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Vaginal Delivery Following Thrombolytic Therapy in the Third Trimester: A Case Report

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INTRODUCTION

Stroke in pregnancy is a leading cause of maternal mortality, as it is estimated that 7.7-15% of all maternal deaths are due to stroke.[1] Risk factors for stroke in women include the prothrombic state of pregnancy and pregnancy-associated complications including preeclampsia and eclampsia.[2] Due to the commonly applied ethical barrier of including pregnant patients in randomized control trials, there are no clear guidelines for the management of pregnancy-associated stroke (PAS). Animal models suggest tissue plasminogen activator (tPA) does not cross the placenta, and a handful of case reports imply favorable outcomes with the use of tPA to treat ischemic infarcts in pregnancy.[3-6]

Despite the increased acceptance of tPA treatment in pregnancy, there remains a gap of knowledge pertaining to the timing of delivery in patients following tPA administration in the late third trimester. This is especially true in patients who have conditions in which immediate delivery is indicated, such as preeclampsia with severe features. The use of neuraxial anesthesia soon after tPA administration poses an additional clinical dilemma in which limited data exists. We present a patient with preeclampsia with severe features and persistent abnormal coagulation studies after tPA administration for presumed ischemic stroke who had an uncomplicated spontaneous vaginal delivery with epidural anesthesia.

CASE REPORT

A 31-year-old gravida 2 para 1 female at 36 weeks and 5 days by last menstrual period confirmed with ultrasound presented to the emergency department with acute onset left sided facial droop and left sided weakness. Past medical history was significant for preeclampsia in a prior pregnancy, sick sinus syndrome with single-lead pacemaker in place and prior ablations, anxiety, and depression. Her current medications included prenatal vitamin and 81 mg aspirin which she had not taken for two days prior to presentation.

Review of systems was unremarkable apart from left sided weakness and left sided facial droop. Vital signs were normal apart from a significant blood pressure of 144/79 mmHG. Subsequent blood pressure readings were within normal limits. Physical exam revealed left facial droop present in both upper and lower face with drift of the left arm and left leg with a National Health Institute stroke scale of 4. There were no sensory deficits. Laboratory values obtained were noncontributory and included a prothrombin time of 13 seconds, partial thromboplastin time of 23 seconds and an international normalized ratio of 1.0. Non-contrast head CT showed no intracranial abnormalities. 2D echocardiogram and carotid studies were unremarkable. At this time, her diagnosis was subradiographic stroke.

The patient received tissue plasminogen activator (tPA) two hours after symptom onset, after which her weakness and facial droop improved. She received 12 mg betamethasone four hours after symptom onset and magnesium 4-gram load followed by 1-gram per hour infusion. The patient was transferred to our tertiary care center and admitted to the neurology intensive care unit where she remained normotensive and afebrile. Given the patient did not have sustained elevated blood pressure readings, with the absence of proteinuria and any serum laboratory abnormalities consistent with preeclampsia, the managing teams felt she did not have preeclampsia and continued expectant management without magnesium sulfate infusion. She was subsequently transferred to the labor and delivery unit for further maternal and fetal monitoring.

Two days after symptom onset, pertinent labs included a hemoglobin of 11.1 gm/dL, platelet count of 204,000 K/uL, AST of 15 u/L, ALT of 17 u/L and 24-hour urine protein of 323 mg. Her aspirin dose had been increased to 325 mg daily, and on hospital day three she started to have sustained mild-range blood pressure readings. She was diagnosed with preeclampsia with severe features based on elevated blood pressure with neurologic changes. Magnesium sulfate was reinitiated with 4-gram bolus followed by 2-gram per hour continuous infusion. Given the patient's history of sick sinus syndrome, a 4-gram magnesium load was opted over a 6-gram load to avoid potential arrythmias. Additionally, the patient had a normal body mass index, an indication that she would be likely to reach therapeutic magnesium levels at a 4-gram load dose. Coagulation studies 48 hours after symptom onset included a PT of 10.4 seconds, PTT of 22.1 seconds, international normalized ratio of 0.9 and a critically low fibrinogen of 82 mg/dL. Thromboelastogram revealed low MA Kaolin at 45.5 (normal > 49.9 MM), reflecting low clot strength, and mildly elevated Lysis30 at 11.1 (normal less than 8.1%), increasing concern for fibrinolysis. A noncontrast MRI head revealed no intracranial abnormalities and a noncontrast head MRV showed no evidence of sinus venous thrombosis. The possibility of Bell's palsy was considered but unlikely due to concomitant limb involvement.

After extensive risk stratification between the threats of preeclampsia with severe features versus induction of labor with high hemorrhage risk, particularly from a critically low fibrinogen level, the multidisciplinary consensus was to follow fibrinogen levels for 24 hours to further assess hemorrhage risk prior to delivery. Had coagulation studies been normal, induction of labor would have been indicated for the patient given her diagnosis of preeclampsia with severe features. The option for Cesarean delivery under general anesthetic was considered too high risk for further neurologic injury. The patient was well informed on the potential risks of neuraxial anesthesia after tPA and remained decisive on an epidural for labor, even if transfusion would be required to obtain one.

In the next 12, 24, and 36 hours, the patient's fibrinogen levels increased to 111 dL/mg, 132 dL/mg, and 131 dL/mg, respectively. Her left sided weakness and facial droop continued to improve throughout this time. On hospital day five, five units of cryoprecipitate and one pack of single donor platelets were transfused and repeat thromboelastogram was normal. Neuraxial anesthesia was placed

immediately after transfusions and labor was induced with oxytocin. Seven hours after transfusions and induction, the patient's fibrinogen was 155 mg/dL. The patient delivered a healthy female infant at 37 weeks and 2 days gestational age 12 hours after induction without complications. Apgar scores at 1 and 5 minutes after delivery were 9 and 9. Venous and arterial cord blood gases were both within normal limits at 7.42 and 7.28, respectively. Additionally, there was no neonatal hemorrhage. Magnesium infusion was continued for 24 hours after delivery.

The patient's fibrinogen level eight hours after delivery was 195 mg/dL. After extensive discussion between our blood bank pathologist and OB anesthesiologist, we transfused another five units of cryoprecipitate, and the epidural was removed without issue. Coagulation labs continued to normalize. The patient was discharged on postpartum day three after a normal repeat CT head and neck. She had met all discharge criteria and instructed to follow up in six weeks.

DISCUSSION

Pregnancy-associated stroke (PAS) is projected to occur at a 3-to-13-fold increase in pregnant people compared to non-pregnant, and evidence suggests the incidence is increasing.[7] For non-pregnant patients, thrombolytic therapy with tPA for ischemic stroke, pulmonary embolism, or myocardial infarction is an acceptable therapy.[8] Despite the increasing acceptance of thrombolytic therapy in pregnancy-associated infarcts, there lacks sufficient data from randomized controlled trials for the use of tPA in pregnancy and a knowledge gap remains for optimizing delivery timing to best reduce risk of hemorrhage.[4-6] Specifically, there are minimal reports discussing the management of third-trimester patients who are treated with tPA that results in prolonged abnormal coagulation studies.

The current guidelines for management of preeclampsia with severe features is to deliver at 34 weeks gestational age if there is no prior indication for delivery.[9] The management becomes unclear when coagulation studies are critically abnormal and postpartum hemorrhage risk is high. The case presented provides a strong example of appropriate timing of delivery for patients with newly diagnosed preeclampsia with severe features when also needing to balance the risk of postpartum hemorrhage. Management becomes even more complex in patients who desire delivery with neuraxial anesthesia, which poses an additional risk of hemorrhage and spinal hematoma.[8] It is estimated that 60% of women chose epidural or combined spinal anesthesia during labor and delivery.[9] There are currently different management guidelines for different types of anticoagulant and antiplatelet therapy, but it is overall accepted that coagulation studies should normalize prior to neuraxial anesthesia.[10] This complicates management plans for patients who desire a vaginal delivery with neuraxial anesthesia who also have critically abnormal coagulation studies.

While the use of thrombolytics to treat ischemic embolisms in pregnancy is becoming more accepted, there is limited research on the risks and benefits of neuraxial anesthesia after thrombolytic therapy. Because of the large percentage of women choosing neuraxial anesthesia during labor and the increase in ischemic embolism during pregnancy, there is a need for research regarding the management of pregnant patients who received thrombolytic therapy.

CONCLUSIONS

There are no clear management guidelines for pregnancy-associated stroke when delivery is indicated due to other risk factors like preeclampsia with severe features. Decisions regarding type of anesthesia and mode of delivery are complex. Risks of performing general anesthesia shortly after a pregnancy-associated stroke need to be weighed against the risks of expectant management and risks of neuraxial anesthesia after treatments like tPA. The case presented is an example of a complex patient with preeclampsia with severe features who underwent an uncomplicated spontaneous vaginal delivery with regional anesthesia after tPA administration. We highlight how additional research is needed to establish clear guidelines on the management of stroke in pregnancy with subsequent abnormal coagulation studies.

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