A Case of Unremitting Orolingual Angioedema in Conjunction with Locked-in Syndrome

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Citation

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Abstract

We describe a case of unremitting orolingual angioedema in conjunction with Locked-in syndrome

CASE SUMMARY

A seventy-three year old Guyanese female presented to the ER with altered mental status, global weakness, and massive tongue enlargement. Her symptoms, as presented by her husband, began overnight with dyspnea, nausea, vomiting, and progressive weakness. While at home, she ingested 81 mg of aspirin without relief of symptoms.

Her past medical history is significant for uncontrolled hypertension and an acute haemolytic transfusion reaction several years ago. An old left cerebellar infarct was additionally discovered with MRI.

The patient was an ordained minister and herbalist who, prior to admission, had not used western medicine aside from an occasional aspirin. Her husband was unaware of any herbal medications she may have used prior to the acute onset of symptoms.

Upon admission, the patient was afebrile, tachycardic at 112 BPM and hypertensive at 195/82 with an oxygen saturation of 91%. Among other less significant findings, MRI demonstrated a large acute infarct involving the medulla and pontomedullary junction. CT of the neck demonstrated a diffusely enlarged and swollen tongue with no definite abscess collection, no lymphadenopathy, and symmetric salivary glands.

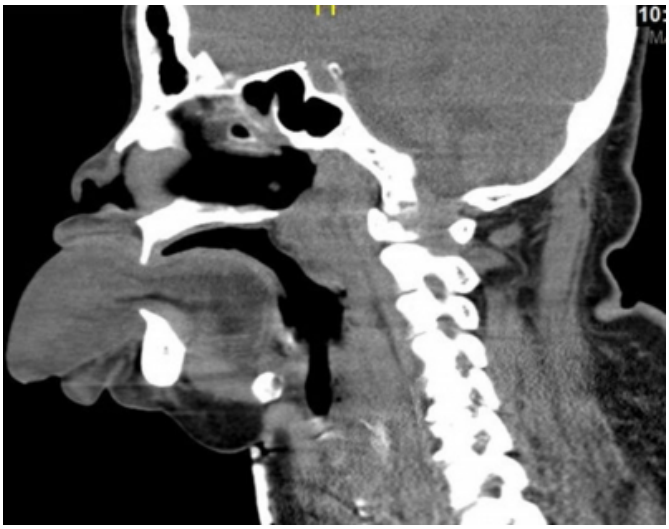
On the basis of clinical and MRI findings, the patient was diagnosed with Locked-in Syndrome (LIS) secondary to acute pontomedullary infarction. Throughout her seventy-nine days in the ICU she endured several additional health challenges, many of which were not unexpected for a person with LIS. However, the significant lingual enlargement was most unusual.

Figure 1

Figure 1: Photograph of patient's tongue following trial of compression

Figure 2

Figure 2: CT of patient's head and neck demonstrating tongue enlargement



DISCUSSION

The coetaneous presentation of lingual angioedema with locked-in syndrome secondary to anterior, rostral medullary

infarction is both intriguing and yet unexplained. The area of infarction is inclusive of or closely related to not only the corticospinal, corticobulbar, and medial lemniscal tracts but several centres of systemic modulation. Blood pressure is modulated by the nucleus tractus solitarius in the dorsomedial medulla, a similar region in the caudal ventrolateral medulla, and most significantly by the major pressor centre in the baroreceptor reflex arc of the rostral ventrolateral medulla[1]. Likewise, respiration is modulated by the nearby Bötzinger and preBötzinger complexes [2, 3]. With such complex systemic regulation imposed by the medulla, we cannot conclude nor exclude the infarction as a direct or contributory cause of tongue oedema.

Albeit myriad cases have been published regarding the incidence of orolingual angioedema secondary to administration of tissue plasminogen activator (tPA) and/or ACE inhibitor after cerebrovascular accident, we were unable to find another case in which tongue enlargement began prior to admission. Moreover, tPA was contraindicated at admission and therefore not administered. Other medications well known to cause angioedema include several NSAIDs with aspirin being most common[4], ACE inhibitors[5¬¬¬], and angiotensin II receptor blockers[6]. A growing list of other drugs and herbal supplements has been documented in the literature. Of the aforementioned medications, aspirin was the only known drug administered prior to admission. However, the patient had used aspirin in the past multiple times without incident. Subsequent massive enlargement of her tongue progressed over the following twenty-four hours and remained enlarged with some fluctuation throughout her seventy-nine day stay in the ICU.

Several aetiologies have been posited and some debate has ensued as to the correct nomenclature of her tongue presentation. Should it be referred to as macroglossia, angioedema, or acute parenchymatous glossitis? We were without reason to cogitate pseudomacroglossia[7]. As described originally by Gupta and reaffirmed by several authors, true macroglossia should be restricted to chronic enlargement of the tongue[8]. Macroglossia, though aesthetically accurate is not applicable diagnostically in this case. The distinction from acute swelling has varied implications in both aetiology and treatment[9]. Murthy appends,

Unfortunately, given the unique nature of the circumstance in which the patient was unresponsive at presentation, history was limited. Her husband was unaware of any herbal remedies she may have ingested but stated she fashioned most of her own medications. Possible aetiologies considered beyond aspirin-induced angioedema, included other allergic reactions, vitamin deficiencies, amyloidosis, hypothyroidism, venous stasis, and even poison. Several avenues were pursued in attempt to elucidate the cause of and subsequently treat her tongue enlargement. We discontinued each medication on a trial basis, attempted treatment with high-dose corticosteroids, IV diphenhydramine, and famotidine, performed a tongue biopsy, and finally attempted a trial of tongue compression within the oral cavity. Neither medication abeyance nor pharmacologic therapy yielded diagnostic or therapeutic result.

Although the acute presentation of tongue enlargement was unlikely secondary to amyloidosis, tongue biopsy to mutually rule out amyloidosis and help explicate the aetiology was eventually performed on the sixteenth day. Amyloidosis has been reported to be the most common cause of macroglossia in adults[10]. The biopsy was negative for amyloid deposition on H&E, Congo red stain, and immunohistochemistry stain for Amyloid A. It did, however, demonstrate submucosal oedema, skeletal muscle fibres separated by oedema, and focal hyperkeratosis and parakeratosis.

The final attempt, compression of the tongue, may have provided the most diagnostic value as the tongue did compress. Unfortunately, due to subsequent facial swelling the procedure was reversed. Upon reversal, facial oedema decreased but lingual oedema returned. From this response, we cautiously concluded the aetiology to be venous stasis in character. Upon analysis of head and neck CT, head and neck MRA, and brain MRI we were unable to identify a structural cause for venous stasis.

CONCLUSION

The simultaneous presentation of lingual enlargement and vascular, locked-in syndrome is a fascinating association of which we have been unable to truly define. We do not know whether aspirin, though previously well tolerated, was responsible. If so, was a stress response contributory? It is additionally unknown whether an herbal supplement was causative or contributory. Mindful of the delicate balance and intricate systemic coordination elicited by the medulla, we do not feel it is unreasonable to hypothesize injury as a direct or contributory cause of tongue oedema. Further investigation is required to establish association.

References

1. Chalmers, J. P., V. Kapoor, I. J. Llewellyn-Smith, J. B. Minson, and P. M. Pilowsky. "Central Control of Blood Pressure." European Heart Journal Supplement A (1992): 2-9.
2. Richter, D. W. "Generation and Maintenance of the Respiratory Rhythm." J. Exp. Biology 100 (1982): 93-107.
3. Lavezzi, A. M., and L. Matturri. "Functional Neuroanatomy of the Human Pre-Botzinger Complex with Particular Reference to Sudden Unexplained Perinatal and Infant Death." Neuropathology 28 (2008): 10-16.
4. Kaplan, A., and M. Greaves. "Angioedema." Journal of the American Academy of Dermatology 53.3 (2005): 373-88.
5. Greaves, M., and F. Lawlor. "Angioedema: Manifestations and Management." Journal of the American Academy of Dermatology 2nd ser. 25.1 (1991): 155-65.
6. Van Rijnsoever, E. W., W. JM Kwee-Zuiderwijk, and J. Feenstra. "Angioneurotic Edema Attributed to the Use of Losartan." Arch Intern Med. 158 (1998): 2063-065.
7. Abdi, R., V. M. Dong, C. J. Lee, and K. A. Ntoso. "Angiotensin II Receptor Blocker–Associated Angioedema: On the Heels of ACE Inhibitor Angioedema." Pharmacotherapy 22.9 (2002): 1173-175.
8. Gupta, O. P. "Congenital Macroglossia." Archives of Otolaryngology 93 (1971): 378-83.
9. Murthy, P., and M. R. Laing. "Macroglossia: Management Depends on the Cause; Many Patients Will Need Long Term Psychological Support." British Medical Journal 309 (1994): 1386-387.
10. Rizer, F., G. Schechter, and M. Richardson. "Macroglossia: Etiologic Considerations and Management Techniques*." International Journal of Pediatric Otorhinolaryngology 8.3 (1985): 225-36.

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