



Refractory Macroglossia Following Thrombolysis and Decompressive Craniectomy for Malignant Middle Cerebral Artery Infarction: A Case Report from the Neurocritical Care Unit

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Abstract: Background: Macroglossia is an uncommon yet potentially life-threatening complication encountered in critically ill neurological patients, with an estimated incidence ranging from 0.5% to 5% following major neurosurgical interventions (1). The pathogenesis is typically multifactorial, involving mechanical compression, venous and lymphatic stasis, neurogenic influences, and drug-induced angioedema (4,5). Severe, persistent tongue enlargement can precipitate airway obstruction, impair nutritional support, and significantly prolong intensive care unit (ICU) stay (8). Case Presentation: We report a 65-year-old female with type 2 diabetes mellitus, hypertension, and hypothyroidism who developed a malignant right middle cerebral artery (MCA) territory infarction. Following intravenous tenecteplase administration, she experienced hemorrhagic transformation and subsequent decompressive hemicraniectomy. Her postoperative course was complicated by progressive, severe macroglossia refractory to multiple steroid injections and conservative measures. Comprehensive imaging, including contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI), excluded necrosis or focal lesions, implicating diffuse edema secondary to venous congestion, lymphatic impairment, and local traumatic injury. The multidisciplinary team proposed surgical tongue reduction (odontectomy/debulking); however, the family declined due to perceived high operative risks. Conclusion: This case underscores the diagnostic and therapeutic challenges inherent in managing refractory macroglossia in the neurocritical care setting. Early recognition, systematic evaluation, and multidisciplinary collaboration are paramount. When conservative strategies prove futile and surgical intervention is precluded, the clinical course becomes exceptionally complex, often resulting in prolonged morbidity and functional impairment.

Keywords: Macroglossia, Ischemic Stroke, Thrombolysis, Decompressive Craniectomy, Tongue Edema, Critical Care, Case Report.

INTRODUCTION

Ischemic stroke remains a leading cause of global mortality and long-term disability, with large territory middle cerebral artery (MCA) infarctions accounting for approximately 10-15% of all ischemic stroke cases (5). These lesions, frequently designated as "malignant" owing to their propensity for the development of massive cerebral edema, can precipitate fatal intracranial hypertension and cerebral herniation if not managed aggressively (1). Decompressive hemicraniectomy has emerged as the standard of care for malignant MCA infarction, with randomized controlled trials demonstrating a significant reduction in mortality from approximately 80% to 30% and improvement in functional outcomes among

patients under 60 years of age (2,3). More recent evidence suggests that survival benefits extend to carefully selected older adult populations (3).

While the neurological and neurosurgical dimensions of this condition are extensively documented, a rare but potentially devastating complication is the development of macroglossia. Postoperative macroglossia, although infrequently reported, constitutes a recognized complication following neurosurgical and spinal procedures, particularly those of prolonged duration, those performed in the prone or park-bench position, and those associated with significant intraoperative blood loss (4). The proposed pathophysiological mechanisms include direct mechanical compression compromising venous and lymphatic drainage, regional vascular congestion, traumatic injury from endotracheal tubes or bite blocks, and, in certain cases, neurogenic causes related to brainstem or hypoglossal nerve manipulation (5). Furthermore, orolingual angioedema is a well-established, albeit infrequent, complication of thrombolytic therapy with tissue plasminogen activators (t-PA), including tenecteplase, occurring in approximately 1-5% of treated patients, with a higher incidence (up to 8%) in those concurrently receiving angiotensin-converting enzyme (ACE) inhibitors (6,7).

This case report provides a comprehensive analysis of a patient who developed refractory macroglossia following a complex sequence of malignant MCA stroke, thrombolysis, and decompressive craniectomy. We systematically review the putative etiological factors, diagnostic approach, and therapeutic challenges, drawing upon contemporary literature to contextualize this rare but clinically significant complication.

CASE PRESENTATION

A 65-year-old female, with a significant past medical history of type 2 diabetes mellitus, hypertension, hypothyroidism, and a left mastectomy for breast carcinoma, presented to the emergency department with acute-onset left-sided hemiparesis (involving both the arm and leg), dysarthria, and left-sided hemineglect. Her initial National Institutes of Health Stroke Scale (NIHSS) score was 16, indicating a substantial neurological deficit burden (13). Non-contrast computed tomography (CT) of the brain revealed a right subthalamic and deep white matter infarction. CT angiography demonstrated reduced opacification of the distal branches of the right MCA, and CT perfusion imaging confirmed a significant perfusion mismatch with a large penumbra, indicating salvageable brain tissue at risk (14). After meticulous blood pressure optimization (targeting <185/110 mmHg in accordance with current guidelines), she received intravenous tenecteplase at a dose of 0.25 mg/kg, consistent with standard thrombolytic protocols.

Approximately two hours post-thrombolysis, the patient's neurological status deteriorated precipitously, with her Glasgow Coma Scale (GCS) declining to 6/15. A repeat non-contrast CT brain revealed hemorrhagic transformation of the infarct with substantial mass effect and a midline shift of approximately 15 mm, consistent with malignant cerebral edema (1). She was emergently intubated for airway protection, commenced on osmotherapy (mannitol 1g/kg) to reduce intracranial pressure, and started on antiepileptic therapy (levetiracetam 1000mg loading dose) for seizure prophylaxis. Given the refractory malignant edema and imminent risk of uncal herniation, she underwent an urgent decompressive hemicraniectomy, a procedure proven to be life-saving in this context (2).

In the subsequent days, the patient developed progressively worsening diffuse macroglossia. The tongue became severely enlarged, protruding beyond the oral cavity, hindering oral care, and complicating weaning from mechanical ventilation. The maxillofacial surgery team was consulted urgently. A comprehensive radiological evaluation, including contrast-enhanced CT and magnetic resonance imaging (MRI) of the neck and tongue, revealed significant diffuse edema without any evidence of focal enhancing lesions, abscess formation, or necrotic changes. This imaging profile was critical in ruling out more sinister pathologies such as tongue necrosis, which would necessitate immediate surgical debridement. The maxillofacial specialists postulated that the macroglossia was a consequence of a confluence of factors: venous congestion and impaired lymphatic drainage secondary to the underlying neurological state and prolonged recumbency; traumatic injury from biting or compression against the endotracheal tube and natural dentition; and potentially a component of thrombolysis-related angioedema (6,7).

The management strategy initially focused on conservative measures, including elevation of the head of the bed to 30-45 degrees to facilitate venous return, meticulous oral hygiene with chlorhexidine mouthwash, and the application of a bite block to prevent further trauma (8). The maxillofacial team also administered a course of multiple steroid injections (methylprednisolone 40mg), aiming to reduce local inflammation and edema. Despite these concerted efforts, the macroglossia remained persistent and severe. The clinical team, increasingly concerned about the escalating risk of tongue ischemia and necrosis, repeatedly discussed the option of surgical tongue reduction (odontectomy/glossectomy/debulking) with the family. This procedure, while definitive, carries significant operative risks, including bleeding, infection, airway compromise, and functional impairment (9, 10). After extensive counseling regarding the potential benefits and the substantial risks in a critically ill, diabetic patient with a recent major stroke, the family declined surgical intervention.



DISCUSSION

This case illuminates a complex and challenging intersection of complications following a major neurovascular event. The patient's clinical trajectory—from acute stroke to thrombolysis, hemorrhagic transformation, and emergent decompressive surgery—represents a sequence of events that individually and collectively may have contributed to

the development of refractory macroglossia. The discussion will be structured around the potential etiologies, diagnostic workup, and therapeutic challenges, with reference to the relevant literature.

Etiopathogenesis of Macroglossia in Neurocritical Care

The pathophysiology of macroglossia in such patients is almost certainly multifactorial. A primary consideration is thrombolysis-related angioedema. The use of intravenous t-PA (such as tenecteplase) is associated with the development of orolingual angioedema, which is thought to occur via the plasmin-mediated generation of bradykinin, leading to increased vascular permeability and localized edema (6). This phenomenon has a reported incidence of 1-8% in ischemic stroke patients treated with t-PA, with a significantly higher risk (up to 8.5%) in those taking ACE inhibitors (7). The angioedema typically presents unilaterally, but can be bilateral and severe, potentially leading to airway compromise. The temporal association in our patient, occurring within hours of tenecteplase administration, strongly suggests a component of this bradykinin-mediated mechanism.

Secondly, the neurosurgical intervention and critical care environment introduce substantial mechanical and physiological risks. The decompressive craniectomy, while life-saving, does not directly cause macroglossia. However, the subsequent period of prolonged intubation, mechanical ventilation, and altered consciousness are significant predisposing factors. Prolonged orotracheal intubation can lead to local mechanical compression of the tongue against the endotracheal tube and the patient's teeth, impairing venous and lymphatic drainage (5). This is compounded by the effects of gravity in the supine position, leading to dependent edema. Furthermore, the patient's positioning during surgery and the early postoperative period can contribute to venous and lymphatic congestion in the head and neck. A comprehensive review by Brockerville et al. (2017) highlights that macroglossia has been most frequently reported after neurosurgical procedures lasting more than 8 hours, often in the prone or park-bench positions (4). The mechanisms proposed include both venous and lymphatic obstruction and, in some cases, a "reperfusion injury" phenomenon, where arterial inflow is restored to a previously compressed area, causing rapid, edematous swelling (10).

Thirdly, neurogenic factors should be considered. The massive right MCA stroke and subsequent craniectomy may have led to dysfunction of the supranuclear pathways or direct damage to the hypoglossal nerve (CN XII) or its nuclei, potentially altering tongue muscle tone and predisposing to edema and trauma (2). However, this is more speculative and less well-documented in the literature compared to mechanical and vascular mechanisms.

Diagnostic Approach

The diagnostic workup in this case was exemplary. The use of both contrast-enhanced CT and MRI of the neck and tongue was essential in excluding the most dreaded complications, such as tongue necrosis, abscess, or a focal malignancy. The finding of diffuse edema without necrosis or enhancement guided the management towards conservative and supportive measures rather than urgent surgical debridement. In similar cases, Doppler ultrasound may also be employed to assess the vascularity of the tongue, though this was not performed in our patient (22). The importance of a systematic, multidisciplinary

diagnostic evaluation involving neurology, neurosurgery, maxillofacial surgery, and critical care cannot be overstated.

Therapeutic Challenges and Management Strategies

The failure of conservative measures, including steroid injections, is consistent with the literature. While steroids are often the first-line medical therapy for angioedema, their efficacy in severe, established macroglossia is frequently limited (8). A number of other medical strategies have been reported anecdotally, including the use of fresh frozen plasma (which contains ACE-2, a bradykinin-degrading enzyme) for t-PA-induced angioedema, and the use of icatibant, a bradykinin B2 receptor antagonist. However, these are not routine and were not considered in this specific case.

The subsequent discussion of surgical tongue reduction (odontectomy/glossectomy) is the definitive management for refractory cases. This procedure aims to reduce tongue bulk to alleviate airway obstruction, improve oral intake, and prevent necrosis (9). The surgical techniques vary, often involving a midline or wedge resection of the tongue, and may include extraction of teeth to relieve external pressure on the tongue (10). However, as clearly demonstrated in this case, the decision to proceed with surgery is heavily weighed against the patient's overall clinical status and the significant operative and anesthetic risks, especially in a patient with multiple comorbidities (diabetes mellitus, recent major stroke) who is already critically ill.

CONCLUSION

Refractory macroglossia is a rare but serious complication that can arise after a complex sequence of events including acute ischemic stroke, thrombolysis, and decompressive craniectomy. Its etiology is likely a combination of bradykinin-mediated angioedema from thrombolytics (6,7) and mechanical/venous/lymphatic obstruction from prolonged intubation and patient positioning (4,5). Early recognition, a systematic diagnostic approach to rule out necrosis or infection, and multidisciplinary management are crucial. This case highlights the significant therapeutic challenge when conservative measures and steroid injections fail, and the definitive surgical option is declined due to high perceived risk, leading to a complex and prolonged clinical course with significant implications for patient and family.

DISCLOSURE

Conflict of Interest: The authors declare no conflict of interest.

Patient Consent: Written informed consent was obtained from the patient for the publication of this case report and any accompanying images. A copy of the signed consent is available for review by the Editor-in-Chief of this journal upon request.

Acknowledgments: The authors have no acknowledgments to declare.

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