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CASE REPORT

A Case of Oropharyngeal Angioedema Following Intravenous Recombinant Tissue Plasminogen Activator (rt-PA) and Mechanical Thrombectomy

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Abstract

A 72-year-old housewife presented with ischemic cerebrovascular stroke. Intravenous thrombolysis using recombinant tissue plasminogen activator (rt-PA) followed by mechanical thrombectomy under general anesthesia were attempted. The patient developed stridor and tongue swelling, in addition to hypotension and bradycardia, 60 min after completion of the rt-PA infusion. The airway was intubated, and intramuscular adrenaline, together with intravenous hydrocortisone and diphenhydramine, were administered. On the second day, the tongue edema subsided, and the cuff leak test was negative. However, extubation was not attempted due to the development of brain edema. A tracheostomy was later performed, and the patient was weaned off mechanical ventilation.

Key Points

Post-thrombolysis oropharyngeal angioedema is a rare but serious complication.

Multiple risk factors aggravate post-thrombolysis oropharyngeal angioedema.

Introduction

Recombinant tissue plasminogen activator (rt-PA) is the treatment of choice for those patients with ischemic cerebrovascular stroke who present within the first 4.5 h of the onset of symptoms [1]. In selected patients, mechanical thrombectomy can be performed within 24 h of symptom onset [2]. Intracranial hemorrhage is not an uncommon complication following reperfusion therapies. Rare complications of these therapies include brain edema, extracranial hemorrhage, oropharyngeal angioedema (OA), and allergic reactions [3]. In this case report, we present a case of OA that occurred after the patient received intravenous rt-PA and underwent mechanical thrombectomy. The patient required endotracheal intubation for the management of OA.

Case Report

The patient was a 72-year-old housewife who had a medical history of paroxysmal atrial fibrillation and hypertension, which were being managed with bisoprolol 5 mg once daily for 5 years and perindopril 10 mg once daily for 3 years. The patient presented to the emergency department (ED) 2 h after sudden onset of slurring of speech and left hemiparesis.

Brain imaging [computed tomography (CT) angiography and magnetic resonance imaging (MRI)] showed complete occlusion of the petrous portion of the right internal carotid artery and right middle cerebral artery (Fig. 1). Thrombolysis was attempted by administering rt-PA at a dose of 0.9 mg/kg, of which 10% was administered as an intravenous bolus followed by intravenous infusion of the remainder of the calculated dose over 1 h. This was followed by mechanical thrombectomy under general anesthesia using propofol and cisatracurium.

The patient's trachea was extubated 60 min following administration of the rt-PA infusion. She developed stridor

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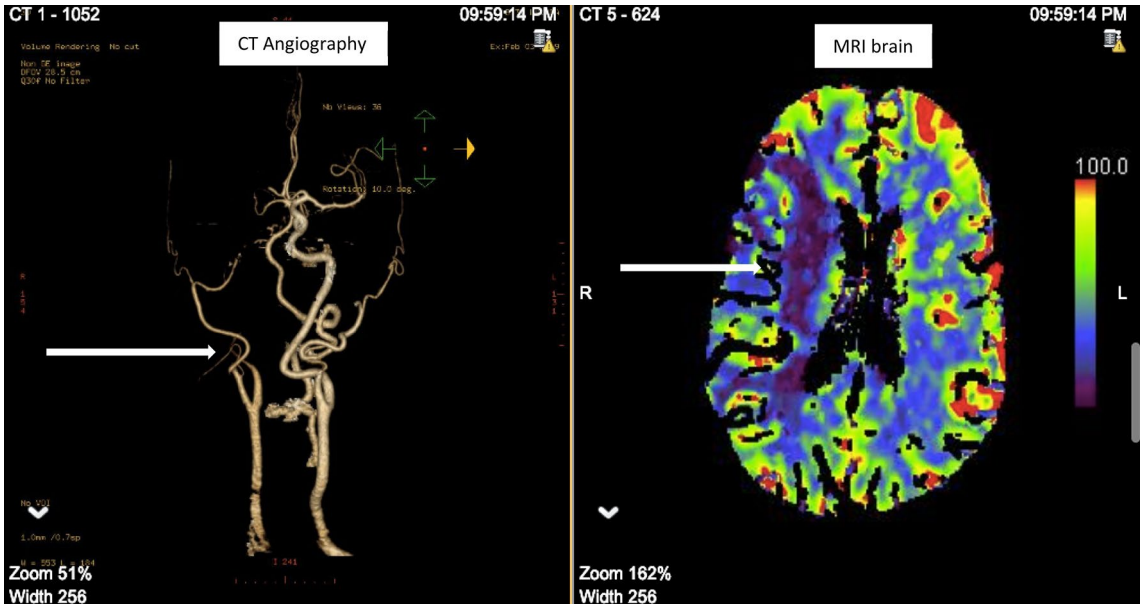

Fig. 1 Computed tomography angiography and magnetic resonance imaging of the brain

soon after extubation, and swelling was noted on the right side of the tongue. In addition, the patient had hypotension and bradycardia. She was re-intubated immediately, and adrenaline 0.5 mg (1:1000) was administered intramuscularly. Additionally, hydrocortisone 200 mg and diphenhydramine 10 mg were administered as intravenous boluses. Subsequently, the patient's hemodynamic status improved.

Examination of the larynx (during endotracheal intubation) revealed oedema of the right vocal cord. The patient was managed in the intensive care unit (ICU), where she was given invasive ventilator support while being sedated with dexmedetomidine infusion. Intravenous infusion of dexamethasone 4 mg was administered every 8 h for the next 3 days.

On the following day, despite resolution of the swelling of the tongue and a negative cuff leak test, extubation of the trachea was not attempted as the patient required elective ventilation because of cerebral oedema, which was seen in a repeat CT of the brain (Fig. 2).

Over the next 9 days, the cerebral oedema was managed with osmotic brain dehydrating medication, which was followed by complete resolution of cerebral oedema. Although the patient was conscious, her trachea could not be extubated as she had pseudobulbar involvement that impaired her cough and gag reflexes. The patient underwent tracheostomy after 16 days of endotracheal intubation.

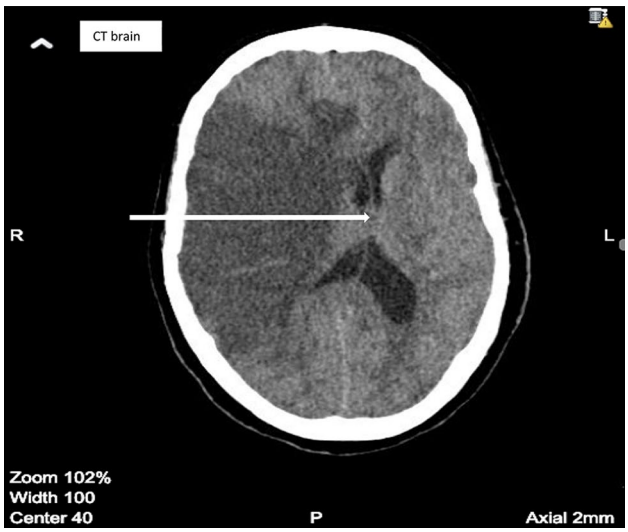

Fig. 2 Follow-up computed tomography of the brain

Discussion

OA after rt-PA is bradykinin-mediated angioedema characterized by sudden onset of swelling of the skin, subcutaneous layers, and the mucous membranes of the mouth and upper airway, and may result in life-threatening airway obstruction. The pathophysiology is the unregulated production of bradykinin caused by the plasmin-mediated cleavage of kininogen to bradykinin [4]. Previous studies have reported a 0.89–7.90% incidence of OA following the administration of rt-PA [5, 6]. In the majority of these cases, OA started hemilingually, contralateral to the side of the infarcted cerebral hemisphere [7].

The risk factors reported for rt-PA-induced OA were prior use of angiotensin-converting enzyme (ACE) inhibitors, prior history of allergy, insular cortex infarction, and female sex [6].

ACE inhibitors inhibit the degradation of bradykinin, des-Arg9-BK (a metabolite of bradykinin), and substance P. The accumulation of these vasodilator substances aggravates the development of OA [8].

The mechanism by which insular cortex infarction can mediate OA was proposed to be due to the imbalance between sympathetic and parasympathetic control [5, 9]. However, a study conducted by Pinho et al. showed that insular infarctions were not significantly correlated with OA [10].

The University of Cincinnati developed a stepwise approach to manage rt-PA-induced OA similar to that for allergic reaction, which involves stopping the infusion, administering diphenhydramine, corticosteroids, and adrenaline, and undertaking an otolaryngology/anesthesia consult if needed [11].

Icatibant, a selective bradykinin B2 receptor antagonist, and plasma-derived C1 esterase inhibitors (C1-INHs) are both used for the treatment of angioedema associated with (C1-INH) deficiency or dysfunction. Both drugs have been successfully used in the treatment of post-thrombolysis OA [12, 13].

In this case, angioedema was noted 1 h after completion of the rt-PA infusion. Thus, OA could have been a symptom of anaphylaxis induced by the contrast dye that was injected during mechanical thrombectomy, the mechanism of which is histamine-mediated type I hypersensitivity reaction [14]. In this case, another possible cause of OA could have been the mechanical effect of the intubation.

Conclusion

If suspected, OA should be managed promptly in patients receiving rt-PA and mechanical thrombectomy, especially in those who are receiving ACE inhibitors and have large insular infarctions.

Compliance with Ethical Standards

Funding No funding grants were received to prepare this case report.

Conflict of interest Mohamed Shirazy, Anis Chaari, Vipin Kauts, Karim Hakim and Kamel Bousselmi declare that they have no conflicts of interest that may be relevant to the contents of this manuscript.

Ethical approval This case report has been approved for submission and publication by the Education and Proficiency Center, King Hamad University Hospital.

Consent Informed written consent to publish this case report has been obtained from the patient's representatives.

References

1. 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(3):870–947.
2. Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 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. 2018;49(3):e46–110.
3. Adams HP Jr, del Zoppo G, Alberts MJ, et al. Guidelines for the early management of adults with ischemic stroke: a guideline from the American Heart Association/American Stroke Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research Interdisciplinary Working Groups: the American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists. Stroke. 2007;38(5):1655–711.
4. Molinaro G, Gervais N, Adam A. Biochemical basis of angioedema associated with recombinant tissue plasminogen activator treatment: an in vitro experimental approach. Stroke. 2002;33(6):1712–6.
5. Lin SY, Tang SC, Tsai LK, et al. Orolingual angioedema after alteplase therapy of acute ischaemic stroke: incidence and risk of prior angiotensin-converting enzyme inhibitor use. Eur J Neurol. 2014;21:1285–91.
6. Wang YX, Li YQ, Chen Y, et al. Analysis of related factors of orolingual angioedema after rt-PA intravenous thrombolytic therapy. Eur Rev Med Pharmacol Sci. 2018;22(5):1478–84.
7. Werner R, Keller M, Woehrle JC. Facial angioedema and stroke. Cerebrovasc Dis. 2014;38:101–6.
8. Byrd JB, Adam A, Brown NJ. Angiotensin-converting enzyme inhibitor-associated angioedema. Immunol Allergy Clin N Am. 2006;26:725.
9. Myslimi F, Caparros F, Dequatre-Ponchelle N, et al. Orolingual angioedema during or after thrombolysis for cerebral ischemia. Stroke. 2016;47(7):1825–30.
10. Pinho J, Alves JN, Oliveira L, et al. Orolingual angioedema after thrombolysis is not associated with insular cortex ischemia on pre-thrombolysis CT. J Neurol Sci. 2016;369:48.
11. O'Carroll CB, Aguilar MI. Management of post-thrombolysis hemorrhagic and orolingual angioedema complications. Neurohospitalist. 2015;5:133–41.
12. Brown E, Campana C, Zimmerman Brooks S, et al. Icatibant for the treatment of orolingual angioedema following the administration of tissue plasminogen activator. Am J Emerg Med. 2018;36(6):1125.e1–2.
13. Pahs L, Droege C, Kneale H, et al. A novel approach to the treatment of orolingual angioedema after tissue plasminogen activator administration. Ann Emerg Med. 2016;68:345–8.
14. Bernstein JA, Moellman J. Emerging concepts in the diagnosis and treatment of patients with undifferentiated angioedema. Int J Emerg Med. 2012;5(1):39.