Clinical Improvement and Successful Pregnancy in a Preeclamptic Patient With Antiphospholipid Syndrome Treated With Pravastatin

To the Editor:

The clinical hallmarks of the antiphospholipid syndrome (APS) are thrombosis and adverse obstetric outcomes. Women with APS have a higher incidence of preeclampsia. Currently, treatment of APS focuses on anticoagulation therapy, treatment mostly given empirically and often ineffective. Similarly, treatment for preeclampsia remains symptomatic and also ineffective. Studies in animal models support the hypothesis that pravastatin may be an effective therapy to prevent pregnancy complications in APS and in preeclampsia. Here, we describe a patient, with a previous history of preeclampsia, thrombosis, and APS, presenting with preeclampsia at 23 weeks’ gestation in her second pregnancy that was treated with pravastatin, which resulted in marked clinical improvement and successful pregnancy outcome.

Case Report

A 30-year-old woman with no previous medical history had a first pregnancy complicated with early preeclampsia with bilateral notching (22 weeks and 0 days) and hypertension and edema at 24 weeks, leading to a still birth at week 26. She developed deep vein thrombosis 2 days postpartum. Based on her history of deep vein thrombosis, early preeclampsia, and twice positive lupus anticoagulant, with an interval of 3 months between the tests, the patient was diagnosed with APS.

The patient received therapeutic doses of low-molecular-weight heparin for 3 months and prophylactic doses while trying to conceive again. Her blood pressure and proteinuria remained normal. Ten months later, she got pregnant and was started on intermediate doses of enoxaparin (0.6 OD) and aspirin (100 mg OD). Blood pressure and proteinuria were normal between pregnancies and at weeks 6 and 11 of gestation. At 13 weeks and 2 days, the uterine artery Dopplers showed increased resistance and bilateral notching that persisted during the scan performed at 21 weeks despite anticoagulation therapy (Figure A). Enoxaparin was increased to therapeutic doses. At 23 weeks and 0 days, she developed early preeclampsia again (proteinuria=360 mg/24 h and hypertension; Figure B and C). Because of her previous poor obstetric history and the fact that she did not respond to anticoagulation, the patient was started on pravastatin. Pravastatin treatment was selected based on the animal work demonstrating the effectiveness of pravastatin in obstetric APS and preeclampsia, and recent data showing that the passage of pravastatin through the placenta is limited. At 23 weeks and 2 days, the patient was started on 20 mg of pravastatin, together with enoxaparin 0.4 BD and aspirin 100 mg OD. At 24 weeks and 3 days, the notch on the right uterine artery resolved and the pulsatility index value was within normal range. On the left side, the pulsatility index remained high (Figure A and D). During pravastatin treatment, proteinuria went down from 360 to 280 mg/24 h at week 26 (Figure B), and at 30th week of gestation, the proteinuria was 220 mg/24 h (Figure B). The blood pressure normalized 1 month after the initiation of pravastatin treatment (Figure C). The patient was monitored closely with blood tests and Doppler scans every 2 weeks. At 36th week, a decline in fetal growth was noticed and labor was induced at 38 weeks and 0 days. Aspirin and pravastatin were stopped 7 days before labor. Proteinuria at 37 weeks was 220 mg/24 h. A live and healthy baby girl weighing 2830 g was delivered vaginally, and no peripartum complications were observed. Enoxaparin was stopped 12 hours before labor and restarted 6 hours postpartum. Interestingly, 4 days postpartum, the proteinuria increased to 426 mg/24 h (Figure B) and hypertension and edema relapsed (Figure C). The patient was put back on pravastatin and aspirin. Eight days postpartum, proteinuria was 489 mg/24 h, and during pravastatin treatment, it went down to 225 mg/24 h on the 20th day postpartum (Figure B). Once again, the patient responded well to pravastatin treatment and is now 120 days postpartum. She is still lupus anticoagulant positive, but her blood pressure and proteins in urine remain within normal limits while on the same therapy (enoxaparin, aspirin, and pravastatin). The baby girl shows a completely normal development, and she is closely followed.

Discussion

To our best knowledge, this is the first report on the effective use of pravastatin in a preeclamptic woman with APS. Pravastatin reversed preeclampsia clinical symptoms allowing the pregnancy to go to term. The recidivism of preeclampsia after stopping the treatment highlights the efficacy of pravastatin in abrogating preeclampsia.

This report supports a likely benefit of statins for the treatment of preeclampsia and APS. Its use may be principally helpful among women who do not respond to anticoagulation treatment. This is a single case report, and further research is warranted to validate our findings in a larger clinical study. Currently, a randomized placebo-controlled clinical trial of statins in preeclampsia, Statins to Ameliorate early onset Preeclampsia (StAMP) trial is recruiting patients in the United Kingdom. In addition, a clinical trial in the United States just started a pilot trial to collect maternal–fetal safety data in high-risk pregnant women receiving pravastatin to prevent preeclampsia (identifier, NCT01717586). Epidemiological data collected to date suggest that statins are not major teratogens. We need to consider that this report is a one-case-only study, and as such, it has intrinsic limitations. Good evidence should be acquired from the clinical trials. If clinical trials confirm the beneficial effects of statins in treating preeclampsia, as observed in this case report, an affordable and fast way to reduce this life-threatening disease may have been identified.

Disclosures

None.

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**Figure.** Proteinuria, blood pressure, and uterine artery Doppler flow variations in the patient during pregnancy and postpartum. A, Uterine artery Doppler flow studies. Doppler velocimetry shows increased pulsatility index (PI) associated with notch in the waveform in the left and right arteries at 13+2 and 21+2 gestational weeks. After pravastatin treatment, uterine arteries Doppler flow measurements were normalized on the right uterine artery, but remained high on the left (24+3, 33+2, 36+4 gestational weeks). B, Urinary protein levels (mg/24h) in the patient during pregnancy and postpartum. Proteinuria dropped dramatically after pravastatin treatment was administered at 23 weeks and 1 day and at day 5 postpartum. Ninety days postpartum, proteinuria values were within normal limits. C, Systolic (SBP) and diastolic (DBP) blood pressure variations in the patient during pregnancy and postpartum. The different treatments that the patient received are also shown. Notice that SBP and DBP dropped significantly after pravastatin treatment at 23 weeks and 1 day and at day 5 postpartum. Ninety days postpartum, blood pressure values were within normal limits. D, Doppler ultrasound imaging of the uterine arteries at 13+2, 21+2 and 24+3 gestational weeks. Enox indicates enoxaparin.
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