

Hypoglossal Nerve Palsy Missed and Misinterpreted: The Hidden Skull Base

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Objective: Dysarthria and tongue swelling may be seen with hypoglossal nerve palsy, and on cross-sectional imaging studies, tongue denervation can be misinterpreted as a primary base-of-tongue mass. Understanding radiological patterns of tongue denervation is important to prevent misinterpretation. Close evaluation of the skull base is critical as hypoglossal palsies resulting from pathology here are often overlooked.

Methods: Neck and brain magnetic resonance imaging studies obtained in 7 adult patients referred to our institution with clinically and/or radiologically suspected tongue base masses were retrospectively reviewed. Outside imaging evaluations were misinterpreted as base-of-tongue tumors in 3 patients, incorrectly read as normal in 2, and skull base pathologies were missed in 5.

Results: All 7 patients showed magnetic resonance imaging findings typical of tongue denervation: T2-weighted hyperintensity of involved hemitongue, protrusion of the tongue into oropharynx, variable fatty infiltration. All 5 skull base masses involved hypoglossal canal (4 metastases, 1 multiple myeloma; 4 newly diagnosed cancers). Two patients had internal carotid artery dissections at the skull base.

Conclusions: To avoid misinterpretation of tongue denervation for tongue base mass, understanding of tongue innervations and classic imaging findings of hypoglossal denervation are essential. Careful inspection of skull base is paramount to avoid overlooking these hidden pathologies.

Key Words: hypoglossal nerve palsy, tongue paralysis, skull base

Abbreviations: ICA - internal carotid artery, SE - spin echo, STIR - short T1 inversion recovery

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Dysarthria, dysphagia, and/or tongue fullness are nonspecific symptoms seen with a spectrum of pathologies including tongue paresis. Tongue denervation may be due to a spectrum of conditions that may be neurological (stroke, demyelination) or related to head and neck pathology, most importantly, oncologic disease.^{1,2} The symptom complex may also represent manifestations of systemic disorders such as rheumatoid arthritis, viral infection, meningitis, and lymphoma due to involvement of the hypoglossal nerve.^{2–4} It is not uncommon for patients with these symptoms to initially be seen by their primary care or an emergency room physician where it may be difficult on initial evaluation to distinguish a stroke from other processes including

primary tongue pathology and tongue denervation. Following clinical assessment, patients are frequently referred for cross-sectional imaging (computed tomography [CT] or magnetic resonance [MR] imaging) of the head and/or soft tissues of the neck to assess for a structural lesion.⁵ Radiologists, especially if biased by a provided clinical history concerning for tongue cancer and unfamiliar with the imaging findings of tongue denervation, may misinterpret the imaging findings as a primary base of a tongue tumor. Misinterpretation of tongue paralysis for a tongue tumor may subsequently result in a failure to identify skull base pathology resulting in tongue paralysis.

This article reviews the physiology of tongue innervation, pertinent skull base anatomy, the normal appearance and anatomy of the tongue (Fig. 1), and the characteristic imaging findings of tongue denervation. An orderly approach to image analysis to avoid the potential pitfalls of misinterpretation is reviewed. Accurate image interpretation is paramount for an expedient diagnosis and focused workup.

MATERIALS AND METHODS

The soft-tissue neck (n = 4) and brain MR (n = 5) imaging studies obtained in 7 patients (5 men, 2 women; mean age, 60 years) referred to our institution with clinically and/or radiologically suspected tongue base masses were retrospectively reviewed. All patients complained of new-onset dysarthria, dysphagia, and tongue fullness.

All brain and neck MR studies were performed on 1.5-T systems. The brain MR included 5-mm-thick sagittal spin echo (SE) T1-weighted and axial turbo SE T2-weighted, axial fluid-attenuated inversion recovery, axial echoplanar imaging diffusion-weighted imaging, and enhanced SE axial T1-weighted sequences and enhanced coronal SE T1-weighted sequences. In 1 patient, additional high-resolution 3-mm-thick axial and coronal SE T1-weighted and enhanced with fat saturation axial and coronal T1-weighted and axial T2 SE with fat saturation of the face soft tissue were added to the brain MR. Neck MR studies consisted of 5-mm-thick sagittal SE T1-weighted, axial SE T1-weighted, axial turbo SE T2-weighted, axial short T1 inversion recovery (STIR), postcontrast fat-saturated axial T1-weighted, and postcontrast fat-saturated coronal T1-weighted. Enhanced MR images were obtained after the intravenous administration of 0.1 mmol/kg of gadolinium-based contrast agent.

All images were reviewed by 2 neuroradiologists (K.O.L., L.A.L.) with expertise in head and neck imaging. Imaging findings of tongue denervation were defined as (1) T2 hyperintensity of the involved hemitongue; (2) linear, demarcated margin in the midline; (3) apparent enlargement of the ipsilateral base of the tongue with protrusion of the tongue into the oropharyngeal lumen; (4) enhancement; and (5) variable T1 hyperintensity due to fatty replacement. Each study was systematically evaluated for an abnormality along the course of the ipsilateral hypoglossal nerve as well as exclusion of a primary oropharyngeal cancer. Medical records were reviewed for demographics, history of primary

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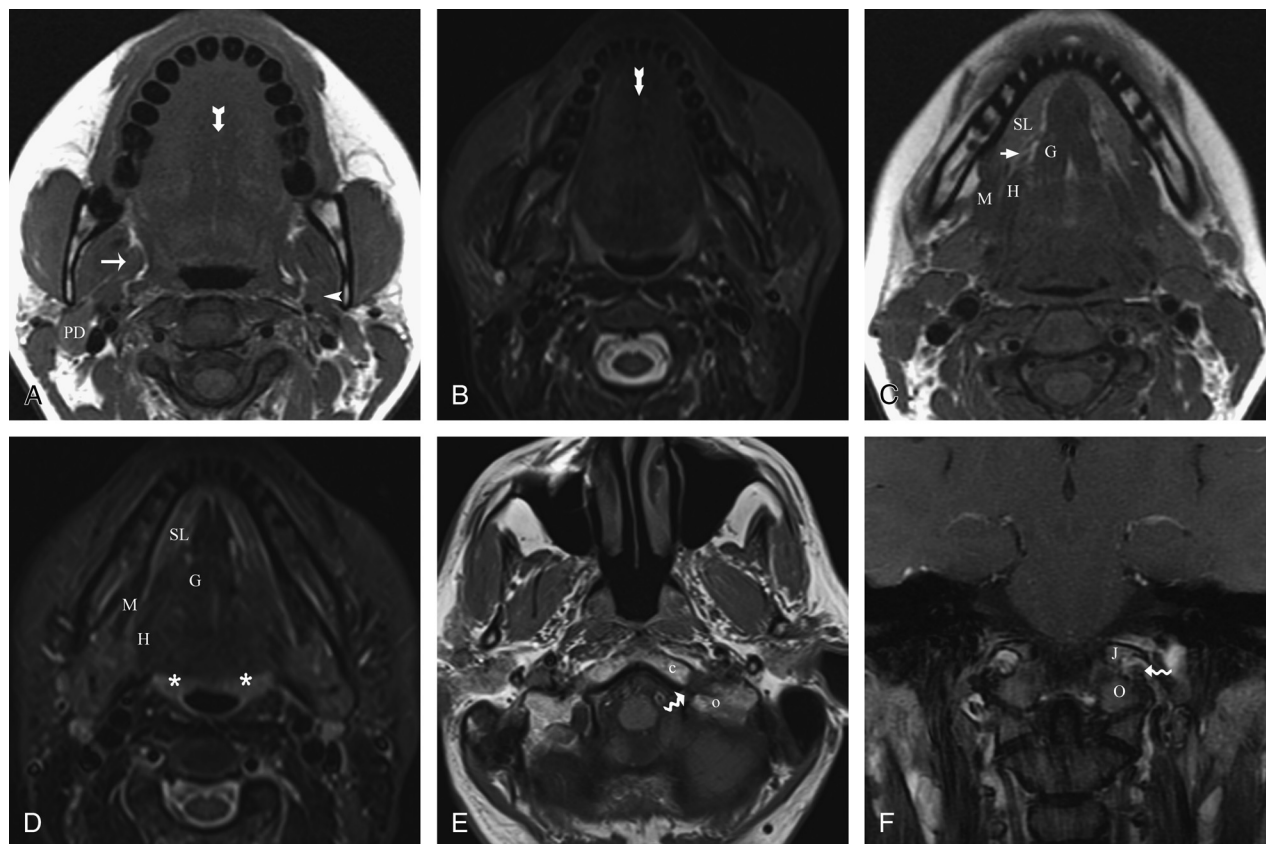


FIGURE 1. Normal tongue and hypoglossal canal. A and B, Axial T1-weighted (T1W) and STIR images of upper tongue: striated architecture of genioglossus and intrinsic tongue musculature on either side of midline lingual septum (bow arrow); styloglossus (arrow), stylopharyngeus (arrowhead), and posterior belly of digastric muscles (PD). C and D, Axial T1W and STIR images of lower tongue and sublingual space: hyoglossus muscle (H) defines the lateral tongue border; sublingual gland (SL) and neurovascular bundle of lingual nerve/CN XII and vessels (short arrow) above the mylohyoid sling (M); genioglossus (G) and lingual tonsils at base of tongue (asterisks). E and F, Axial T1W and enhanced coronal T1W fat-suppressed images of the skull base: occipital condyle (O), occipital clivus (C), and jugular tubercle (J) define the boundary of hypoglossal nerve canal (squiggly arrow).

carcinoma, metastatic disease, and findings on physical examination and endoscopy.

RESULTS

The MR imaging in all 7 patients showed findings characteristic of tongue denervation (4 left-sided, 3 right-sided). Image analysis also revealed the underlying etiology for the hypoglossal nerve palsies (Table 1). Imaging findings for tongue denervation in all patients included T2-weighted hyperintensity in the involved hemitongue with abrupt linear demarcation of the signal alteration in the midline (Fig. 2) and apparent enlargement of the ipsilateral base of the tongue, which causes protrusion of the tongue into the oropharyngeal lumen (Fig. 4). Mild increase in enhancement of the paralyzed hemitongue was evident in 3 patients with symptom duration of 2 weeks to 4 months. Remaining 4 patients showed no increase in enhancement of the affected hemitongue with symptom duration of 2 to 4 months. Variable degrees of T1-weighted hyperintensity due to fatty infiltration were noted in all patients (Fig. 5).

Evaluation for pathology along the course of the affected hypoglossal nerve revealed that 3 patients had skull bases masses centered in the ipsilateral occipital condyle (Figs. 2–4), and 2 patients had small masses in the ipsilateral occipital portion of the clivus. All 5 skull base masses extended to the hypoglossal canal. Four patients on subsequent workup represented osseous

metastases and 1 multiple myeloma (Table 1). In 4 patients, this was the initial presentation of newly diagnosed cancers; in 1 patient with a history of renal cell carcinoma, this was the first presentation of metastatic disease. The skull base mass also involving the mastoid segment of the temporal bone in the patient with multiple myeloma was initially interpreted as cholesteatoma (Fig. 3). Misinterpretation of tongue denervation for base-of-tongue tumor resulting in “missed skull base lesions” resulted in a delay of diagnoses in most of the patients. After accurate identification of tongue paralysis and a skull base mass in 1 patient, subsequent workup that began with a positron emission tomography–CT revealed a small breast mass with axillary nodal and multiple bone metastases (Fig. 2).

In the remaining 2 cases, internal carotid artery (ICA) dissections at the skull base resulting in cranial neuropathy (1 unilateral and 1 bilateral dissections with pseudoaneurysms) accounted for tongue denervation (Fig. 5). In 1 patient, the dissection was spontaneous and unsuspected. In the other patient, the carotid dissections were sequela of violent cough related to an asthma attack 2 weeks earlier. This patient also had a left vocal cord paresis related to concurrent vagus nerve palsy.

DISCUSSION

The tongue is composed of a fibrous skeleton consisting of the lingual septum, as well as intrinsic and extrinsic musculature

TABLE 1. Summary of Patient Demographics and Clinical Workups

No.	Age, y/Sex	Clinical Work-up Resulting From Misinterpretation of Tongue Denervation	Clinical Workup Leading to Diagnosis	Diagnosis
1	64/F	Panendoscopy	Laboratory evaluation including serum monoclonal protein, bone marrow biopsy, skeletal survey	Multiple myeloma
2	71/F	Panendoscopy	CT body, PET CT, breast and axillary lymph node biopsy	Breast cancer
3	66/M	Panendoscopy	PSA, bone scan, CT body, PET CT, skull base biopsy	Prostate cancer
4	76/M	Panendoscopy	CT body, PET CT	Unknown primary
5	47/M	Panendoscopy	CT body, bone scan	Renal cell carcinoma
6	40/M	Correct tongue denervation interpretation	Neck CTA	Bilateral ICA dissections
7	55/M	Panendoscopy and mucosal biopsy	Neck MRA	Left ICA dissection

CTA indicates computed tomography angiography; F, female; M, male; MRA, magnetic resonance angiography; PET, positron emission tomography.

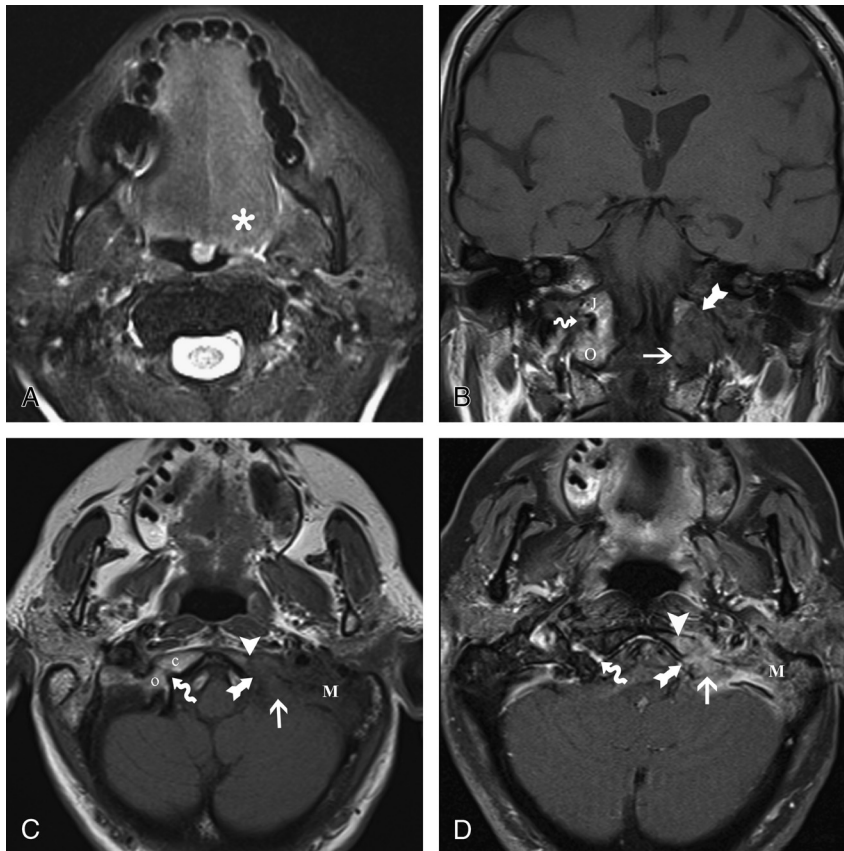


FIGURE 2. A 71-year-old female patient presented 5 months after empiric treatment for left ear infection with similar otalgia and new dysphagia and was referred for evaluation of tongue lesion. A, Axial T2W fat-saturated image demonstrates sharply demarcated T2 hyperintensity of the left hemitongue (asterisk). B, Coronal T1W image of the skull base shows T1 hypointensity lesion of the left occipital condyle (arrow) with extension to the hypoglossal canal (bow arrow). C and D, Unenhanced and fat-saturated enhanced T1W axial images of the skull base show abnormal T1 hypointensity marrow and enhancing mass of left occipital condyle (arrow) with extension to hypoglossal canal (bow arrow), occipital clivus (arrowhead), and mastoid (M). Note normal right occipital condyle (O), occipital clivus (C), and hypoglossal canal underneath the jugular tubercle (J) with vascular enhancement (squiggly arrow). Patient had metastatic breast cancer.

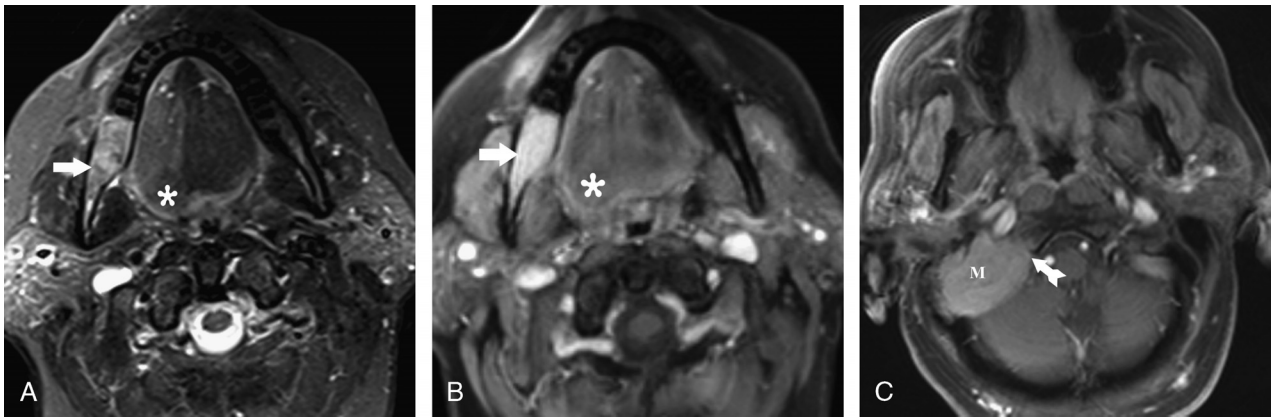


FIGURE 3. A 64-year-old female patient with remote history of ear infection and recent diagnosis of cholesteatoma was referred for base of tongue cancer with new right tongue symptom. A and B, Axial STIR and fat-saturated enhanced T1W images demonstrate sharply demarcated T2 hyperintensity of the right hemitongue with mild enhancement (asterisk), consistent with tongue paralysis. Note right mandible marrow replaced lesion (arrow). C, Fat-saturated enhanced T1W image of the skull base shows enhancing lesion of the right occipital condyle and mastoid (M) with extension to the hypoglossal canal (bow arrow), accounting for ipsilateral tongue paralysis. Further workup revealed multiple myeloma.

(Fig. 1). There are 4 paired extrinsic muscles named after their origins and insertions: the genioglossus, hyoglossus, styloglossus, and palatoglossus. The bulk of the tongue is made up by the

genioglossus muscle, a fan-shaped muscle arising from the genial tubercle and inserting at the dorsum of the tongue. When contracted, the genioglossus depresses and protrudes the tongue out,

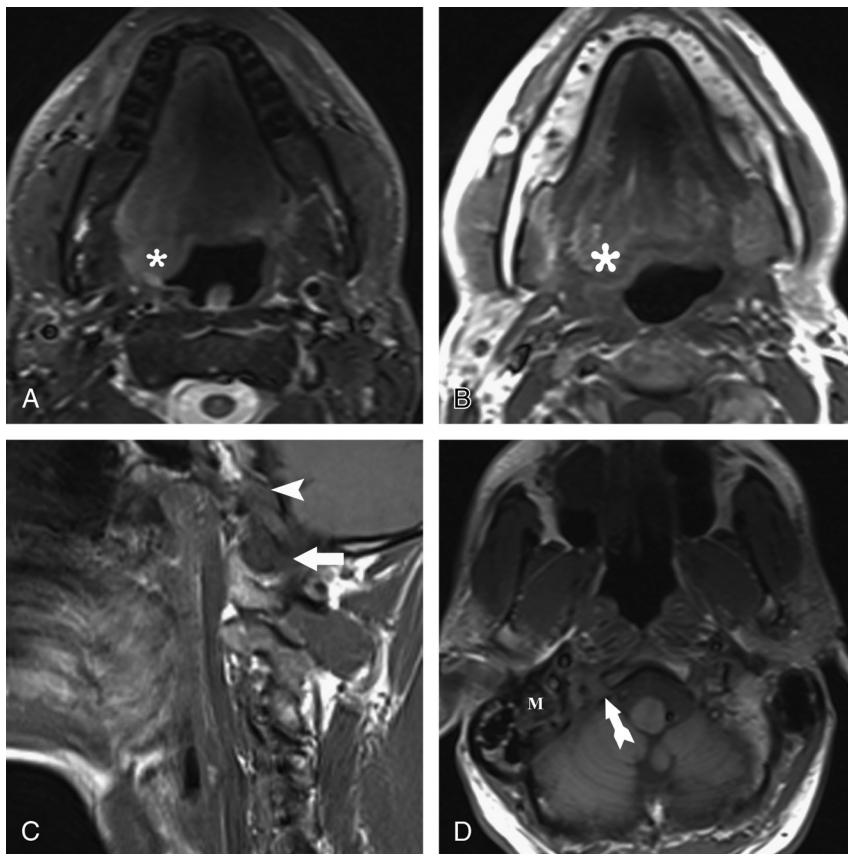


FIGURE 4. A 67-year-old man with right tongue symptoms was referred with radiological diagnosis of base-of-tongue mass. A and B, Axial STIR and T1W images demonstrate sharply demarcated T2 hyperintensity with normal internal architecture of the right hemitongue protruding into oropharynx (asterisk). C, Sagittal T1W image shows replacement of the marrow in the right condyle (arrow) and occipital clivus (arrowhead). D, Axial T1W image at the skull base demonstrates extraosseous tumor extension into the right hypoglossal canal (bow arrow) and mastoid (M), accounting for ipsilateral tongue paralysis. Skull base biopsy shows prostate cancer.

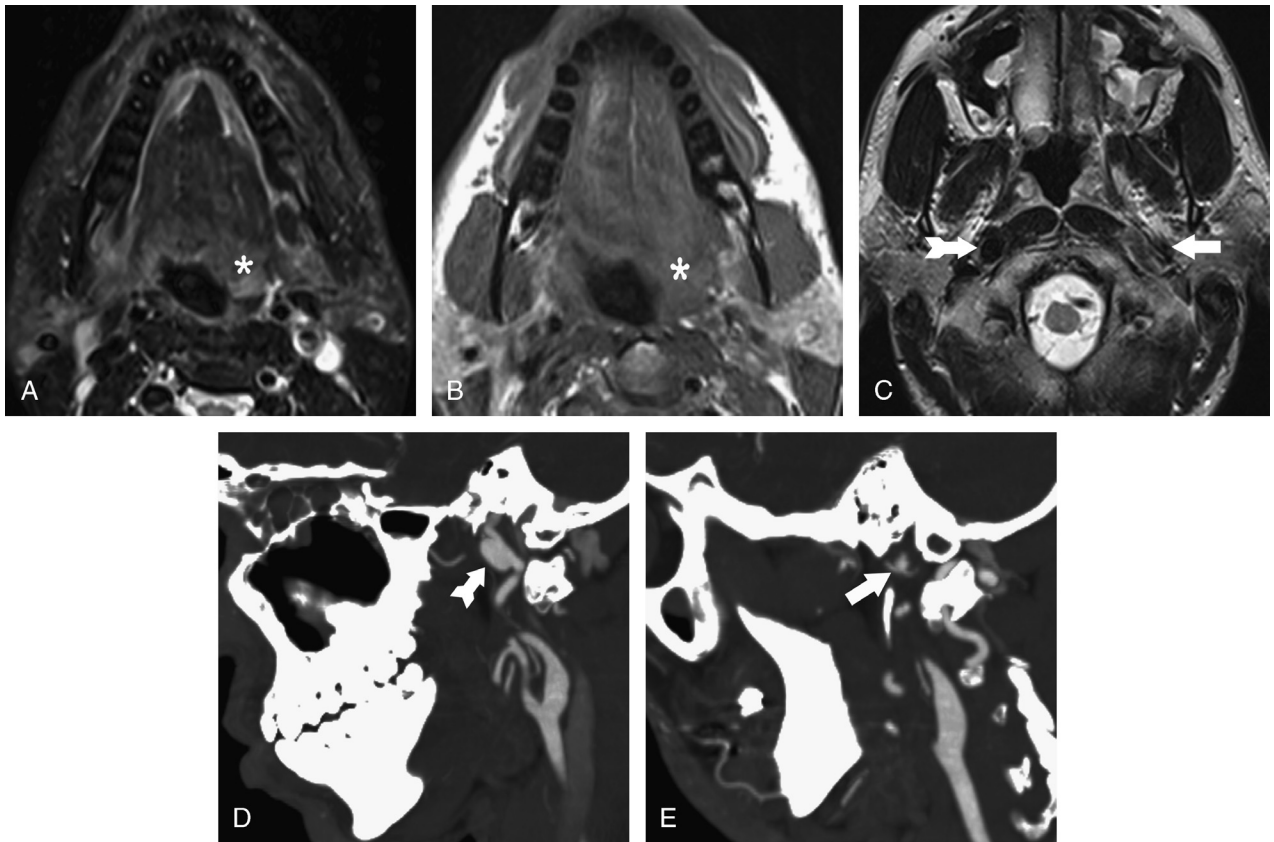


FIGURE 5. A 40-year-old man with dysarthria and dysphagia and tongue weakness concerning for mass lesion. A and B, Axial STIR and T1W images of the tongue show bulbous protrusion of left hemitongue into oropharynx (asterisk) and mild fatty atrophy of right hemitongue (arrowhead). C, Axial T2W image of the skull base shows focal dilatation of right ICA (bow arrow) and string-like narrowing of left ICA (arrow). D and E, Computed tomography angiogram sagittal maximal intensity projection images at the skull base confirm bilateral ICA dissections with large right pseudoaneurysm (bow arrow) and luminal narrowing of left ICA with small pseudoaneurysm (arrow).

keeping the oropharyngeal airway open. Paralysis results in mass-like posterior protrusion of the tongue into the oropharynx. The hyoglossus muscle originates from the greater horn of the hyoid bone and passes vertically upward to insert on the side of the tongue. This muscle defines the lateral aspect of the tongue and depresses and retracts the tongue. Interdigitating with the hyoglossus muscle is the styloglossus that originates from the styloid process, passes between the internal and external carotid arteries, and inserts on the side of the tongue near the dorsal surface. The styloglossus muscles draw up the sides of the tongue to create a trough for swallowing. Dysphagia can result from denervation of these muscles. The palatoglossus muscles arise from the anterior surface of the soft palate adjacent to the uvula, pass anterior to their respective palatine tonsils, and insert into the posterolateral tongue. This muscle forms the anterior pillar of the tonsil and has mucosa covering its surface. It aids in the initiation of swallowing. The intrinsic muscles are composed of the superior longitudinal fibers, which can be identified on MR imaging beneath the lingual mucosa, as well as other transverse, vertical, and inferior longitudinal fibers, which intermingle within the tongue and cannot be differentiated radiologically.⁶

The palatoglossus muscle is innervated by the vagus nerve. All of the other muscles are innervated by the hypoglossal nerve. Both the vagus and hypoglossal nerve nuclei are located in the dorsal medulla anterior to the fourth ventricle.³ The paired

hypoglossal nerves exit the medulla in the pre-olivary sulci and travel in the pre-medullary cistern before entering the hypoglossal canals at the skull base. The inferior border of the hypoglossal canal is located between the occipital condyle posteriorly and the occipital portion of the clivus anteriorly. Its roof is formed by the jugular tubercle (Figs. 1E–F). Pathology of the occipital condyle and occipital clivus can extend to involve the hypoglossal canal and nerve because these structures are anatomically contiguous with each other.

The hypoglossal nerve and contents of the jugular foramen enter the carotid space at the level of the nasopharynx and travel together inferiorly. At the angle of the mandible, the hypoglossal nerve exits the carotid space and loops around the occipital artery, lying inferior to the posterior belly of the digastric muscle where it becomes superficial.⁴ At the level of the hyoid bone, the nerve crosses the lingual artery and curves anteriorly to run lateral to the hyoglossus muscle and deep to the mylohyoid muscle within the sublingual space. As it passes anteriorly, the nerve lies on the surface of genioglossus before penetrating the muscle. Therefore, malignant tumors arising from the oral tongue, base of the tongue, or sublingual gland tumors can result in hypoglossal palsies.

The intrinsic tongue muscles are intermediate in signal intensity on T1-weighted images and hypointense on T2-weighted images with a striated appearance (Figs. 1A–B). There is a

midline frenulum and normal fat surrounding the neurovascular bundles on either side of the tongue between the genioglossus and hyoglossus muscles. With acute to subacute denervation (days to several months), the affected hemitongue shows T2 hyperintensity, swelling, and various degrees of fatty infiltration as well as abnormal enhancement⁷ (Figs. 2–5). In our series, the symptom durations ranged from 2 weeks to 4 months. All 7 patients' affected hemitongue had variable degrees of T2 hyperintensity with abrupt linear demarcation of the signal alteration at the midline (Figs. 2 and 3) and apparent enlargement of the ipsilateral base of the tongue. This geographic border of tongue paralysis is in contrast to the ill-defined infiltrative margin of neoplasm with loss of normal muscle striation.⁶ The presence of increased enhancement of the affected hemitongue occurred in less than half of our patients. Mass-like enlargement and posterior protrusion of the paretic hemitongue into the oropharyngeal lumen may mimic a base-of-tongue mass, especially if there is associated enhancement. However, careful analysis of the affected tongue for its preserved normal architecture and the lack of an endophytic or exophytic neoplasm is paramount in establishing the correct diagnosis of tongue denervation.

When tongue denervation is correctly identified, an orderly search for pathologies that may account for hypoglossal nerve palsy should follow. The course of the hypoglossal nerve from the dorsal medulla along the skull base through the hypoglossal canal, in the carotid sheath to the sublingual space must be interrogated.

In adults, the bone marrow is predominantly fatty-replaced. Therefore, the hyperintensity of skull base bone marrow on unenhanced T1-weighted imaging reflects its normal fatty marrow content. Hematopoietic cellular bone marrow has low signal intensity on unenhanced T1-weighted imaging and is normally seen in childhood and adolescents. Fatty conversion is usually seen by the age of 20 years.^{8,9} Low signal intensity in the skull base marrow of an adult strongly suggests the presence of abnormal marrow with an infiltrative process.⁹

Familiarity with the normal MR imaging appearance and anatomy of the hypoglossal canal is essential. Following the administration of intravenous contrast agents, the hypoglossal canal enhances related to the basilar venous plexus surrounding the hypoglossal nerve. The enhancement is usually bilateral and extends anteriorly into the prevertebral and nasopharyngeal space.¹⁰

Internal carotid artery dissections may result in isolated or multiple palsies of cranial nerves IX, X, and/or XII because of direct stretching injury, expansile mass effect related to an associated carotid pseudoaneurysm, and/or interruption of vascular supply to the nerves.^{1,11–15} Imaging findings of ICA dissection include intimal flap (often not seen), crescentic wall thickening due to mural thrombus, tapered luminal narrowing, and secondary pseudoaneurysm formation¹⁶ (Fig. 5).

In Keane's² study of 100 cases of hypoglossal nerve palsy, nearly half were caused by neoplasm; the majority was malignant. Other common etiologies included trauma, spontaneous or traumatic carotid artery dissection, neurological conditions such as stroke and multiple sclerosis, and infection.^{2,13} Only 15% of patients experienced complete or near-complete recovery, and among those who had complete resolution, viral neuritis was most common.²

The role of the radiologist is paramount in correctly establishing the diagnosis of tongue paralysis and identifying the underlying etiology. In our series, failure to correctly identify tongue paralysis resulted in exhausted workups including pan-endoscopy, and 1 patient also underwent mucosal biopsies because of misinterpretation of tongue paralysis for tongue tumor.

Furthermore, overlooked skull base lesions are not uncommon. Loevner and Yousem¹⁷ reported a series of patients with headaches and/or neck pain whose occipital condyle lesions were missed on multiple imaging studies. Because the skull base anatomy is intricate and at the edge of radiological images, skull base pathologies are often overlooked.¹⁷ All of our patients had either skull base bony metastasis and myeloma or ICA dissection, which accounts for the tongue paralysis. Of 5 oncologic patients, 4 had no prior oncologic diagnosis, and the fifth had no known metastatic disease. When the correct imaging interpretation of tongue denervation is made, the hypoglossal canal and ICA should be carefully scrutinized for pathology to avoid incorrect and delayed diagnoses.

CONCLUSIONS

Missed or misinterpretation of tongue denervation for "base-of-tongue masses" on CT and MR imaging is not uncommon. To avoid this pitfall, an understanding of the innervation of the tongue and the classic imaging findings of denervation are essential. The T2 and unenhanced T1-weighted images are most helpful, demonstrating sharply demarcated T2 hyperintensity of the denervated and swollen hemitongue with preserved internal architecture. When tongue denervation is identified, a careful search for pathology involving the hypoglossal nerve is essential. Familiarity with the complex anatomy and normal imaging appearance of the skull base is critical. Correct identification of tongue denervation and detection of skull base masses will allow a tailored, succinct clinical workup and lead to an expedient diagnosis.

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