Delayed Diagnosis of Giant Cell Arteritis in the Setting of Isolated Lingual Necrosis

Clinical Medicine Insights: Case Reports
Volume 12: 1–5

DOI: 10.1177/1179547619857690

Logan Christopher DeBord[1], Ilene Chiu[2] and Nelson Eddie Liou[3]

[1]Department of Dermatology, University of Colorado School of Medicine, Aurora, CO, USA. [2]Department of Otolaryngology—Head and Neck Surgery, University of Texas Southwestern Medical Center, Dallas, TX, USA. [3]Bobby R. Alford Department of Otolaryngology—Head and Neck Surgery, Baylor College of Medicine, Houston, TX, USA.

ABSTRACT

BACKGROUND: Lingual necrosis is a rare complication of giant cell arteritis (GCA).

METHODS: A 77-year-old woman presented for treatment of a painful and discolored tongue, odynophagia, and dehydration refractory to antimicrobials over 2 weeks. An extensive, well-demarcated necrotic area was visualized on the anterior tongue upon admission. Leukocytosis, thrombocytosis, and elevated erythrocyte sedimentation rate were present. Computed tomography angiogram of the head and neck revealed an undulated-beaded appearance of the distal internal carotid arteries and vertebral arteries bilaterally.

RESULTS: High-dose intravenous steroids were initiated for suspected vasculitis. Temporal artery biopsy confirmed the diagnosis of GCA. The patient's condition improved and the anterior tongue was well healed at 1 month follow-up.

CONCLUSIONS: An atypical presentation of GCA (eg, isolated lingual necrosis) risks a delay in diagnosis and increased morbidity. Any patient above the age of 50 years presenting with tongue necrosis, in the absence of known cause, should undergo expedited workup for GCA.

KEYWORDS: giant cell arteritis, vasculitis, lingual necrosis, tongue necrosis

RECEIVED: May 23, 2019. **ACCEPTED:** May 24, 2019.

TYPE: Case Report

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

CORRESPONDING AUTHOR: Nelson Eddie Liou, Bobby R. Alford Department of Otolaryngology—Head and Neck Surgery, Baylor College of Medicine, 6501 Fannin St. NB302, MS: NA-102—Houston, TX 77030, USA. Email: nelson.liou@bcm.edu

Introduction

Giant cell arteritis (GCA) is a large-vessel vasculitis often presenting with headache, jaw claudication, and temporal scalp tenderness. If unrecognized and left untreated, the disease process can progress to potentially irreversible cranial ischemic complications. These may include permanent loss of vision (most commonly due to anterior ischemic optic neuropathy),[1] extraocular motility disorders resulting in diplopia,[2] and uncommonly, cerebral infarct in either the vertebrobasilar or internal carotid artery distributions.[3]

Lingual necrosis is a known but rare initial manifestation of GCA, and due to the rich vascular supply of the tongue, bilateral lingual necrosis is even more unusual.[4,5] This uncommon manifestation of GCA should not be overlooked due to the potential complications related to untreated disease.

Here, we present a rare case of a patient ultimately diagnosed with GCA whose only initial presenting symptom was lingual ischemia and necrosis.

Case Report

A 77-year-old woman presented to the emergency room for treatment of oral tongue pain, odynophagia, and dehydration. She reported a 2-week history of progressively worsening tongue pain with ulceration and odynophagia. The patient stated that her tongue was blue in color before the onset of ulceration (Figure 1). She denied having any associated fevers, chills, malaise, scalp or jaw tenderness, headaches, or vision changes. Initially, the patient was treated by her primary care physician for a presumed infection and was prescribed Bactrim, then Augmentin, with progression of her symptoms. Her odynophagia led to severe dehydration that required a short hospitalization at an outside facility 1 week prior to presentation. The patient was seen by an infectious disease physician and underwent continued antimicrobial treatment with addition of acyclovir and fluconazole as an outpatient.

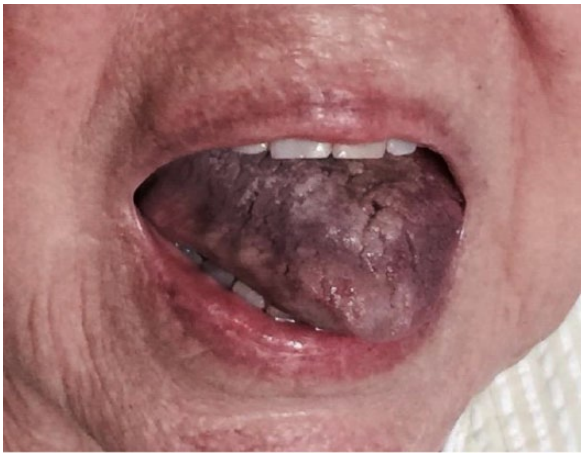

Figure 1. Ischemic changes to the anterior tongue.

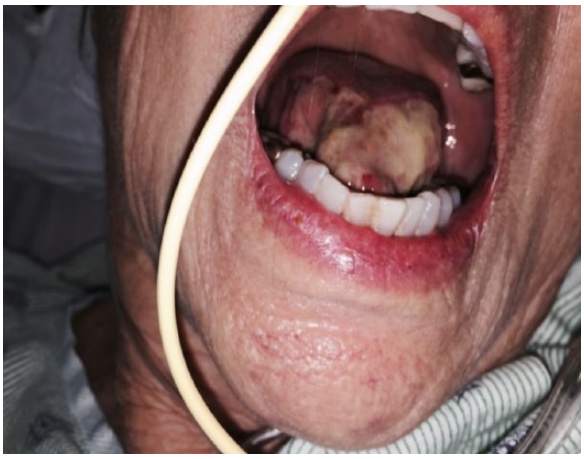

Figure 2. Lingual necrosis present upon initial presentation.

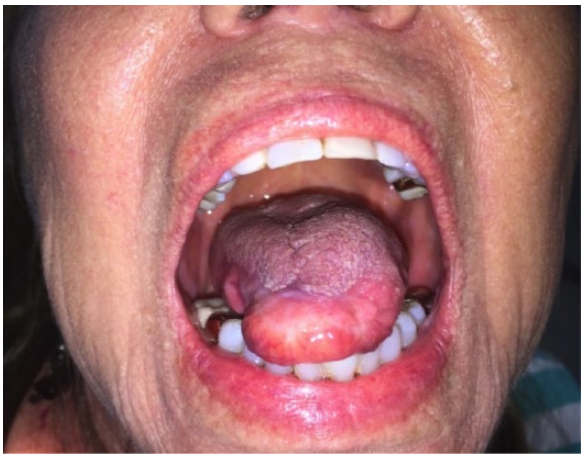

Figure 3. Six months after initial presentation and long-term steroid treatment.

Upon evaluation by the otolaryngology service, the patient was noted to have dry mucous membranes, and there was an extensive, but well-demarcated, area of necrosis involving the anterior one-third to half of the oral tongue (Figure 2). The tongue was tender to palpation.

Laboratory studies revealed that the patient had a leukocytosis of 22 K/μL, thrombocytosis of 716 K/μL, and erythrocyte sedimentation rate (ESR) that was elevated to 65 mm/h. Computed tomography (CT) angiogram of the head and neck revealed an undulated-beaded appearance of the distal internal carotid arteries and vertebral arteries bilaterally. Biopsy of the tongue revealed marked acute inflammation and granulation tissue with focal loss of the squamous mucosa above the basal layer. No fungal elements were identified with staining, and no viruses (cytomegalovirus, herpes simplex virus, or varicella zoster virus) were identified with immunohistochemistry markers.

The rheumatology service was consulted due to concern for vasculitis and the patient was started on high-dose intravenous steroids. A transthoracic echocardiogram was not performed due to low suspicion for an emboligen cardiopathy in the absence of an arrhythmia or artificial valve. The patient was taken to the operating room for a left superficial temporal artery biopsy. Histology revealed reduction of the vessel lumen caliber due to intimal hyperplasia, fragmentation of the internal elastic lamina, and transmural mononuclear cell infiltrate, confirming the diagnosis of GCA. With long-term high-dose steroids, the patient's pain resolved and the tongue necrosis stopped progressing. She eventually recovered and the anterior edge of the tongue was well-healed 6 months after presentation (Figure 3).

Discussion

Giant cell arteritis, also historically known as temporal arteritis, cranial arteritis, or Horton disease, is a large-vessel vasculitis. This disease typically affects older adults above the age of 50 years, affects women twice as often as men, and has an overall disease prevalence of 1:500.[6] Associated constitutional symptoms may include fever, malaise, arthralgia, weight loss, and night sweats. More specific symptoms include temporal headaches, transient monocular visual loss or amaurosis fugax, tongue or jaw claudication, or scalp tenderness with or without necrosis. Lingual necrosis is a rare manifestation of GCA, with only 29 previously reported cases in the literature.[7–10] The tongue receives its main vascular supply from branches of the external carotid artery, which is preferentially affected in GCA. Due to rich vascular feed from branches of the lingual, facial, pharyngeal and palatine arteries, unilateral presentation of lingual necrosis is more common than bilateral presentation.

During the medical workup for GCA, an elevated ESR is often seen, but on rare occasions may still be normal.[11] Serum C-reactive protein (CRP) is another acute phase marker that may be correlated to disease activity. The traditional gold standard for diagnosis of GCA is temporal artery biopsy; the classic histopathologic finding of mononuclear cell infiltration of the artery wall is diagnostic.[12] The American College of Rheumatology recommends that 3 out of the 5 following criteria are necessary for diagnosis: aged above 50 years, new onset of localized headache, tenderness or decreased pulse in the temporal artery, ESR >50 mm in the first hour, and classic findings on temporal artery biopsy.[6] Meller et al[13] found that fluorodeoxyglucose (FDG) uptake greater than or equal to that of liver uptake could also be used as criterion to detect vascular inflammation and was more reliable than magnetic resonance imaging (MRI) in a subset of patients. While the threshold of significance has not yet been determined for this application of FDG-positron emission tomography (PET), this imaging modality may offer a non-invasive way to diagnose GCA in the future.[14]

Treatment of GCA involves induction therapy, typically starting the patient on high-dose glucocorticoids as soon as GCA is clinically suspected. This is followed by maintenance therapy with lower dose steroids and management of flares should they occur.[15] Notably, necrotic tongue ulcerations may occur in delayed fashion even after 1 week or more of

Table 1. Case reports describing lingual necrosis as the primary initial clinical manifestation of giant cell arteritis.

AUTHOR	PATIENT AGE	PRESENTATION	PERTINENT PHYSICAL AND LAB FINDINGS	TREATMENT	OUTCOME
DeBord et al (current study)	77	Painful tongue for 2 weeks with development of blue discoloration on the anterior portion with dysphagia	ESR: 65 mm/h. Leukocytes: 22.2 K/μL. CTA: undulated-beaded appearance of distal internal carotid arteries and vertebral arteries bilaterally. Temporal artery biopsy on hospital day 8: histology consistent with GCA	Oral trimethoprim-sulfamethoxazole and amoxicillin-clavulanate as an outpatient, followed by acyclovir and fluconazole. After admission and rheumatology consult, Solu-Medrol 1 mg/kg/day IV, then transitioned to oral prednisone 60 mg daily	Pain improved with initiation of steroids and patient was able to tolerate a soft diet upon discharge. Anterior edge of tongue was well-healed 1 month later
Kumarasinghe et al[4]	74	Progressively painful, swollen, and discolored tongue that impaired function over 24 hours, with history of transient left-sided numbness of the tongue and sore throat days prior	ESR: 103 mm/h. C-reactive protein: 37 mg/L. Leukocytes: 15.4 K/μL. *Candida* species grown on tongue swab. Temporal artery biopsy 8 days after presentation: transmural infiltrate of lymphocytes and histiocytes with giant cells and focal disruption of the internal elastic lamina	Antihistamines and corticosteroids in ER (suspected hypersensitivity reaction); fluconazole and nystatin oral suspension after swab results. Prednisolone 40 mg daily with aspirin following rheumatology consult. Debridement of necrotic tissue 8 days after presentation	Following initiation of steroids, tongue became more necrotic with severe pain and uptrending inflammatory markers. After eventual debridement, patient was discharged on hospital day 16. Attainment of near-normal speech and function at discharge despite loss of tongue tissue. Discharged on aspirin and prednisolone taper
Husein-Elahmed et al[20]	76	Painful, swollen, and discolored tongue for 17 days and generalized weakness	ESR: 87 mm/h. Leukocytes: 168 g/L. Temporal artery biopsy: histology consistent with GCA	Prednisone and debridement of necrotic tissue	Delayed diagnosis resulted in subtotal necrosis of the mobile part of the tongue. Symptoms improved quickly following treatment but patient remained morbid
Brodmann et al[22]	81	New-onset progressive ulcer (2.1 × 0.7 cm) on the right side of the tongue, with additional fatigue, for 2 weeks	ESR: 52 mm/h. Temporal artery pulses relatively decreased on the right side. Color-coded duplex sonography of temporal artery: "halo" sign of intimal edema. FDG-PET negative. Temporal artery biopsy: histology consistent with GCA	Glucocorticoid therapy for 2 months	Ulcer showed a slow but constant healing accompanied by improvement in fatigue
Schurr et al[5]	66	Grayish-purple discoloration of the anterior two-third of the tongue, in addition to slowed, slurred speech and worsening dysphagia for 2 weeks	ESR: 120 mm/h. C-reactive protein: 23.9 mg/L. Mildly increased AST (64 U/L) and ALT (48 U/L). Creatine kinase: 621 U/L. Normal CK-MB and Troponin T. Diffusely narrowed and stenosed external carotid arteries bilaterally on CTA, MRA, and Doppler. Temporal artery biopsy: moderate fibrous thickening of the intima without granulomatous inflammation. Markedly decreased temporal artery pulsation bilaterally	Prophylactic heparin and antibiotics initially; prednisone 500 mg IV following imaging. Dose reduced to 100 mg after 3 days	Loss of anterior two-third of tongue with satisfactory healing 2 weeks following initiation of therapy. ESR decreased to 30 mm/h, accompanied by return to baseline of C-reactive protein and leukocyte count
Sainuddin and Saeed[19]	88	Painful, swollen, and discolored tongue and generalized weakness for 10 days	ESR: 78 mm/h. Leukocytes: 186 g/L. Temporal artery biopsy: inflammation of the tunica media with giant cells	Prednisone 40 mg daily; debridement of necrotic tissue	Complete resolution; prednisone was reduced to 15 mg daily and tongue had regained normal color at time of discharge
Kusanale et al[21]	86	Painful, swollen, and dark tongue that turned pale and necrotic days later, with addition of dysarthria	ESR: 25 mm/h. Temporal artery biopsy: histology consistent with GCA	High-dose steroids	Recovery of near-normal speech and function despite loss of tongue tissue
Ciantar and Adlam[18]	74	Painful, burning, and swollen tongue impairing tongue mobility, with additional neck pain	ESR: 79 mm/h. CRP: >250 mg/L. Leukocytes: 17.7 K/μL. Temporal artery biopsy: consistent with GCA with pronounced intimal proliferation and narrowing of the lumen. MRA: lingual vascular abnormality	Oral and IV antibiotics initially; maintenance dose of methylprednisolone 1 g daily following diagnosis	Oral candidosis and jaw claudication on follow-up, with persistently high ESR and C-reactive protein. Outpatient prednisone and methotrexate increased to 60 mg daily and 12.5 mg weekly. Tongue well-healed with some superficial ulceration 9 weeks later

Abbreviations: ACR, American College of Rheumatology; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK-MB, creatine kinase-muscle/brain; CRP, C-reactive protein; CTA, computed tomography angiogram; ESR, erythrocyte sedimentation rate; FDG-PET, fluorodeoxyglucose-positron emission tomography; GCA, giant cell arteritis; MRA, magnetic resonance angiogram.

appropriate glucocorticoid treatment.[7] Mahr et al[16] in 2007 published a meta-analysis from pooled data from 3 randomized control trials and found that adjunctive treatment using methotrexate may lower the risk of relapse and reduce the overall dose of steroids administered to the patients. Methotrexate has also been chosen as early adjuvant therapy for GCA in part due to the presence of lingual necrosis, which portends worse prognosis.[8] The recent GiACTA trial found that the addition of tocilizumab, an interleukin (IL)-6 inhibitor, to a prednisone taper was superior to both short- and long-term prednisone alone for the primary outcome of sustained remission at 52 weeks.[17]

Table 1 provides a summary of case reports in which lingual ischemia and necrosis was the primary initial manifestation of GCA, occurring either in the absence of, or prior to, classic symptoms such as headache, visual disturbances, or jaw claudication. Herein, we focus only on cases of isolated lingual necrosis that resulted in delay of diagnosis, rather than attempting a review of all cases of lingual necrosis complicating GCA such as the one performed by Sobrinho et al.[8] Such an atypical presentation risks a delay of appropriate care, as evidenced by the fact that antimicrobial therapy was also an initial treatment of choice in several other instances.[4,5,18] The differential for tongue necrosis includes other ischemic causes such as embolism or hemorrhage, septic or cardiogenic shock, malignant tumors, infection or abscess, intake of ergotamine drugs, previous history of radiation to the head and neck, or other vasculitides such as granulomatosis with polyangiitis or polyarteritis nodosa.[18–20] However, it would behoove the clinician to be aware that GCA is likely the most common cause of lingual necrosis when it does present.[21]

Although a diagnosis of GCA was not immediately apparent in any of the 7 previous cases, the majority of patients satisfied at least 3 diagnostic criteria as set by the ACR (Table 1). However, empiric steroids should never be delayed to await confirmation if there is high clinical suspicion.[4] Temporal artery biopsy is not a perfectly sensitive method due to the segmental nature of lesions in GCA, and in one case, the authors considered the diagnosis definitive only after observing excellent therapeutic response to prednisone and exclusion of differential diagnoses.[5] In any patient presenting with lingual necrosis, it is important to undergo repeated, specific questioning regarding the possible coexistence of more vague classic manifestations of GCA that may otherwise go unreported.[4] Brodmann et al[22] recommends ESR and duplex sonography of the temporal arteries in the setting of any unexplained tongue necrosis, with subsequent biopsy in the event of uncertainty. In the CT angiography of our patient, the undulated-beaded appearance of the distal internal carotid and vertebral arteries bilaterally was more consistent with skip lesions occurring secondary to a vasculitic process than diffuse atherosclerosis. While CTA is less sensitive than MRI for diagnosing cerebral vasculitis,[23] the presence of intracranial vascular lesions in a segmental pattern provided enough grounds for initiation of glucocorticoids and scheduling a superficial temporal artery biopsy rather than evaluation for cardioembolic or infectious origin.

Conclusions

Giant cell arteritis may present with vague constitutional symptoms including fever, malaise, arthralgia, weight loss, and night sweats. High clinical suspicion is necessary to diagnose and treat the disease before irreversible ischemia and blindness occur. Bilateral lingual ischemia and necrosis is a rare manifestation and potentially reversible complication of this disease. It is imperative that otolaryngologists be able to recognize cases of GCA in which lingual necrosis is the only presenting symptom to mitigate morbidity and mortality resulting from delayed diagnosis. The authors recommend that any patient above the age of 50 years presenting with tongue necrosis, in the absence of known cause, should undergo expedited workup for GCA.

Author Contributions

I.C. and N.E.L. conceived the the project. L.C.D. collected clinic information and data, and wrote the manuscript with the support of I.C. and N.E.L. L.C.D., I.C., and N.E.L. contributed to the final version of the manuscript.

Acknowledgements

This paper was presented as a Poster Submission to the American Academy of Otolaryngology—Head and Neck Surgery Annual Meeting in San Diego, CA, September 18-21, 2016.

Informed Consent

The patient provided informed consent for the authors to publish images and discuss the case presentation.

ORCID iD

Logan Christopher DeBord https://orcid.org/0000-0002-5474-9100

REFERENCES

1. Hayreh SS, Podhajsky PA, Zimmerman B. Ocular manifestations of giant cell arteritis. *Am J Ophthalmol*. 1998;125:509–520.
2. Jonasson F, Cullen JF, Elton RA. Temporal arteritis. A 14-year epidemiological, clinical and prognostic study. *Scott Med J*. 1979;24:111–117.
3. Gonzalez-Gay MA, Vazquez-Rodriguez TR, Gomez-Acebo I, et al. Strokes at time of disease diagnosis in a series of 287 patients with biopsy-proven giant cell arteritis. *Medicine (Baltimore)*. 2009;88:227–235.
4. Kumarasinghe AP, Hepburn A, Reuther WJ, Pratt C. Temporal arteritis presenting with tongue necrosis. *BMJ Case Rep*. 2012;2012:bcr2012007241.
5. Schurr C, Berthele A, Burghartz M, Kiefer J. Spontaneous bilateral necrosis of the tongue: a manifestation of giant cell arteritis? *Eur Arch Otorhinolaryngol*. 2008;265:993–998.
6. Hunder GG, Bloch DA, Michel BA, et al. The American College of Rheumatology 1990 criteria for the classification of giant cell arteritis. *Arthritis Rheum*. 1990;33:1122–1128.
7. Truffaut L, Lefebvre P. Tongue necrosis in giant-cell arteritis. *N Engl J Med*. 2018;378:2517.
8. Sobrinho RAB, de Lima KCA, Moura HC, Araujo MM, de Assis CMRB, Gouveia PADC. Tongue necrosis secondary to giant cell arteritis: a case report and literature review. *Case Rep Med*. 2017;2017:6327437. doi:10.1155/2017/6327437.
9. Larsen JM, Aabenhus K. [Ischaemic necrosis of the tongue due to temporal arteritis]. *Ugeskr Laeger*. 2017;179:V01170041.
10. Fongaufier C, Guffroy A, Lutz J-C. Tongue and scalp necrosis: simultaneous initial complications revealing giant cell arteritis. *J Rheumatol*. 2018;45:873–874. doi:10.3899/jrheum.171321.

11. Smetana GW, Shmerling RH. Does this patient have temporal arteritis? *JAMA*. 2002;287:92–101.
12. Lie JT. Illustrated histopathologic classification criteria for selected vasculitis syndromes. *Arthritis Rheum*. 1990;33:1074–1087.
13. Meller J, Strutz F, Siefker U, et al. Early diagnosis and follow-up of aortitis with [(18)F]FDG PET and MRI. *Eur J Nucl Med Mol Imaging*. 2003;30:730–736.
14. Soussan M, Nicolas P, Schramm C, et al. Management of large-vessel vasculitis with FDG-PET: a systematic literature review and meta-analysis. *Medicine (Baltimore)*. 2015;94:e622.
15. Weyand CM, Goronzy JJ. Clinical practice. Giant-cell arteritis and polymyalgia rheumatica. *N Engl J Med*. 2014;371:50–57.
16. Mahr AD, Jover JA, Spiera RF, et al. Adjunctive methotrexate for treatment of giant cell arteritis: an individual patient data meta-analysis. *Arthritis Rheum*. 2007;56:2789–2797.
17. Stone JH, Tuckwell K, Dimonaco S, et al. Trial of tocilizumab in giant-cell arteritis. *N Engl J Med*. 2017;377:317–328.
18. Ciantar M, Adlam DM. Glossodynia and necrosis of the tongue caused by giant cell arteritis. *Br J Oral Maxillofac Surg*. 2008;46:231–233.
19. Sainuddin S, Saeed NR. Acute bilateral tongue necrosis–a case report. *Br J Oral Maxillofac Surg*. 2008;46:671–672.
20. Husein-Elahmed H, Callejas-Rubio J-L, Rios-Fernandez R, Ortego-Centeno N. Tongue infarction as first symptom of temporal arteritis. *Rheumatol Int*. 2012;32:799–800.
21. Kusanale A, Boardman H, Khoshnaw H. Tongue necrosis: a rare presentation of temporal arteritis. *Age Ageing*. 2008;37:119.
22. Brodmann M, Dorr A, Hafner F, Gary T, Pilger E. Tongue necrosis as first symptom of giant cell arteritis (GCA). *Clin Rheumatol*. 2009:S47–S49.
23. Abdel Razek AA, Alvarez H, Bagg S, Refaat S, Castillo M. Imaging spectrum of CNS vasculitis. *Radiographics*. 2014;34:873–894.