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DIAGNOSIS AND MANAGEMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS IN PREGNANCY: A CASE REPORT

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ABSTRACT Systemic lupus erythematosus (SLE) is a heterogenous autoimmune disorder with a complex pathogenesis that results in interactions between susceptibility genes and environmental factors. Almost 90 percent of SLE cases are in women; especially in child bearing age. It is a chronic inflammatory disease with multisystemic involvement in which immune complex deposition causes damage to the tissues involved. Maternal and fetal mortality and morbidity are still significantly high despite improvements in outcomes. Maternal morbidity includes higher risk of disease flares, preeclampsia and other pregnancy-related complications. Fetal issues include higher rates of preterm birth, fetal growth restriction, and neonatal lupus syndromes. Management option is limited to few safer drugs. A multidisciplinary approach, with close medical, obstetric and neonatal monitoring, is essential for optimal outcomes. This case report describes a 27 years old primigravida diagnosed with SLE for the first time in pregnancy, evaluated and managed with a good feto-maternal outcome.

KEYWORDS : fetal growth restriction, neonatal lupus syndrome, multidisciplinary approach

INTRODUCTION

Lupus is a chronic inflammatory disorder in which connective tissue damage is caused by deposition of immune complexes, global loss of self tolerance with activation of auto reactive T and B cells leading to production of pathogenic autoantibodies and tissue injury. The overactive B lymphocytes are responsible for autoantibody production and immunosuppression is impaired, which includes regulatory T-cell function.(Charles A Janeway et al., 2001) Lupus is variable in presentation, course and outcome. Findings may be confined to one organ system, and others become involved later or, the disease may first be multisystemic. Frequent findings are malaise, arthralgia, rash, anaemia, thrombocytopenia, renal abnormalities, fever, pleuropericarditis, photosensitivity and cognitive dysfunction. Identification of antinuclear antibodies (ANA) is the best screening test, however positive result in not specific for SLE. Antibodies to double stranded DNA (dsDNA) and to Smith antigens (Sm) are relatively specific for SLE.(Kumar et al., 2009) During the past several decades, pregnancy outcomes with SLE have improved remarkably. Factors favouring good outcomes are lupus activity quiescent for 6 months before conception, no renal involvement, absence of APLA or lupus anticoagulant and no superimposed preeclampsia.

Case Report

A 27 years old primigravida conceived spontaneously, married since 2 years, booked case at Government Medical College and Hospital, Nagpur, Maharashtra, India with 3 ANC visits and Daga hospital, Nagpur with 2 ANC visits with normal BP record was admitted at 30 weeks of gestation with complaints of edema feet since 1 month and joint pain since 2 days. Patient was a known case of Sickle cell trait (AS pattern). There was no history of any blood transfusion or hospital admission in past. On examination, the patient was conscious oriented afebrile, extremely pale and had a tachycardia of 120/min and BP 120/70. She had grade 2 edema feet since 1 month worsened to grade 3 since 1 week. On abdominal examination, abdominal wall edema was present and height of uterus was corresponding to 28 weeks of gestation (FGR-Fetal growth restriction as the expected height of uterus was 30 weeks), cephalic presentation, uterus was well relaxed and fetal heart rate was around 140/min regular. During her monitoring in the inpatient ward, her blood pressure was normal and there were no premonitory signs and symptoms of pre-eclampsia and deep tendon reflexes were normal. Her investigation profile was as follows-

On admission

1- Hb 3.2 g/dl and platelets 30,000/microlit (severe anaemia and thrombocytopenia). 3 blood transfusions and 5 doses of multivitamin injections (containing Vitamin B12 and Folic acid) were given.
2- Peripheral smear examination showed mild to moderate anisopoikilocytosis, normocytic to microcytic RBCs with macro-ovalocytes and pencil cells, moderate hypochromia, platelets and WBCs normal
3- Reticulocyte count normal (1.2).
4- LFT- serum bilirubin- 1.5 g/dl, liver enzymes- normal, KFT- blood urea 18mg/dl and serum creatinine 0.8mg/dl.
5- Urine albumin estimation by dipstick method was 1+ (>30mg/day).
6- Urine routine microscopy showed no proteinuria or bacteriuria.
7- 24 hour urine protein estimation sent- 360mg in 24 hours (subnephrotic proteinuria).
8- Urine protein creatinine ratio was 0.075 (normal).
9- 75 gm Glucose tolerance test of the patient was normal
10- USG abdomen-pelvis s/o mild hepatosplenomegaly.
11- ANA profile- Anti Sm antibody positive
12- Obstetric USG report

At gestational age of 30 weeks- BPD- 27 weeks /HC- 28 weeks /AC- 26 weeks /FL- 28 weeks/ liquor adequate/ placenta fundal/ EFW 1.05 kg Physician and Rheumatologist consulted and patient was started on Tab. Ecosprin 75mg OD and Tab HCQ 200mg BD. Patient was discharged on Hb 7.4 g/dl and platelet count 1,98,000/ microlit and advised to continue HCQ and aspirin, oral iron and calcium supplementation, amino acid supplementation, plenty of oral fluids, weekly follow up. Antenatal monitoring in the form of biweekly Non-Stress test and weekly USG Doppler was done. Patient was followed up

and readmitted at 38 weeks gestation for elective termination of pregnancy.

On readmission

1- Hb 8.9 g/dl, platelets 99,000/microlit, INR LFT KFT normal
2- Obstetric USG report

At gestational age of 38 weeks- BPD- 33 weeks /HC- 33 weeks /AC- 30 weeks /FL- 34 weeks/ liquor adequate/ placenta fundal/ EFW 2.1 kg Aspirin 75 mg OD was withheld a day prior to surgery as per physician's advice. Elective LSCS was planned and female baby with 2.2 kg birth weight was born. The intraoperative and postoperative period was uneventful with minimal bleeding. Neonatologist was called in for examination of the baby. APGAR score at birth was- 8, at 5 min- 9. No evidence of any bleeding tendencies or signs of neonatal lupus. 2D Echo of the baby advised- normal. Patient reviewed by physician, asked to omit Aspirin and continue Tab. HCQ 200 mg BD. Patient was indoor upto day 5 of LSCS and discharged after checking healthy suture line.

DISCUSSION

During pregnancy, lupus improves in a third of women, remains unchanged in a third and worsens in the remaining third. High level of suspicion is essential in diagnosing the disease when presents with multisystem involvement for the first time in pregnancy. The patient discussed above was evaluated for anaemia, proteinuria and FGR to begin with. The anaemia did not improve significantly even after blood transfusions and haemolytic profile was within normal limit. The proteinuria as detected on bedside dipstick test and further confirmed by 24-hour urine protein estimation suggested subnephrotic range proteinuria. Urine routine microscopy and culture sensitivity ruled out urinary tract infection. Diabetic nephropathy as a differential for subnephrotic proteinuria ruled out by 75 gm OGTT. Owing to the multisystem involvement in the form of anaemia, thrombocytopenia, arthralgia, nephritis, hepatosplenomegaly- autoimmune etiology was suspected and ANA profile was sent. Patient was diagnosed with SLE at 32 weeks gestation with anti Sm antibody positive. After consulting the physician and rheumatologist, patient was started on Tab. Ecosprin 75mg OD and Tab HCQ 200mg BD.

CONCLUSION

By using the Nationwide Inpatient Sample from 2000 to 2003, Clowse et al. compared maternal and pregnancy complications for all pregnancy-related admissions for women with and without SLE.(Clowse et al., 2006) Among patients with lupus, maternal mortality was 20-fold higher and risks for thrombosis, infection, thrombocytopenia and transfusion were each 3- to 7-fold higher. Lupus patients also had a higher risk for caesarean sections (odds ratio: 1.7), preterm labour (odds ratio: 2.4), preeclampsia (odds ratio: 3.0), and were more likely to have other medical conditions, including diabetes, hypertension, and thrombophilia. (Clowse, 2007) The rates of adverse perinatal outcome- spontaneous abortions, preterm delivery, IUFD, fetal growth restriction, stillbirth, preeclampsia and eclampsia and neonatal lupus syndrome are significantly increased in pregnancies complicated by SLE. A coordinated approach, with close monitoring by a multidisciplinary team is essential for optimal outcomes. Aims of the treatment are to maintain lupus disease quiescent during and after pregnancy and to improve the outcome of the fetus. Preconception assessment is a vital aspect of pregnancy planning in women with SLE. Maternal and fetal risk factors should be evaluated prior to conception and the patient should be counselled about all the risks including lupus flares and development or worsening of lupus nephritis. Any drug with teratogenic potential should be stopped before pregnancy. Ideally, conception should only be attempted in the state of disease remission, minimizing the need of drug use during pregnancy.

Following drugs can be used in women suffering with SLE in pregnancy

Steroids	Prednisolone Methylprednisolone Betamethasone Dexamethasone
Antimalarials	Hydroxychloroquine
Antiplatelets	Aspirin
Anticoagulants	Heparin
Immunosuppresives	Azathioprine Cyclosporine Tacrolimus
Antihypertensives	Methyldopa Labetalol Nifedipine Hydralazine (with caution) Beta-adrenergic blocking agents (with caution)
Anti-inflammatory drugs	Acetaminophen NSAIDS
Miscellaneous	Calcium supplements Vitamin D

The lowest possible dose of corticosteroids during pregnancy, preferably <20mg per day should be used, and stress doses at delivery in patients on long-term corticosteroid therapy. In cases of lupus flare, intravenous pulse methylprednisolone should be given.(Lateef & Petri, 2012) Hydroxychloroquine should be continued during pregnancy in all patients with SLE due to its safety and efficacy.

Discontinuation of this drug leads to increased disease activity.(Østensen, 2006) Control of blood pressure in pregnancy may minimize the progression of disease and prevent the adverse pregnancy outcomes seen in those with hypertension.(Moroni & Ponticelli, 2016) . Aspirin reduces the risk of pre-eclampsia and perinatal death and increases the birth weight in those with risk factors including renal disease. The use of low-dose aspirin is recommended in all pregnant women with chronic kidney disease without contraindications(Day et al., 2000). In case of previous thromboembolic event full anticoagulation with low molecular weight is recommended. In case of massive proteinuria, low molecular weight heparin at prophylactic doses (with Factor Xa monitoring) for duration of pregnancy and 6 weeks post-partum, especially in patients of antiphospholipid-antibody syndrome.

Most immunosuppressive agents are contraindicated in pregnancy, but if need arises azathioprine can be given in low doses to suppress lupus flare. NSAIDs and other anti-inflammatory agents can be given with caution after evaluation of renal function. Thus diagnosis, evaluation and management of SLE in pregnancy needs a multidisciplinary approach, one to one patient care, intensive monitoring of the mother and the fetus for optimal feto-maternal outcome.

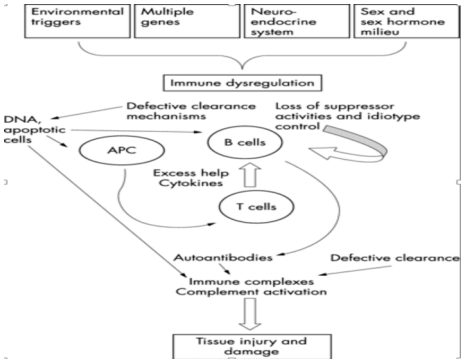

Fig 1- Figure depicting pathophysiology of SLE

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