerance. Variations in immune mechanisms may have severe adverse effects on fetus resulting abortion and neonatal lupus and in mother resulting in SLE reactivation

In healthy pregnancy, Th 2 cells seen predominantand also suppresses cytotoxic T cells thus helps in maintaining the pregnancy. In SLE, defect in immune system disturb T regulatory cells function which plays a central role in regulation of immune system.

Two types of T regulatory cells are secreted; Natural T regulatory cells synthesized from thymus and Induced T regulatory cells produced in the periphery. Main role of T regulator cells is to control immune cells like macrophages, cytotoxic CD8 cells, and NK cells. Treg cells acts on maternal fetal interface with increased concentration in the decidua. T regulatory cells inhibits allogenic fetal rejection thus helps in maintaining the pregnancy. Whereas absence of Treg cells results in fetal rejection/miscarriage. In normal pregnancy, Treg cell count was found to be increased but decreased inpregnancy loss and preeclampsia.

The decline in the number and action of Treg cells may present with obstetrics complication in women with SLE.

In SLE, inactive Treg cells causes defect in maintenance of fetal immune tolerance and result in adverse effects like abortion, pre eclampsia and preterm delivery.

Diagnosis

SLE is suspected by clinical features and confirmed by serological markers. In 2019, New criteria for diagnosis of SLE formulated by European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR). Each criterion is given points from 2 to 10. Patients with at least one clinical criterion and 10 or more points are classified as having SLE.

Table 1: European League Against Rheumatism (EULAR) criteria

Domain[11]	Criteria	Points
Constitutional	Fever	2
	Leukopenia	3
Hematologic	Thrombocytopenia	4
	Autoimmune Hemolysis	4
Neurologic	Delirium	2
	Psychosis	3
	Seizure	5
Cutaneous	Alopecia	2
	Oral Ulcers	2
	Subacute Cutaneous/Discoid	4
Serositis	Pleural/Pericardial Effusion	5
Arthritis	Synovitis +2 Joints	6
Renal	Proteinuria >0.5g/24hours	4
	Class 2/5 Lupus Nephritis	8
	Class3/4 Lupus Nephritis	10
Antiphospholipid Antibody	Anti - Cardiolipin Antibodies Or Anti - B2gp1 Antibodies Or Lupus Anticoagulant	2
Complement Proteins	Low C3 Or Low C4	3
	Low C3 And Low C4	4
High Specific	Anti - dsDNA Antibody Or Anti - Smith Antibody	6

Management of SLE

Preconception counselling and risk stratification must be performed for all women diagnosed with SLE ideally with both obstetrician and rheumatologist.

Key features[3] to be considered at preconception are:

1) Evaluation of disease activity
2) Any major organ involvement with comorbidities.
3) Antibodies profile.

Antenatal care should begin early with frequent antenatal visits every fortnight in first and second trimester followed by weekly in 3rd trimester should be advised. Fetal growth and well being should be assessed using ultrasound every 3 weeks until delivery[12].

Fetal surveillance should be initiated at 30 - 32 weeks.

Low dose aspirin can be used throughout the pregnancy. Steroids like prednisolone or methyl prednisolone can be used[7].

Low molecular weight heparin recommended as it does not cross placenta. Heparin reduces the risk of abortion by 54%. Heparin in addition to its anticoagulant effect, prevention of placental thrombosis also block the activation of complement targeted to decidual tissues[4]. It also preserves trophoblastic function, reduce generation of inflammatory mediators and thus prevent obstetrics complication[1].

Delivery should be conducted at term. Postpartum SLE flare should be looked for and should be treated early[12].

5. Conclusion

Active SLE is often associated with serious maternal and fetal consequences. Hence pregnancy should be planned when the disease is under controlled for atleast 6months. The success of antenatal and postnatal period in our case without any complications defines the importance of low dose aspirin and low molecular weight heparin which was considered safe during pregnancy to improve maternal and fetal outcome.

Conflicts of Interests

The authors declare that there are no competing interests.

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Logeswari. B. M - Critical analysis
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Mahalakshmi - Data collection
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