Thrombolysis of a stroke patient with history of rtPA-associated angioedema

Felipe De Los Rios La Rosa, MD; Amy K. Starosciak, PhD; Brian Wolf, MD

Orolingual angioedema in acute ischemic stroke patients following IV recombinant tissue plasminogen activator (rtPA) treatment is a potentially life-threatening complication. It is estimated to occur in 1.7%–7.9% of all cases.^{1,2} This complication is considered to be anaphylactoid as opposed to true anaphylaxis.³ It is thought to be a product of increased levels of bradykinin and histamine mediated in part by IV rtPA and potentiated by other factors such as stroke location involving the insular cortex causing dysfunction of the autonomic system, concomitant medications such as angiotensin-converting enzyme inhibitors (ACEI), and personal predisposition.^{2,4} Treatment includes antihistamines, steroids, complement inhibitors, and airway protection.⁵ Comprehensive reviews on rtPA-related orolingual angioedema fail to describe previous occurrences as a risk factor for its development.^{2,4} Furthermore, this complication is not a formal contraindication to rtPA and we failed to find case reports on this issue. We suspect some acute ischemic stroke patients may be denied this treatment due to history of rtPA-related orolingual angioedema. We report such a case where a patient with previous rtPA-related orolingual angioedema was successfully treated with IV rtPA without adverse reactions.

Case report

An 83-year-old woman had previously experienced an acute ischemic stroke (NIH Stroke Scale [NIHSS] 15) secondary to a right middle cerebral artery cardiac embolus in the setting of atrial fibrillation. At the time, her home medications included benazepril (ACEI) and the area of ischemia included the right insular cortex (figure, A). She had a known allergy to aspirin. She was treated with IV rtPA and experienced considerable orolingual angioedema requiring intubation for airway protection 69 minutes after rtPA initiation. Ultimately, she had substantial improvement with minimal residual symptoms. Now, 3 years later (at 86 years old), she presented with acutely worsening left-sided weakness, right gaze preference, extinction, and dysarthria (NIHSS 9). She had been noncompliant with her oral anticoagulant and was not on an ACEI or angiotensin receptor blocker. She received IV rtPA with substantial improvement. She was discharged home 5 days later with an NIHSS of 3. No prophylactic treatment for orolingual angioedema was prescribed and there was no tongue or facial swelling. The brain MRI demonstrated embolic acute infarcts on the right precentral and postcentral gyri as well as on the right cerebellum (figure, B).

Practical Implications

It is reasonable to recommend IV recombinant tissue plasminogen activator (rtPA) for patients with disabling acute ischemic strokes even with previous rtPA-associated orolingual angioedema as long as the tongue and mouth are monitored closely for this complication and practitioners who are able to secure an airway are available to assist if necessary.

Neuroscience Center (FDLRLR, AKS, BW) and Center for Research & Grants (AKS), Baptist Health South Florida, Miami-Dade County.

Funding information and disclosures are provided at the end of the article. Full disclosure form information provided by the authors is available with the **full text of this article at Neurology.org/cp**.

Correspondence to: felipedl@baptisthealth.net

Figure Brain MRIs in 2014 and 2017

All images are diffusion-weighted images. (A) MRI of the brain in 2014 at first presentation of acute ischemic stroke. (B) MRI of the brain in 2017 at next presentation of acute ischemic stroke.

DISCUSSION

Even though repeated exposure to rtPA is believed to be safe after 3 months from an acute ischemic stroke, or possibly earlier after a minor stroke,^{6,7} the risks of recurrent orolingual angioedema associated with rtPA are unknown. These risks are likely to vary within an individual depending on their active medications and the location of brain ischemia. Furthermore, if orolingual angioedema is managed promptly, it rarely leads to death or permanent injury.^{3,7} At our institution, and as recommended in the literature,^{3,5,8} we discontinue the alteplase infusion upon identification of angioedema, administer diphenhydramine 50 mg IV together with famotidine 20 mg IV stat once, and if angioedema continues to progress, then we prescribe methylprednisolone 125 mg IV $\times$ 1 stat. If there are any further increases in angioedema, then epinephrine 0.3 mg subcutaneous $\times$ 1 is considered and anesthesiology is called for emergency airway protection interventions.

Given the above stated facts, and the well-established benefits of rtPA, it is reasonable to recommend IV rtPA for patients with disabling acute ischemic strokes in the setting of previous rtPA-associated orolingual angioedema. The tongue and mouth should be monitored closely for signs of angioedema and practitioners who are able to secure an airway should be available to assist if severe orolingual angioedema were to develop.

REFERENCES

1. Lekoubou A, Philippeau F, Derex L, et al. Audit report and systematic review of orolingual angioedema in post-acute stroke thrombolysis. *Neurol Res* 2014;36:687–694.
2. Hurford R, Rezvani S, Kreimei M, et al. Incidence, predictors and clinical characteristics of orolingual angio-oedema complicating thrombolysis with tissue plasminogen activator for ischaemic stroke. *J Neurol Neurosurg Psychiatry* 2015;86:520–523.

3. Hill MD, Barber PA, Takahashi J, Demchuk AM, Feasby TE, Buchan AM. Anaphylactoid reactions and angioedema during alteplase treatment of acute ischemic stroke. *CMAJ* 2000;162:1281–1284.
4. Correia AS, Matias G, Calado S, Lourenco A, Viana-Baptista M. Orolingual angioedema associated with alteplase treatment of acute stroke: a reappraisal. *J Stroke Cerebrovasc Dis* 2015;24:31–40.
5. Pahs L, Droegge C, Kneale H, Pancioli A. A novel approach to the treatment of orolingual angioedema after tissue plasminogen activator administration. *Ann Emerg Med* 2016;68:345–348.
6. Cappellari M, Moretto G, Bovi P. Repeated intravenous thrombolysis after recurrent stroke: a case series and review of the literature. *J Neurol Sci* 2014;345:181–183.
7. Arsava EM, Topcuoglu MA. De-novo thrombolysis for recurrent stroke in a patient with prior history of thrombolysis. *Blood Coagul Fibrinolysis* 2010;21:605–607.
8. Jauch EC, Saver JL, Adams HP Jr, et al. Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2013;44:870–947.

Received April 10, 2017. Accepted in final form June 20, 2017.

AUTHOR CONTRIBUTIONS

F. De Los Rios La Rosa: manuscript concept and case review. A.K. Starosciak: critical revision of manuscript for intellectual content. B. Wolf: critical revision of manuscript for intellectual content.

STUDY FUNDING

No targeted funding reported.

DISCLOSURES

F. De Los Rios La Rosa serves as a consultant for Gerson Lehrman Group. A.K. Starosciak has received funding for travel from Bristol-Myers Squibb. B. Wolf reports no disclosures. Full disclosure form information provided by the authors is available with the **full text of this article at Neurology.org/cp**.

Share Your Knowledge

Neurology® Clinical Practice encourages readers to share their insights, expertise, and experiences.

- How are you employing drugs and devices in your field?
- What ethical challenges do you face?
- Do you have a case report that is illustrative of a clinical challenge?
- What challenges have you faced or successes have you enjoyed in bringing greater efficiency to your practice?

If you are interested in delivering a high-quality, peer-reviewed message to your colleagues in practice, submit your paper **online**.