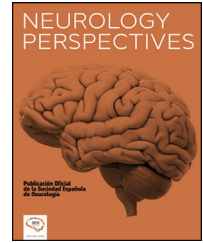




# NEUROLOGY PERSPECTIVES

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## SCIENTIFIC LETTER

### Upper airway bleeding after rt-PA use in stroke management: a case report

### Sangrado de la vía aérea superior luego del uso de rt-PA en el tratamiento del ictus Agudo: Un reporte de Caso

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#### Clinical case

A 79-year-old right-handed female presented to the ER with sudden onset of decreased level of consciousness, loss of postural tone, and left hemiparesis. The patient was last seen well one hour before. Code stroke was activated. The syncope lasted 30 s with spontaneous recovery, without consequences, and it was followed by slurred speech, headache, and left hemiparesis. Blood pressure was 211/125 mmHg with normal glucose levels. Neurologic examination was remarkable for a National Institutes of Health Stroke Score (NIHSS) of 13 (level of consciousness (+1), horizontal gaze (+2), facial palsy (+2), arm drift (+4), leg drift (+1), dysarthria (+1), and extinction (+2) and a modified Rankin Score of 3. Her past medical history included hypertension, ischemic stroke 4 years ago without residual deficits, coronary artery disease, COPD, former smoker (>40 years), undiagnosed auricular fibrillation

without treatment by previous transthoracic echocardiogram and stable angina pending revascularization.

A head CT (Supplemental fig. 1) showed a hyperdense right middle cerebral artery (MCA) with an ASPECT score of 6. A CT angiography (CTA) revealed a cervical internal carotid artery obstruction with passage of the contrast media, with filiform flow in the petrous and cavernous carotid and complete occlusion in carotid ophthalmic segment and right MCA. Blood pressure readings of 160/80 mmHg were achieved after 20 mg of labetalol. A dose of 0.9 mg/kg of rt-PA were infused and, according to weight of 65 kg, 6 mg were administered in the first minute and 52 mg in the next 59 min. Initial workup was normal (Table 1). Following CTA findings, mechanical thrombectomy was performed with 3 solitaire passes and 1 penumbra aspiration with a door to groin time of 117 min (Supplemental fig. 2).

A TIC1 grade 3 was achieved after clot retrieval. During the procedure a massive bleeding from the nasal and oral cavities was observed. Compression maneuvers with gauzes and hydrogen peroxide didn't control it. The patient became hemodynamically unstable and there was a 4 units drop in hemoglobin levels that required a 2-unit red blood cell

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**Table 1** Laboratory data on the day of admission.

Blood count				
	Hemoglobin (mg/dL)	Hematocrit (%)	Platelets (per mm <sup>3</sup> )	White cell count
On admission	15.2	47.5	308,000	13,100
During thrombectomy	8.8	27.4	243,000	13,700
After intervention	11	33.9	149,000	13,100
Blood count				
	PT (control)	PTT (control)	INR	Fibrinogen (mg/dL)
On admission	10.3 (10.9)	23 (25.9)	0.95	–
During thrombectomy	–	–	–	187.7
After intervention	11 (10.9)	25.7 (26.3)	1.02	246
Serum electrolytes				
	Sodium (mEq/L)	Chloride (mEq/L)	Potassium (mEq/L)	Calcium (mmol/L)
On admission	138	108	3.47	–
During thrombectomy	–	–	–	–
After intervention	141	109	3.08	1.14

transfusion. Otorhinolaryngology was called for assistance. Video-laryngoscopy showed a friable lesion on the anterior commissure of the glottis and a massive pulsatile bleeding from the right vocal fold affecting the thyroarytenoid muscle (Fig. 1). Electrocautery was unsuccessful in controlling the bleeding, so robotic CO<sub>2</sub> laser were used to achieve adequate hemostasia. Fibrin glue (Tisseal<sup>®</sup>) was applied on the vaporized area and the entire glottis to reinforce hemostasia. A 3-L blood loss was estimated. After bleeding control, the patient was intubated and transferred to the intensive care unit.

A post-stroke head CT didn't show new acute findings or hemorrhagic transformation. Carotid Doppler Ultrasound evidenced improved bilateral flow dependent on high pressures. Due to high bronchoaspiration risk, a temporary tracheostomy was placed, during which a 30% stenosis of the glottis and granulation tissue in the anterior surface of the vocal cords were noted. On day 3 a new video laryngoscopy was performed by the oral cavity, passing the uvula



**Fig. 1** Video endoscopic of the larynx in the operating room. Source: Authors.

and progressing to the larynx without active bleeding. On postoperative day 7, the patient was awake and opened her eyes to verbal stimuli.

By postoperative day 9, the patient's condition improved with a NIHSS of 6 and dabigatran 150 mg BID was started. On day 70 the patient was discharged and continued follow-up as an outpatient with a modified Rankin of 4.

## Analysis and discussion

### General principles

Pharmacological thrombolysis is mediated through plasminogen activation. Side effects include internal or external bleeding, including symptomatic intracranial hemorrhage (sICH), arterial puncture, recent surgical incision and oral mucous bleeding.<sup>1</sup> Between 4.7–11.4% of stroke patients undergoing intravenous thrombolysis experience sICH and 1.6–3.6% have major systemic bleeding.<sup>2</sup> Bleeding events tend to happen between 2–24 h after thrombolysis. This interval overlaps with the period of early fibrinogen degradation coagulopathy and is associated with decreased fibrinogen concentrations.<sup>3</sup> Risk factors for symptomatic hemorrhage include: age, male gender, obesity, stroke severity, diabetes, hyperglycemia, uncontrolled hypertension, dual antiplatelet therapy, large areas of early ischemic change, auricular fibrillation, congestive heart failure and leukoaraiosis.<sup>1</sup>

### Differential diagnosis

An adverse event related to alteplase administration was suspected, possibly bleeding gums, however, this was discarded as the patient became hemodynamically unstable and compression maneuvers were unsuccessful. Cervical spinal hemorrhage was also considered as it causes neurological worsening and airway compromise.<sup>4</sup> This was

discarded as a cervical hematoma was not observed and massive bleeding from oral and nasal cavities were present.

A case report of spontaneous sternocleidomastoid muscle hematoma after thrombolytic therapy was found. This complication was attributed to chronic inflammation from a mycobacterial infection.<sup>5</sup> However, there was no involvement of superficial neck muscles in our patient. There are few cases reported of upper digestive tract hemorrhage following rt-PA use for acute stroke.<sup>6</sup> One of these involved a patient with intramural hematoma of the esophagus.<sup>7,8</sup> Another neck structure that has been involved after rt-PA use in ischemic stroke is the thyroid gland. The case reported was a thyroid hemorrhage that caused tracheal and vascular compression causing acute airway obstruction and respiratory failure.<sup>9</sup> Our patient also had this presentation, however, the thyroid gland was uninjured.

Lingual artery hemorrhage has been reported and associated with a previous history of laryngoscopic trauma. However, this was discarded as intubation was performed after the bleeding was observed.<sup>10</sup> In our patient, a friable lesion on the glottis was seen before identifying the bleeding source on the vocal fold. Therefore, a previously undiagnosed vascular lesion was suspected but was considered unlikely as our patient had no history of dysphonia or laryngeal-related symptoms. However, external laryngeal trauma with the compromised submucosal vessel is a cause of vocal cord bleeding secondary to coagulation disorders. Vocal fold varix, telangiectasias, or irregularities should also be considered as the cause of bleeding in this case.<sup>11,12</sup>

4 cases of hemorrhage from upper airway structures were found involving thrombolytic therapy.<sup>13</sup> However, most of these involved streptokinase use and were associated with recent local trauma.<sup>14</sup> Another important complication of thrombolytic therapy in ischemic stroke is cardiac tamponade due to hemopericardium.<sup>4</sup>

## Conclusions

Up to our knowledge, this is the first reported case of an upper airway hemorrhage with severe hemodynamic decompensation following rt-PA. The source of the bleeding was the right vocal fold. The hemorrhage was difficult to control and required local treatment with laser coagulation, surgical intervention, and multiple blood transfusions. Optimal recovery of hemodynamic status was achieved without other hemorrhagic complications. After 2 months, the patient was discharged and continued ambulatory stroke rehabilitation.

## Protection of human and animal subjects

The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

## Confidentiality of data

The authors declare that they have followed the protocols of their work center on the publication of patient data.

## Right to privacy and informed consent

The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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## Ethical considerations

We declare the center's protocols on the publication of patient data were followed. Informed consent was obtained before the writing of this article.

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## Declaration of Competing Interest

The authors declare they do not have any financial or non-financial competing interests.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.neurop.2023.100113>.

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