Intravenous Recombinant Tissue Plasminogen Activator in a Pregnant Woman With Cardioembolic Stroke

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Background and Purpose—Historically, the use of tissue plasminogen activator (tPA) thrombolysis in pregnancy has been regarded as relatively contraindicated. Underlying this stance has been the concern over the risk of bleeding complications in both mother and child.

Summary of Case—We report the successful use of intravenous recombinant tPA (rtPA) thrombolysis in a pregnant woman with acute cardioembolic stroke.

Conclusions—The patient improved clinically, did not develop complications after receiving rtPA, and at 37 weeks’ gestation, delivered a healthy infant, demonstrating that rtPA thrombolysis may be used safely in pregnant women.

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Key Words: thrombolysis ■ tissue plasminogen activator

Although not addressed specifically in the latest guidelines for tissue plasminogen activator (tPA) thrombolysis in acute ischemic stroke, the use of tPA in pregnant patients historically has been regarded as relatively contraindicated. The fundamental risks underlying opposition to thrombolytic therapy in pregnancy include placental abruption, retroplacental hemorrhage, abortion, peripartum uterine bleeding, and postpartum hemorrhage. For these reasons, no large controlled trials of thrombolytic agents in pregnant patients have been undertaken. To date, only case reports and case series have been published, citing myriad indications for thrombolysis and thrombolytic agents. Of these reports, there have been 3 citing the use of thrombolytics specifically in the setting of acute arterial ischemic stroke. Two cases reported thrombolytic use in women with first-trimester pregnancies, noted improvement in the patients’ stroke symptoms after intervention, and reported the birth of healthy infants at term. However, both cases were complicated by the development of intracerebral hemorrhages after lysis. A third case reported the successful use of intra-arterial recombinant tPA (rtPA) in a woman pregnant for 37 weeks, demonstrating that rtPA may be used throughout pregnancy. In this case, a healthy infant was delivered only 3 days after treatment.

Herein we report the successful use of intravenous rtPA thrombolysis, uncomplicated by hemorrhage development, in a woman who was 13 weeks pregnant with acute cardioembolic ischemic stroke secondary to presumed prosthetic mitral valve thrombosis.

Case Report

The patient was a 33-year-old, right-handed white woman who presented to an outlying community hospital at 25 to 30 minutes after developing acute onset of right-sided hemiparesis and expressive aphasia. At that facility, she was found to have normal vital signs, and laboratory studies revealed normal peripheral cell counts, electrolytes, and coagulation values. A noncontrast head computed tomography scan was remarkable only for a hyperdense left middle cerebral artery sign.

Recording of the patient’s medical history revealed that 3 years previously, she had undergone mitral valve replacement surgery for a history of mitral valve prolapse. Subsequently the patient had been placed on long-term Coumadin therapy, which was later switched to subcutaneous heparin when she was found to be pregnant. At presentation, the patient was G0P1, and 13 weeks’ pregnant. She was noted to have delivered a healthy baby only 6 months before via induced vaginal delivery after a pregnancy then complicated by gestational diabetes mellitus.

After obtaining informed consent from the patient’s domestic partner, intravenous rtPA was administered per standard protocol (0.9 mg/kg over 60 minutes as a 10% bolus and 90% infusion). Subsequently the patient was transferred via LifeFlight to the OSF Stroke Center for potential receipt of intra-arterial tPA and for tertiary-level neurological care. On her arrival, the patient was found to have a right-sided hemiparesis and fluctuating expressive aphasia with a maximum National Institutes of Health Stroke Scale (NIHSS) score of 13. Because 6 hours had elapsed since the onset of symptoms, the decision was made to forgo intra-arterial thrombolysis.

The following morning, a noncontrast computed tomography scan revealed hypodensities in the left caudate, putamen, globus pallidus, anterior limb of the internal capsule, and adjacent white matter, with effacement of the left frontal

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horn. No evidence of hemorrhage was seen. Carotid Doppler findings were normal, and a transthoracic echocardiogram was remarkable only for a mechanical mitral valve prosthesis and moderate tricuspid regurgitation.

Clinically, the patient improved to an NIHSS of 11 and was placed on prophylactic therapeutic enoxaparin 80 mg subcutaneously twice daily. She was then transferred to an outlying rehabilitation facility, restarted on warfarin therapy, and ultimately improved to an NIHSS of 4. Six months after her stroke and after an uncomplicated pregnancy, the patient delivered a 37-week, healthy male infant via repeat cesarean section.

Discussion
Although pregnancy has historically been widely regarded as a relative contraindication to thrombolytic therapy, >200 pregnant patients have been reported to have received such therapy and overall with low maternal mortality (1%), low fetal loss (6%), and a low incidence of preterm delivery (6%). Furthermore, in a series of 172 pregnant patients who had received thrombolytics, infants were reported to be normal on their initial examinations.

To date, most reported cases have involved the use of streptokinase for thrombolysis, with fewer using urokinase. Fewer cases yet have involved the use of rtPA and other newer, more fibrin-specific and less antigenic thrombolytic agents. Even so, the safety data in favor of these agents are fairly compelling and have led other authors to view the use of tPA in pregnancy as at least tenable and likely safe. On the basis of this case, we affirm such may be the case and speculate that the use of relatively newer agents, like rtPA, may add an additional margin of safety by virtue of their fibrin specificity and, at least versus streptokinase, less antigenic profile.

As Ahearn et al reported, at least as of 2002, there were 6 published reports of pregnant women who had received rtPA for various indications, including thrombosed prosthetic valves, myocardial infarction, and pulmonary embolism. None of these cases was associated with adverse maternal outcomes, and although a single case of fetal death was reported, it was unrelated to the use of rtPA. Additionally, Elford et al reported on the use of intra-arterial rtPA in a right middle cerebral artery distribution thromboembolic stroke related to ovarian hyperstimulation syndrome. Although the patient developed a hematoma after lysis, she did gradually improve neurologically and delivered a healthy, term infant.

Therefore, based on the evidence to date, the use of thrombolysis may be feasible in pregnant patients. Given that a significant proportion of all maternal deaths are attributable to ischemic arterial stroke and furthermore, that an estimated 42% to 63% of pregnancy-associated stroke survivors have residual neurological deficits thereafter, the benefits of rtPA thrombolysis may outweigh the risks when given to pregnant women when indicated, even as early as the first trimester and as late as the late third trimester. Further exploration of the benefits of rtPA thrombolysis in this setting is warranted.

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