Should Intravenous Thrombolysis be Considered the First Option in Pregnant Women?

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The current package insert for tissue plasminogen activator (t-PA) indicates that consideration of its use in pregnancy must include risks weighed against anticipated benefits. Major risks in the current patient include a bad functional outcome from an evolving stroke with a National Institutes of Health Stroke Scale of 12 and known M2 occlusion, risk of intracerebral hemorrhage from thrombolytic agent or other reperfusion therapy if used, major uterine hemorrhage with risk to mother and baby, and risk to the unborn baby from hemorrhage or spontaneous abortion, although t-PA does not cross the blood-placenta barrier.1 The major potential benefits are restoration of blood flow to ischemic brain and a likely excellent clinical outcome if reperfusion is complete and timely. And a good functional outcome for the mother not only makes a successful pregnancy and delivery of a healthy baby more likely but, as importantly, also increases the likelihood that the pregnant woman can care for her child after delivery and beyond.

Unfortunately, the literature to guide our decision making is limited to several small published retrospective series of report on pregnant women with stroke, including a handful of patients treated with intravenous (IV) t-PA and intra-arterial t-PA or urokinase.1-3 Most of these patients were treated in the first trimester, not late in the second trimester as the current patient. The patients presented in the literature are also very different from the case presentation, in that MR perfusion/diffusion imaging and vascular imaging at initial presentation are not described. The majority of reported pregnant stroke patients treated with thrombolytic therapy had a good outcome although symptomatic intracerebral hemorrhage did occur in 1 of 11 treated women.3 Series of patients with thromboembolism of various types treated with t-PA report a major hemorrhage rate of 8%.4,5 Study of aborted fetuses has not provided much information about the potential effects of lytic agents in utero.

I think that there is little disagreement that the pregnant patient presented here should be treated with reperfusion therapy as quickly as possible. In my opinion, there are certain principles that should guide the decision to use IV t-PA or endovascular therapy, which I list in order of greatest weight: (1) the therapy most likely to open the M2 occlusion as quickly as possible, (2) the therapy that minimizes intracranial and extracranial hemorrhagic complications, and (3) the therapy that minimizes risk to the unborn baby. The data underlying the first principle are that the benefit of IV t-PA and endovascular approaches to reperfusion is linked most strongly to chronologic and physiological time from onset to reperfusion.5-6 Additionally, I wonder whether the case described is hypothetical or an actual case, in that the decision-making point is 90 minutes from symptom onset with a complete set of MR diffusion/perfusion/angiographic images. If this is an actual case, I give kudos to the center that accomplished this rare event.

I would use either endovascular or IV t-PA therapy, as determined by the situation, to treat this patient as quickly as possible. If the angiographic team is on site and ready, I would send the patient immediately for endovascular treatment. The superiority of endovascular treatment over IV t-PA alone in terms of recanalization of M2 occlusions is not as well defined as it is for occlusions of the internal carotid artery terminus or M1.7 Regardless, successful reperfusion can be achieved rapidly with newer clot retriever devices and the Penumbra aspiration catheter without the need of any thrombolytic therapy in many cases or, at the most, very small amounts of t-PA in the intracranial circulation. Although this does not likely decrease the risk of symptomatic intracerebral hemorrhage associated with reperfusion, it would likely decrease the risk of uterine hemorrhage. The risk of significant hemorrhage at the puncture site is ≈1% to 2% and should be manageable without risk to the unborn baby. Ideally, endovascular therapy should be performed under sedation rather than generalized anesthesia to minimize risk to mother and baby.8 Thus, the delay in time to treatment (about median of 40–45 minutes from groin puncture to start of reperfusion therapy) when compared with starting IV t-PA immediately is more than balanced by the equal or greater chance for reperfusion with endovascular therapy and minimization of the risks of extracranial hemorrhage associated with t-PA. If, on the contrary, the angiographic team is 30 to 60 minutes from arrival to the hospital, I would treat this woman with IV t-PA and consider additional endovascular therapy subsequently depending on how the patient does.

In summary, treatment of a pregnant stroke patient who has an arterial occlusion is dependent on the individual situation (time...
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from symptom onset, location of clot, availability of endovascular team, imaging findings, other medical conditions, etc). Both endovascular therapy and IV t-PA are good choices, but when everything is lined up properly and ready to go in a patient with a major arterial occlusion, I would choose endovascular therapy.

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References

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