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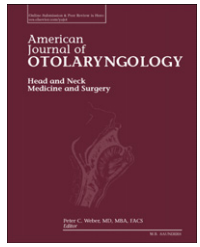

Persistent, severe post-thrombolysis angioedema: Simple management of a difficult problem☆,☆☆

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ARTICLE INFO

Article history:
Received 30 April 2015

ABSTRACT

Post-thrombolysis orolingual angioedema in the setting of managing acute stroke is reported in the literature as most often being mild and self-limiting. We present a case of severe angioedema resulting in persistent macroglossia, representing a different end of the spectrum of disease than that referenced in the literature. Despite the severity of the tongue edema in our case, it did resolve with a relatively simple intervention. In addition to highlighting that post-thrombolysis angioedema can be potentially life threatening, this report reviews the pathophysiology of this condition and discusses management options for macroglossia in this setting.

1. Introduction

Angioedema is a vascular reaction involving the deep dermis of the skin or the submucosal tissues, characterized by vessel dilatation and increased capillary permeability culminating in localized edema typically involving the lips, tongue and soft palate. It may progress rapidly and present as a life-threatening emergency. The etiology of angioedema is varied, including both hereditary and acquired forms. One well-established category is medication-induced angioedema. Angiotensin converting enzyme (ACE) inhibitors are the most well known culprits, producing angioedema through a kinin-mediated pathway. But there are other medications, including tissue plasminogen activator (t-PA), which can result in this clinical presentation.

t-PA is indicated in the early management of acute myocardial infarction and acute ischemic stroke. Its most feared complication is life threatening intracranial hemorrhage. However its administration is also known to be associated with orolingual angioedema. Despite most reports of t-PA associated angioedema being mild and self-limiting, rarely it may be massive and life threatening. We present a case of severe angioedema following t-PA administration requiring emergency airway intervention, followed by a prolonged course of severe macroglossia. Fortunately this complication can be managed simply when it does occur, as demonstrated in our case.

☆ Disclosures: Nil disclosures.
☆☆ Financial support: Nil.

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http://dx.doi.org/10.1016/j.amjoto.2015.05.004
0196-0709/

2. Case report

A 48-year-old female presented to the emergency department with sudden onset of left hemiparesis and slurred speech. She was otherwise well and not taking any regular medications, in particular she was not taking an ACE inhibitor. Shortly after presentation, the patient underwent a CT scan of the head, which demonstrated early ischemic changes in the territory of the right middle cerebral artery. She was treated emergently with recombinant t-PA. Almost 30 min after the injection she developed sudden, severe swelling of the left side of the tongue and face. Despite medical therapy including corticosteroids and anti-histamines she had progressive orofacial edema, threatening her airway and necessitating orotracheal intubation with the head and neck surgical service on standby for possible tracheotomy. In the ensuing hours to days, the tongue swelling continued despite on-going medical therapy. CT angiography of the head and neck was performed and this excluded both lingual hematoma and arteriovenous malformation as potential causes for the macroglossia. Thus it was deduced that this presentation represented persistent, severe macroglossia secondary to post-thrombolysis angioedema. The severity of her disease course was likely due to venous obstruction of the tongue by the impinging incisor teeth. The CT imaging confirmed that the tongue base was relatively spared of the edematous changes. Due to the persistent tongue edema, she was converted to a surgical tracheostomy three weeks after her initial presentation. By this time, the tongue protruded significantly beyond the incisors and was associated with excoriation of the tongue and pain (Fig. 1). Regular saline soaked dressings were continued for the protruding tongue in an attempt to free the tongue of the impingement from the teeth with the hope of improving venous return from the obstructed anterior tongue.

Six weeks after her initial presentation, the tongue was still well beyond the incisor teeth and she was referred to our tertiary head and neck service for opinion regarding management options. Whilst multiple options were considered, it was initially decided to insert a bite-block under general anesthesia to prevent the teeth from biting on the tongue. The result was dramatic with the tongue swelling subsiding over five days. She has since been decannulated and is eating a normal diet (Fig. 2).

3. Discussion

Acute ischemic stroke is a potentially devastating presentation of cerebrovascular disease, which can be associated with significant morbidity and even mortality. In 1996 the United States Food and Drug Administration approved recombinant t-PA for the management of acute ischemic stroke [1]. Whilst its efficacy is almost without doubt [2], it does have a number of potential side effects [3]. Inherent with its mechanism of action, the most common, and indeed most feared, complication of thrombolysis for stroke is intracranial hemorrhage. Plasmin-mediated fibrinolysis is intended to dissolve the offending blood clot and restore cerebral circulation, however this does put the ischemic site at risk of hemorrhagic transformation. This complication is seen in 2%–9% of t-PA administrations. Bleeding at other sites, including the upper airway and even within the tongue has also been reported, although their frequency is not well understood.

In contrast to intracerebral hemorrhage, life-threatening angioedema as a complication of t-PA administration is mentioned infrequently [4]. In a meta-analysis of the literature, despite thousands of t-PA administrations orolingual angioedema was identified in only 41 cases [1]. This is consistent with other reports that suggest angioedema complicates 1.3%–5% of t-PA administrations [5,6]. Its onset is usually within one hour of t-PA infusion and symptoms ordinarily resolve within 24 h [7]. Post-thrombolysis orolingual angioedema is typically reported to be mild, transient and self-limiting [4]. At the severe end of the spectrum, however, it may cause life threatening upper airway obstruction, with up to 20% requiring intubation or

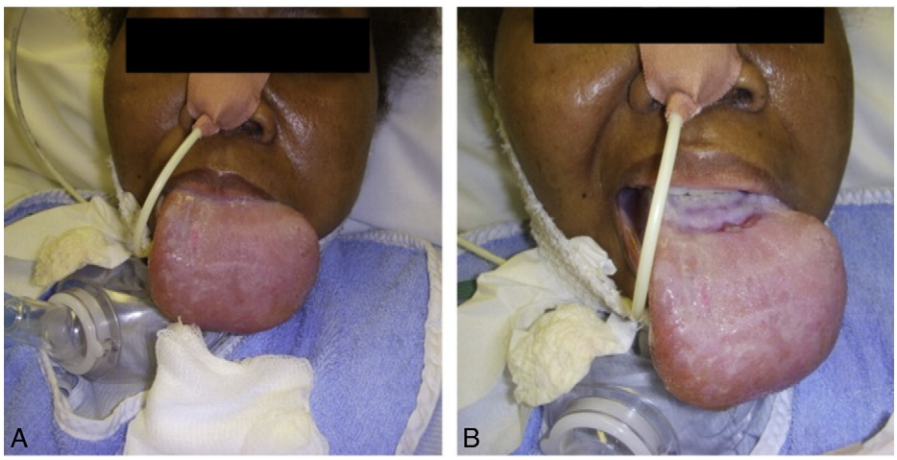

Fig. 1 – Severe post-thrombolysis angioedema. (A) The predominant left side edema (hemiparetic side) characteristic of post-thrombolysis angioedema for stroke. (B) Note the impression of the incisor teeth and significantly increased edema anterior to the occlusal plane.