Case Report

Hemilingual Angioedema after Thrombolysis in a Patient on an Angiotensin II Receptor Blocker

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Orolingual angioedema (OLAE) is a rare adverse effect of alteplase. Previous studies have associated the occurrence of OLAE with thrombolysed patients maintained on angiotensin converting enzyme inhibitors. We report a case of a 60-year-old male presenting with hyperacute ischemic stroke developing hemilingual edema after thrombolysis. He was previously maintained on an angiotensin II receptor blocker (ARB), losartan. The swelling resolved over 2 days with immediate administration of intravenous steroids and antihistamine drugs. Our case is the third documented case of OLAE occurring in a thrombolysed patient concurrently taking an ARB. The presence of hemilingual edema in a post-thrombolysis patient maintained on losartan suggests a possible association between OLAE and ARBs.

Key Words: Alteplase—orolingual angioedema—tongue swelling—thrombolysis—acute stroke

Introduction

Orolingual angioedema (OLAE) is rare adverse effect of alteplase, occurring in about 0%-2.2% of thrombolysed patients.[1-4]

Case Report

We report a case of a 60-year-old male with a prior history of stroke 5 years ago presenting with left-sided weakness. He was discharged with a Modified Rankin Scale of 0. He continued taking losartan, an angiotensin II receptor blocker (ARB), but discontinued aspirin a year ago. He now complains of sudden onset right-sided weakness and numbness with associated occipital headache, diplopia, and dysarthria. The brain attack team was activated upon emergency room arrival 120 minutes after onset of symptoms. He was alert and following commands but had dysarthria, gaze evoked bidirectional nystagmus, right hemiparesis, and hemisensory loss with a total National Institutes of Health Stroke Scale score of 6. A cranial computed tomography scan ruled out a hemorrhage and demonstrated a chronic infarct in the right frontal region. He had a more than twice elevated neutrophil to lymphocyte ratio of 6.07.[5] With a consideration of hyperacute pontine infarct, he was treated with intravenous alteplase (.90 mg/kg) at 185 minutes postictus. His National Institutes of Health Stroke Scale score decreased to 1 for dysarthria after thrombolysis. However, 1 hour and 20 minutes after the drip was completed, worsening dysarthria was noted. Inspection of the oral cavity showed swelling limited to the right side of his tongue. (Fig 1) There was no hypoxemia or stridor. Intravenous doses of hydrocortisone (100 mg every 12 hours) and diphenhydramine (50 mg single dose) were instituted. The tongue swelling gradually subsided within 2 days and he was discharged with a Modified Rankin Scale of 0.

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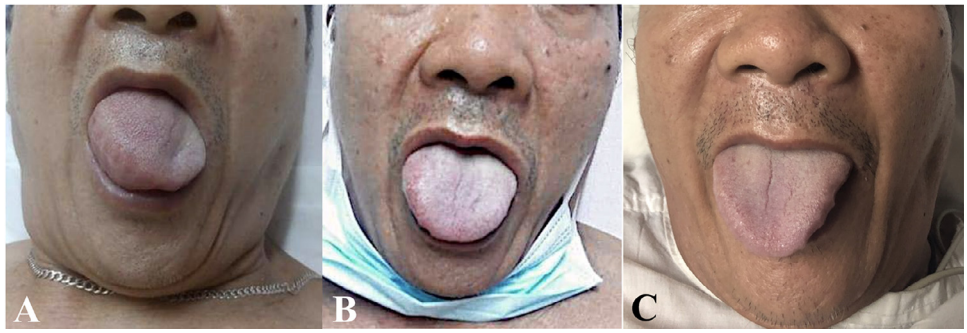

Figure 1. *Photographs showing the course of hemilingual edema. (A) Initial hemilingual edema at 100 minutes (1 hour and 20 minutes) after alteplase drip was consumed (B). Resolving edema 24 hours after thrombolysis (C). Normal tongue morphology 48 hours after thrombolysis.*

Discussion

Previous use of angiotensin converting enzyme inhibitors has been associated with the development of post-thrombolysis OLAE.[6] In contrast, the occurrence of OLAE with the use of ARB in these patients has only been documented in 2 other reports—one with irbesartan and another in an unknown ARB.[7,8] The development of OLAE in patients given alteplase is related to the drug's ability to activate a plasmin-mediated release of bradykinin, a vasodilatory peptide that mediates edema.[9] Angioedema has been reported with the use of ARBs[10] including losartan[11] in nonthrombolysed patients. We hypothesize that the kinin generating effects of alteplase may have been amplified by losartan. Furthermore, his elevated lymphocyte ratio, a known marker of inflammation and poor prognostic factor for stroke patients, may have also played a role.[12] Invasive airway interventions such as endotracheal intubation are reported in 2.4%-13.3% of patients who have post-thrombolysis OLAE.[1,13] The rest are managed successfully with anti-histamines and corticosteroids.[13]

Conclusions

This report documents the first reported case of OLAE in a post-thrombolysis patient maintained on losartan.

References

1. Hill MD. Thrombolysis for acute ischemic stroke: results of the Canadian Alteplase for Stroke Effectiveness Study. Can Med Assoc J 2005;172:1307-1312.
2. Myslimi F, Caparros F, Dequatre-Ponchelle N, et al. Orolingual angioedema during or after thrombolysis for cerebral ischemia. Stroke 2016;47:1825-1830.
3. Tsivgoulis G, Zand R, Katsanos AH, et al. Safety of intravenous thrombolysis in stroke mimics: prospective 5-year study and comprehensive meta-analysis. Stroke 2015;46:1281-1287.
4. Zinkstok SM, Engelter ST, Gensicke H, et al. Safety of thrombolysis in stroke mimics. Stroke 2013;44:1080-1084.
5. Lee JS, Kim NY, Na SH, et al. Reference values of neutrophil-lymphocyte ratio, lymphocyte-monocyte ratio, platelet-lymphocyte ratio, and mean platelet volume in healthy adults in South Korea. Medicine 2018;97:e11138.
6. 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.
7. Tan C-H, Tang S-C, Lin R-J, et al. Orolingual angioedema after alteplase therapy in a stroke patient concurrently using angiotensin II receptor blocker. J Neurol Neurosurg Psychiatry 2010;81:1079. 1079.
8. Hill MD, Lye T, Moss H, et al. Hemi-orolingual angioedema and ACE inhibition after alteplase treatment of stroke. Neurology 2003;60:1525-1527.
9. Molinaro G, Gervais N, Adam A. Biochemical basis of angioedema associated with recombinant tissue plasminogen activator treatment. Stroke 2002;33:1712-1716.
10. The ONTARGET Investigators. Telmisartan, ramipril, or both in patients at high risk for vascular events. N Engl J Med 2008;358:1547-1559.
11. Acker CG, Greenberg A. Angioedema induced by the angiotensin II blocker losartan. N Engl J Med 1995;333:1572. 1572.
12. Zhang J, Ren Q, Song Y, et al. Prognostic role of neutrophil−lymphocyte ratio in patients with acute ischemic stroke. Medicine 2017;96:e8624.
13. Yayan J. Onset of orolingual angioedema after treatment of acute brain ischemia with alteplase depends on the site of brain Ischemia: a meta-analysis. N Am J Med Sci 2013;5:589.