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Case Report

Rare case of active lupus nephritis with mixed connective tissue disease in pregnancy

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ABSTRACT

This was a case report of a 32 years old pregnant woman with 9+6 weeks of gestation presented with hyperemesis gravidarum who was diagnosed of lupus nephritis with mixed connective tissue disorder (MCTD) 7 months back. Renal biopsy-lupus nephritis class 4 with activity score of 9/24 and chronicity score of 0/12. She was advised contraception in view of active lupus nephritis with MCTD but she presented to us with 9+6 weeks gestation with conception being within 20 days of her last dose of cyclophosphamide. She was managed with oral immunosuppressants by constant supervision of obstetricians and nephrologist. The management of MCTD and lupus nephritis in pregnancy presents a diagnostic and therapeutic challenge for providers. Women with prior lupus nephritis and MCTD can have safe, successful pregnancies with excellent, immaculate, collaborative care between obstetricians, nephrologists, and multidisciplinary staff.

Keywords: Pregnancy, Lupus nephritis, Mixed connective tissue disorder

INTRODUCTION

The management of lupus nephritis in pregnancy presents a diagnostic and therapeutic challenge for providers. The incidence of lupus nephritis in pregnancy is 1.4-21.9 and prevalence is 7.4-159.4 per 100000 people.[1] Pregnancy creates a series of physiologic changes in the immune system and kidney that may result in an increased risk of disease flare, cutaneous disease (25-90%), arthritis (20%), hematologic disease like thrombocytopenia (10-40%) and adverse maternal and fetal outcomes, such as preeclampsia (30%), fetal loss (29%) and preterm delivery (26%).[2,3]

Mixed connective tissue disease (MCTD) has been recognized as a distinct condition since the discovery of anti-U1RNP antibodies in 1974. Its evolution during pregnancy is less well understood, due to its rarity and the varying clinical presentations associated with U1RNP antibodies (rheumatoid, lupus, polymyositis, and scleroderma pattern).

Systemic lupus erythematosus (SLE) is an autoimmune disease that predominantly affects women of reproductive age. Pregnancy and its outcome are a major concern to most SLE patients. Queries regarding the risk of disease flares during pregnancy, chance of fetal loss, and the safety of various drugs are often raised. With the improvement in the understanding of the pathogenesis of SLE and the judicious use of immunosuppressive drugs, better disease control can now be achieved and SLE patients should not be deprived of the opportunity for bearing children.

CASE REPORT

A 32 years old pregnant woman with 9+6 weeks of gestation presented with complaints of excessive vomiting. On admission, tachycardia with severe dehydration was noted.

Lab investigations were done, showed UKB positive; urine routine showed albumin 4+, pus cells 60-80 with granular

casts; urine PCR 2.30 mg/mg CRT; anti ds DNA antibody 114.35 IU/ml; CBC normal; RFT, LFT, TFT, RBS, serum electrolytes were normal.

Early obstetric scan was done and it showed a single live intrauterine gestation of 11weeks, NT=1.4 mm, nasal bone ossification noted, CRL=4 cm.

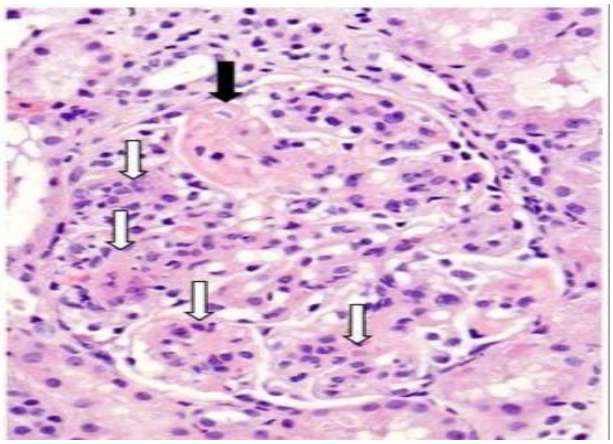

Figure 1: Renal biopsy.

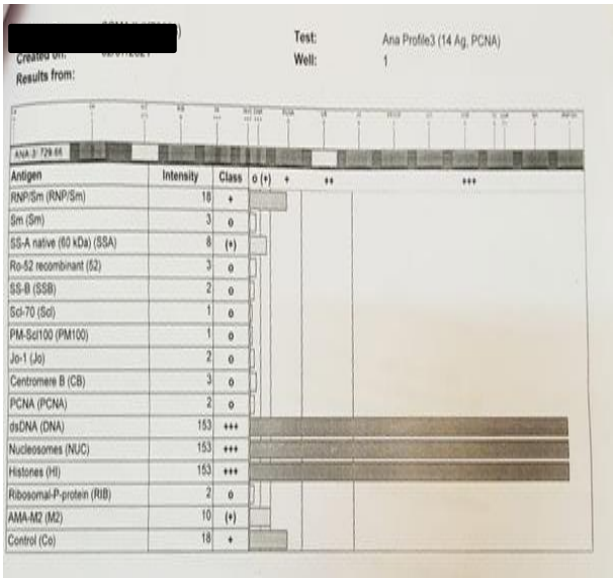

Figure 2: ANA blot.

She was diagnosed of lupus nephritis with MCTD 7 months back. Renal biopsy was done and it showed lupus nephritis class 4 with activity score of 9/24 and chronicity score of 0/12 (Figure 1). ANA blot showed RNP/sm-positive; dsDNA, nucleosomes, histones-strongly positive; AMA-M2 borderline positive (Figure 2). She was started on cyclophosphamide 500 mg IV infusion for 6 cycles. Last dose (6th) was given on 2 November 2021.

Pregnancy management

Hyperemesis was managed and nephrologist was consulted and started on tablet prednisolone 40 mg 1-0-0 and tablet HCQ 200 mg 1-0-1 to be continued throughout pregnancy. She was discharged with folic acid and tablet aspirin 75 mg OD.

She was on regular follow up (once in a fortnight) with obstetricians and nephrologist. At 26 weeks of gestation, she developed hypertension and was started on tablet labetolol 100 mg BD and tablet amlodipine 10 mg OD. Anomaly scan was normal and following growth scans normal.

She was admitted at 37 weeks of gestation with pre-eclampsia. All baseline investigations sent were normal and PGE2 gel induction was done in view of Pre-eclampsia. She underwent emergency LSCS in view of non-progression of labor, delivered an alive female baby of 2.6 kg; baby initially shifted to NICU, was later given mother side.

DISCUSSION

Our case was advised contraception in view of active lupus nephritis with MCTD but she presented to us with 9+6 weeks gestation with conception being within 20 days of her last dose of cyclophosphamide. Conception after 12-18 months (minimum 6 months) of remission, pregnancies have favourable outcome.[4] WHO LN classes I, II, and V are known to have low activity and chronicity indices, whereas classes III and IV tend to be more aggressive and are associated with an increased incidence of LN flare.[2]

Differentiating lupus nephritis from preeclampsia often presents as a conundrum, but lupus nephritis can be confirmed by the presence of decreasing complement levels and increasing double- stranded DNA (dsDNA) antibody levels in addition to new onset hypertension and proteinuria.[5]

According to a meta-analysis of 37 studies on maternal and fetal outcomes in SLE patients, maternal complications of significance during pregnancy included lupus flare (25.6%), hypertension (16.3%), nephritis (16.1%), and preeclampsia (7.6%). Severe complications, including eclampsia, stroke, and death, were observed in approximately 1% of patients. Adverse fetal outcomes included an increased risk of fetal loss (23%; including spontaneous abortion, neonatal death, and stillbirth), preterm delivery (40%), and IUGR (13%).[6] European league against rheumatism (EULAR) guidelines also suggested the increased risks for fetus and mother.[7]

In a case series done by Tardif et al "mixed connective tissue disease in pregnancy: a case series and systematic literature review", during pregnancy 37.1% had active MCTD and 26.7% had relapsed. Maternal complications included caesarean section (31.1%, n=19), preeclampsia (17.6%, n=13), thromboembolism events, and death (2.5%, n=2 for each). Fetal complications included prematurity (48.1%, n=25), intrauterine growth restriction (38.3%, n=19), and neonatal lupus (28.6%, n=18,

including chondrodysplasia punctata). More than half (n=10) of the neonatal lupus cases were explained by anti-U1RNP only. The perinatal mortality rate was 17.7% (n=14). Pregnant women with active disease had higher rates of prematurity (OR=7.60; 95% CI [1.93; 29.95]) and perinatal death (OR=16.83; 95% CI [1.90; 147.70]).[8] McHugh observed in MCTD: live birth rate was 72%, 18.7% miscarriages, 8.9% stillbirths and 5.4% cases with intrauterine growth restriction.[9,10] Maternal pregnancy outcomes were as follows: 3.9% developed preeclampsia, 0.9% developed eclampsia, 15.3% developed gestational hypertension and 1.5% developed gestational diabetes.

The recently published PROMISSE study from Jill Buyon's group is a large prospective study occurring in the United States and Canada that included 385 women from multiple ethnic and racial backgrounds.

The study results highlighted some crucial messages for women with lupus or quiescent lupus nephritis. Overall, 81% of 236 women had uncomplicated pregnancies, and fetal and infant deaths were rare. Severe maternal flares in the second and third trimesters occurred only in 2.5% and 3.0%, respectively. The study identified what constituted risk for adverse pregnancy outcomes. Of the 129 women who were non-Hispanic white, not receiving antihypertensive agents, lupus anticoagulant (LAC)-negative, had a physician's global assessment score of ≤1 (i.e., mild or no disease activity) at screening, and a platelet count of atleast 100×109 cells/l, only 10 (7.8%) had adverse pregnancy outcomes; the fetal or neonatal death rate was also low (only 3.9%) for this group. In contrast, in the 50 women who were either LAC-positive or LAC-negative, non-white or Hispanic, and treated with anti-hypertensive agents, the adverse pregnancy outcome rate was very high at 58% with a high proportion of events occurring between 23 and 35 weeks gestation, and the fetal or neonatal death rate was 22%. Clearly, this will be relevant to many women with prior lupus nephritis, many of whom will be on anti-hypertensive agents, but what needs to be stressed to patients, however, is that the majority of these women had quiescent disease, were in specialist centers, and were nearly all on hydroxychloroquine.[11]

CONCLUSION

Women with prior lupus nephritis and MCTD can have safe, successful pregnancies. The prognosis for both mother and child is best when SLE is quiescent for at least 6 months before the pregnancy and when the mother's underlying kidney function is stable and normal or near normal. As in our case, even without preconceptional control of lupus nephritis for 6 months as advocated in a case of diffuse grade 4 lupus nephritis, successful pregnancy is possible.

Excellent, immaculate, collaborative care between obstetricians, nephrologists, and multidisciplinary staff is essential.

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