Case Report

**Angioedema in the neurointerventional suite**☆

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**Abstract**
A 68-year-old woman with acute ischemic stroke presented for mechanical thrombectomy, after failed thrombolysis with intravenous recombinant tissue plasminogen activator. The procedure was completed successfully with dexmedetomidine infusion. However, she developed acute angioedema toward the end of the procedure requiring emergent fiberoptic-guided endotracheal intubation. Angioedema has been reported to occur after administering intravenous recombinant tissue plasminogen activator with an incidence of 1.3%-5.1% in patients with acute stroke.

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1. Introduction

An increasing number of stroke patients undergo intraarterial stroke therapy. These emergent procedures pose various challenges for anesthesiologists. There is limited time to complete the preoperative evaluation including detailed history of allergic reactions. This point becomes especially difficult or impossible in a patient with altered mental status or aphasia. A case of emergent angiography in a patient who needed immediate airway rescue after the development of orofacial angioedema is presented. Informed written consent was obtained from the patient to publish this case report.

2. Case

A 68-year-old woman with medical history of hypertension and atrial fibrillation presented to the emergency department with sudden onset of right arm and leg weakness along with dysarthria and aphasia. Her home medications included metoprolol, aspirin, and digoxin. The National Institute of Health Stroke Scale (NIHSS) score was 18 at presentation, and the head computed tomography (CT) revealed neither bleed nor ischemia. Subsequently, intravenous recombinant tissue plasminogen activator (rtPA) was administered; and the patient was transferred for further management and possible intraarterial stroke therapy.

Upon presentation, the patient was slightly drowsy and continued to have an NIHSS score of 14. Repeat head CT showed loss of architecture in the left caudate and lentiform nuclei, consistent with an acute ischemic stroke of the left middle cerebral arterial territory. She was immediately transferred to the neurointerventional suite for mechanical thrombectomy during monitored anesthesia care. All standard American Society of Anesthesiologists monitors were connected, and a left radial arterial line was placed for continuous blood pressure monitoring. Dexmedetomidine infusion was started at 0.5 μg/kg per hour and titrated to achieve patient comfort and sedation.

Mechanical thrombectomy was successfully performed by a neurointerventionalist within 3 hours of administering rtPA. Toward the end of the procedure, she complained of difficulty breathing. Considerable facial and neck swelling was observed. A quick examination also revealed swelling of the tongue. Her vital signs, including blood pressure, remained stable; and no wheezing was heard on auscultation. In view of progressive symomatic orofacial edema, awake fiberoptic intubation was performed. Significant swelling of all supraglottic structures were observed through the fiberoptic bronchoscope. A size 6 endotracheal tube was passed over the bronchoscope to secure the airway. Once the airway was secured, 50 mg of diphenhydramine and 10 mg of dexamethasone were administered intravenously. Immediate a postprocedural CT scan was done, which ruled out intracranial complication. However, a CT of the neck showed soft tissue swelling and obscuration of the nasopharyngeal and oropharyngeal airway around the endotracheal tube (Figure). She was transferred to the neurosurgical intensive care unit, where she remained intubated for 37 hours, until the facial swelling subsided and then she was extubated. She had an uneventful recovery and was discharged home on sixth day of her hospital stay. She had an NIHSS score of 1 at discharge with mild aphasia.

3. Discussion

Angioedema is defined as a sudden onset and well-circumscribed swelling of skin and its subcutaneous layers...
with associated involvement of mucus membranes. It often manifests in the head and neck region and may result in life-threatening airway obstruction. It is classified based on pathophysiology into histamine-mediated, bradykinin-mediated, and nonhistamine, and nonbradykinin-mediated angioedema (Table 1) [1]. Histamine-mediated angioedema primarily occurs through an allergic mechanism, specifically type I hypersensitivity reaction. Bradykinin-mediated angioedema occurs either due to unregulated production of bradykinin or due to decreased degradation of bradykinin. This is specifically seen in hereditary angioedema and in angiotensin-converting-enzyme (ACE) inhibitor–induced angioedema. Our patient was neither taking ACE inhibitors nor was initiated on any new home medication in the recent past. The plausible causes of angioedema in our patient seem to be either rtPA or contrast dye or other medications administered during the procedure, namely, dexmedetomidine and fentanyl.

Angioedema has not been reported to occur after administration of either dexmedetomidine or fentanyl. Contrast dye may result in a type I hypersensitivity reaction and in histamine-mediated angioedema. This is usually accompanied by systemic manifestations like urticaria, bronchospasm, and hypotension. Angioedema has also been reported to occur after administration of rtPA. Recombinant tissue plasminogen activator shares the exact same structure as patient's own tissue-type plasminogen activator and thus is not immunogenic. Recombinant tissue plasminogen activator hydrolyzes plasminogen to plasmin, resulting in the fibrinolysis, which is the desired effect. Plasmin causes cleavage of high molecular weight kininogen to bradykinin. Bradykinin, which causes vasodilation and increased vascular permeability, is thought to be the primary cause for manifestation of angioedema after rtPA [2]. The incidence of angioedema after rtPA for stroke ranges from 1.3%–5.1% [3-5]. The occurrence of angioedema after rtPA has been associated with use of ACE inhibitors and also with ischemia in the insular and frontal cortex [3]. However, it has also been reported to occur without any of these predisposing factors as illustrated by our case.

Engelter et al [5] retrospectively looked at 121 patients who received alteplase for acute ischemic stroke and found 2 (1.7%) patients with angioedema. It developed within half an hour of starting the rtPA infusion. The presentation was mild in 1 patient, whereas it was rapidly progressive in the other requiring emergent orotracheal intubation. Further, Hill and Buchan [4] reports a 1.3% incidence of orolingual angioedema among 1135 patients who were part of the Canadian Alteplase for Stroke Effectiveness Study. Of the 15 patients who developed angioedema, 2 required emergent airway management—one patient required intubation and the other required cricothyroidotomy. Hill et al [3] in a prospective observational study of 176 patients found an incidence of 5.1%, but most of the cases were mild, and none of them required airway intervention. The higher incidence in this study has been attributed to the prospective nature of the study, resulting in identification of very mild symptoms, which would otherwise have been overlooked. Nevertheless, angioedema resolved with medical management in most of the cases reported in literature, and the requirement for airway instrumentation has been rare. Although rtPA is administered for other indications, most reports of angioedema have been in the context of acute ischemic stroke. Except for 1 case report, administration of rtPA for reasons other than stroke, like myocardial infarction, has not been reported to result in angioedema [6].

In all the previously reported cases, angioedema developed in the emergency department or intensive care unit. Our case is unique in that the patient developed angioedema in the neurointerventional suite while undergoing thrombectomy. Respiratory distress or angioedema in the neurointerventional suite presents unique challenges due to various differential diagnoses that have to be simultaneously considered and the need to secure the airway in the setting of an ongoing complex procedure.

With advances in neurointerventional procedures, there is an increasing trend toward endovascular therapy in acute ischemic stroke. These procedures may be either performed under general anesthesia or conscious sedation. Conscious sedation has the advantages of reducing delays in treatment and allowing neurologic assessment during or immediately after the procedure. Goals of sedation are to provide patient immobility, alleviation of anxiety, and controlling pain associated with contrast injection into cerebral arteries. A variety of techniques and drugs can be used to achieve optimal sedation depending on the anesthesiologist’s choice of and goals of sedation. They include benzodiazepines, remifentanil infusion, or propofol and also newer agents like dexmedetomidine. However, general anesthesia may need to be instituted in patients who are combative or noncooperative and also in obtunded patients who need airway protection. Procedures requiring complete patient immobility would also need general anesthesia. Although certain retrospective investigations evaluating intraarterial stroke therapy report poorer outcome with general anesthesia, it has not been studied prospectively [7,8]. Decreasing time to intervention and minimizing hemodynamic perturbations should be the goal, irrespective of anesthetic technique [9]. Management of these patients with a constantly changing

<table>
<thead>
<tr>
<th>Histamine mediated:</th>
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<tr>
<td>Allergic angioedema</td>
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<tr>
<td>Angioedema with urticarial vasculitis</td>
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<td>Bradykinin mediated:</td>
<td></td>
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<tr>
<td>Hereditary angioedema (type I, II, and III)</td>
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<tr>
<td>Acquired angioedema</td>
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<td>ACE inhibitor–induced angioedema</td>
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<tr>
<td>Nonhistamine nonbradykinin mediated</td>
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<tr>
<td>Idiopathic angioedema</td>
<td></td>
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<tr>
<td>Pseudoallergic angioedema</td>
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Abbreviation: ACE, angiotensin-converting enzyme.
clinical condition in the absence of a definitive airway can be quite challenging.

Patients undergoing neurointerventional procedures generally require standard American Society of Anesthesiologists monitors, in addition to invasive arterial blood pressure monitoring. Nasal end tidal or transcutaneous carbon dioxide monitoring is beneficial for monitoring ventilation, especially when the procedure is performed during sedation. Table 2 enumerates various causes of respiratory depression or obstruction, which could occur in the neurointerventional suite. Central respiratory depression can occur in these patients due to evolution of stroke, cerebral edema, or intracranial hemorrhage. This is usually associated with signs of raised intracranial pressure like nausea and vomiting, worsening headache, and Cushing response. Extravasation of contrast noticed by the neurointerventionalist may be an early clue to developing hemorrhage. Other plausible causes like bronchospasm in patients with asthma or chronic obstructive pulmonary disease, upper airway obstruction, or oversedation also need to be explored. In the setting of acute orofacial swelling, presence of urticaria would point toward histamine-mediated angioedema. Angioedema without urticaria would be bradykinin mediated. Our patient did not have urticaria or any hemodynamic instability; and, thus, the etiology of angioedema is less likely to be histamine mediated or allergic in etiology. Recombinant tissue plasminogen activator seems to be more likely the cause of angioedema due to lack of systemic manifestations and due to the known association between angioedema and rtPA in stroke patients. Various studies have attempted to classify severity of angioedema and determine risk factors for intubation [10-12]. Supraglottic or base of tongue edema in addition to ominous symptoms like hoarseness, dysphonia, and stridor is indicator for prompt intubation. Rapidity of progression to ominous symptoms like hoarseness, dysphonia, and stridor [10-12]. Supraglottic or base of tongue edema in addition to securing the airway, medical treatment includes possibility of a surgical airway needs to be considered. In the context of recent rtPA use. If difficulty is encountered, the intubation carries the risk of epistaxis and is best avoided in the context of recent rtPA use. If difficulty is encountered, the possibility of a surgical airway needs to be considered. In addition to securing the airway, medical treatment includes intravenous antihistamines and corticosteroids. Although epinephrine has been reported to be safely administered in this context [14], it is best avoided due to the possibility of precipitating intracerebral hemorrhage.

### Table 2  Differential diagnosis of respiratory distress in neurointerventional suite

<table>
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<tr>
<th>Central causes</th>
<th>Peripheral causes</th>
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<tbody>
<tr>
<td>New onset stroke</td>
<td>Decreased airway muscle tone</td>
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<tr>
<td>Evolution of stroke</td>
<td>Bronchospasm</td>
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<tr>
<td>Cerebral edema</td>
<td>o Asthma</td>
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<tr>
<td>Intracranial hemorrhage</td>
<td>o Chronic obstructive pulmonary disease</td>
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<tr>
<td>Oversedation</td>
<td>o Allergic reaction</td>
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<td></td>
<td>o Angioedema</td>
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The development of angioedema in patients with acute stroke who were treated with rtPA poses the unique challenge of avoiding hemodynamic perturbations and airway bleeding, which could be brought on by airway instrumentation. Decreased blood pressures carry the risk of decreased perfusion to the ischemic brain, whereas increased blood pressures can lead to increased risk for hemorrhagic conversion and cerebral edema. Thus, close attention needs to be paid in maintaining hemodynamic goals, while airway management is underway. The American Heart Association/American Stroke Association 2013 guidelines recommend maintaining systolic and diastolic blood pressure lower than 180 and 105 mm Hg, respectively, in acute ischemic stroke patients who have received rtPA. They also caution against blood pressure lower than 15%-25% of baseline values. If the patient has not received rtPA, then the recommended upper limit of blood pressure is 220/120 mm Hg [13].

In the event of a developing angioedema, awake fiberoptic-guided orotracheal intubation would be the technique of choice for securing the airway, as it gives the ability to inspect and diagnose airway edema as well as to secure the airway. Nasal intubation carries the risk of epistaxis and is best avoided in the context of recent rtPA use. If difficulty is encountered, the possibility of a surgical airway needs to be considered. In addition to securing the airway, medical treatment includes intravenous antihistamines and corticosteroids. Although epinephrine has been reported to be safely administered in this context [14], it is best avoided due to the possibility of precipitating intracerebral hemorrhage.

### References


