Is Hypoglossal Nerve Palsy Caused by Craniocervical Junction Degenerative Disease an Underrecognized Entity?


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Is Hypoglossal Nerve Palsy Caused by Craniocervical Junction Degenerative Disease an Underrecognized Entity?


ABSTRACT

SUMMARY: Isolated hypoglossal nerve palsy is uncommon, and underlying craniocervical junction degenerative disease has rarely been reported as an underlying cause. To improve understanding of this entity, we present a retrospective series of 18 patients with hypoglossal palsy in whom twelfth cranial nerve compression within the premedullary cistern or hypoglossal canal, or both, was found secondary to craniocervical junction juxta-articular cysts, retro-odontoid fibrous pseudotumors, and osteophytes. The imaging techniques and characteristic craniocervical junction degenerative disease lesion imaging findings presented here might help clinicians interpreting hypoglossal palsy imaging studies avoid perceptual and interpretive errors commonly found in the present series.

ABBREVIATIONS: CCJ = craniocervical junction; CCJDD = craniocervical junction degenerative disease; JAC = juxta-articular cyst; ROFP = retro-odontoid fibrous pseudotumor

Hypoglossal nerve palsy is an infrequent clinical presentation, most commonly occurring in combination with other lower cranial nerve palsies. By using a segmental approach,1 the underlying etiologic factors can be subdivided by location as involving the brain stem, premedullary cistern, skull base, nasopharynx or oropharynx, or sublingual regions. Hypoglossal nerve palsy secondary to craniocervical junction (CCJ) juxta-articular (synovial and ganglion) cysts2-8 and osteophytes9,10 has been described in isolated case reports; yet, these pathologies are not classically included in the differential diagnosis for hypoglossal palsy. Distinguishing CCJ degenerative lesions from other hypoglossal nerve pathologies might have important diagnostic and treatment implications. To improve understanding of this disorder, a case series of 18 patients with hypoglossal palsy and ipsilateral twelfth cranial nerve compression secondary to CCJ juxta-articular cysts (JACs), retro-odontoid fibrous pseudotumors (ROFPs), and osteophytes is presented.

CASE SERIES

Patients

This Health Insurance Portability and Accountability Act–compliant retrospective case series was approved by the Mayo Clinic Institutional Review Board. Initially, 4 neuroradiologists (S.M.W., C.P.W., D.R.D., J.M.H.) provided 7 known cases of hypoglossal palsy secondary to craniocervical junction degenerative disease (CCJDD) from their teaching files. Next, a retrospective Boolean search of radiology reports from 3 affiliated tertiary medical centers between January 1, 2005, and December 31, 2014, was performed, combining the words “hypoglossal” or “tongue” and “palsy,” “atrophy,” or “denervation.” From this list, patients were excluded if hypoglossal palsy could not be confirmed through review of the electronic health record. Patients with prior head and neck or skull base tumor, radiation therapy, or surgery also were excluded. For the remaining patients with hypoglossal palsy, imaging studies that included the CCJ were reviewed for possible twelfth cranial nerve compression by an underlying CCJDD lesion (JAC, ROFP, or osteophyte). Eleven additional cases were discovered from this 10-year multicenter retrospective review. Three physicians with neuroradiology subspecialty board certification (S.M.W., C.P.W., J.M.H.) performed a consensus imaging review for all patients with hypoglossal palsy believed secondary to CCJDD to confirm and characterize the offending lesions.
each patient with hypoglossal palsy caused by CCJDD, our institution’s first MR imaging or CT report was reviewed to ascertain whether the initial differential diagnosis included the consensus diagnosis.

**Clinical Findings**

A total of 18 patients with hypoglossal palsy related to CCJDD were included in this case series (12 women and 6 men; mean age, 74 years; range, 52–89 years). Symptoms at presentation to our institutions most commonly included tongue weakness or deviation (13/18), dysarthria (12/18), and dysphagia (6/18) (On-line Table 1). Neurologic examination confirmed hypoglossal palsy in all patients. Among the 4 patients in whom the underlying lesion was addressed surgically, the duration between symptom onset and surgery was 3 months (n = 1), 11 months (n = 2), and 7 years (n = 1), respectively. In the final patient, surgical delay was due to lesion misdiagnosis as a hypoglossal schwannoma until the correct diagnosis of JAC was rendered 1 month before surgery. New-onset or worsening headache or suboccipital pain was an associated concern for 13 patients. No patient had a history of rheumatoid arthritis, psoriatic arthritis, gout, or calcium pyrophosphate deposition disease.

**Imaging Findings**

For the 18 patients with CCJDD hypoglossal palsy, the brain, head and neck, and cervical spine imaging studies from our institution and outside facilities spanning 12 years included 17 MR imaging (15 with contrast medium) and 12 CT scans using diverse techniques. Underlying CCJDD lesions included atlanto-occipital JACs (n = 10), atlantoaxial JACs (n = 2), ROFPs (n = 4), and C1-occipital osteophytes (n = 2) (On-line Table 2). All 18 patients had cranio-occipital and/or upper cervical degenerative disease on imaging studies. Altered cervical biomechanics in 4 of 18 patients was secondary to congenital nonsegmentation in 2 patients (C1-occipital and C2–C3) and prior surgical fusion in 2 patients (C2–C5 dorsal fixation and C6–C7 anterior cervical discectomy and fusion).

CCJ JACs appeared as well-circumscribed extradural lesions extending cephalad into the foramen magnum to encroach on the hypoglossal canal internal ostium. They showed lobular projections that were at least partially divergent from the expected twelfth cranial nerve course (Fig 1). On MR imaging, all 12 JACs were T1-hypointense and T2-hyperintense relative to the brain stem and lacked central contrast enhancement. On CT, cysts typically appeared predominantly hypoattenuated (5/6). In 4 of 12 JACs, twelfth cranial nerve compression was limited to the hypoglossal canal internal ostium, where 50% or more of the ostium was covered by JAC in every case. More commonly (8/12), CCJ JACs extended into the hypoglossal canal and caused focal smooth canal widening on CT in 3 of 8 patients (Fig 2). On axial T2-weighted images, the mean CCJ JAC size was 12.3 mm in maximal dimension (range, 7–19 mm). For the 10 patients with CCJ JAC and MR imaging follow-up (mean, 542 days; SD, 855), 4 cysts had decreased in size, 2 were stable, and 4 were enlarged. In 2 of 12 cases, the JAC was not described in the initial radiology report. More often (6/12), the JAC was seen but not correctly identified in the initial radiology report differential diagnosis. In these cases, the correct diagnosis was made at follow-up imaging or at prior examination review.

ROFPs (n = 4) uniformly appeared hyperattenuated on unenhanced CT (3/3) and often extended into the hypoglossal canal (3/4), causing focal irregular bony erosion (2/3) or smooth remodeling (1/3) (Fig 3). On MR imaging, relative to the adjacent brain stem, these masses were T1 iso-hypointense (3/3), T2 hypointense (2/3), or T2 iso-hyperintense (1/3) and showed some internal enhancement in 3 of 4 cases. The ROFP was correctly included in the initial radiology report differential diagnosis in 3 cases. In the fourth case, the offending ROFP was not seen despite radiologist identification of ipsilateral hypoglossal atrophy.

Two patients with hypoglossal...
palsy with advanced CCJDD had C1-occipital joint osteophyte encroachment on the ipsilateral hypoglossal canal external os-
tia. In these patients, C1-occipital arthrosis and osteophytes
narrowed the hypoglossal canal and caused erosions of its
walls. The osteophytes appeared hypointense on T1- and T2-
weighted MR imaging, and hyperattenuated on CT (Fig 4).
Degenerative osteophyte encroachment on the hypoglossal ca-
nal was correctly identified within the initial radiology report
for 1 patient. For the other patient, the offending osteophyte
was not seen, though tongue hemiatrophy was noted in the
radiology report.

Surgical Correlation
Four patients underwent surgical treatment for hypoglossal nerve
compression by CCJ JACs. Two patients had atlanto-occipital
JAC resection, with pathologic evaluation confirming synovial
cysts. In another 2 patients with CCJ JAC, the hypoglossal palsy
was considered irreversible, and occipital-C2 posterior fusion was
performed to prevent additional cranial nerve injury by potential
cyst enlargement. Postfusion MRI demonstrated resolution of 1
atlanto-occipital JAC and decreased size for the other. Surgery
was not performed in patients with hypoglossal palsy caused by
underlying ROFPs or osteophytes.

DISCUSSION
Hypoglossal nerve palsy is uncommon, and diagnosis of the underlying cause
can be problematic for clinicians and radiologists. High-resolution imaging and
a detailed understanding of twelfth cranial nerve anatomy are critical to the
identification of causative lesions and to formulating an educated differential di-
agnosis. Overall, tumors are the most common cause of hypoglossal nerve
palsy, accounting for nearly 50% of cases. Hypoglossal nerve palsy second-
ary to premedullary cistern or hypoglossal canal pathology is most frequently caused by hematogenous
skull base metastasis. Skull base invasion of nasopharyngeal carcino-
ma, radiation-induced neuropathy, hypoglossal neuritis, and schwannomas or secondary nerve compression by meningioma,
aneurysm, arachnoid cyst, and occipital condyle fracture are also
commonly included in the differential diagnosis.1,2,4,5,8-10 Our
series of 18 patients with hypoglossal palsy secondary to JACs,
ROFPs, and osteophytes is, to our knowledge, the largest series
with underlying CCJDD pathologic causes. In this retrospective
series, perceptual and interpretive errors in diagnosis led to an
underreporting of these lesions as the cause for hypoglossal palsy.

Juxta-Articular Cysts
Isolated case reports have described hypoglossal palsy resulting
from CCJ juxta-articular synovial2,4,5 and ganglion3,6-8 cysts
arising from either the atlanto-occipital2,4,8 or the atlantoax-
ial3 joints. Although synovial and ganglion cysts can be distin-
guished histologically, differentiation by imaging is neither
feasible nor clinically important. Therefore, it is practical to
adhere to the convention proposed by Kao et al11 and simply
identify either synovial or ganglion cysts as JACs. Spinal degen-
eration and segmental instability are thought to have an im-

FIG 3. Retro-odontoid pseudotumor of patient 2. This patient was an
87-year-old woman with a 2-month history of dysphagia. MR imaging
sagittal views show the retro-odontoid soft tissue mass (large arrows) to
be T2 hypointense (A), and nonenhancing (B). C, Axial T1-weighted image
shows isointense soft tissue eroding the skull base (large arrow) with
encroachment of the hypoglossal canal (arrowhead). CT axial soft tissue
(D) and coronal bone (E) reformations show hyperattenuated pseudotu-
mor mass (D, large arrow) causing bone erosions (small arrows), with
extension into the hypoglossal canal (E, arrowhead). F, For patient 8, axial
enhanced T1-weighted image shows retro-odontoid mass heterogeneous
enhancement (arrow), as seen in 3 of our 4 patients with ROFPs.

FIG 4. C1-occipital osteophyte of patient 7. This patient was a 77-year-old man with a 3-month
history of tongue weakness and dysarthria. CT axial (A) and coronal (B) images show severe
C1-occipital arthrosis with osteophyte encroachment at the hypoglossal canal external ostium
(arrows).
important role in JAC development, having a predilection for the most mobile levels in the cervical spine.12 Our series included 1 patient with developmental occipitalization of C1, which might have contributed to the patient’s atlantoaxial JAC formation.

Most of our patients with CCJ JAC (8/12) were women (mean age, 70.2 years; range, 52–89 years). Our findings are consistent with the female predilection13 and higher seventh-decade prevalence12,13 previously reported for lumbar spinal JACs. Of interest, though the association of headache and JAC was noted previously in a case report,5 10 of 12 patients with CCJ JAC reported new or worsening ipsilateral headache or suboccipital pain initiating in close relation to their hypoglossal palsy onset.

CCJ JACs appeared as well-defined extradural lesions with extension into the hypoglossal canal and narrow connections with the parent atlanto-occipital or atlantoaxial joint best visualized on thin-section, coronal T2-weighted images and oblique 2D or 3D reformations parallel to the hypoglossal canal. JACs were most conspicuous on T2-weighted images, where they uniformly showed a thin hypointense cyst wall and central hyperintensity. On postcontrast T1-weighted images, cysts showed only peripheral rim enhancement. These findings are consistent with those reported in a large imaging review of lumbar synovial cysts.13 On CT, CCJ JACs were mostly hypoattenuated (6/7). All CCJ JACs encroached on the hypoglossal canal internal ostium by 50% or more, with most (8/12) extending into or through the hypoglossal canal. Secondary hypoglossal canal smooth remodeling, as previously reported in lumbar synovial cysts,13 was seen in 3 of 8 patients. Ten patients had follow-up MR imaging without intervening surgery, revealing JAC size to be enlarged in 4, unchanged in 2, and decreased in 4. Synovial cyst size variation has been reported previously in the lumbar spine, where decreased size13 or complete resolution14 might be attributed to diminished synovial inflammatory fluid production or spontaneous cyst rupture.

CCJ JACs that cause hypoglossal palsy can be treated with surgical resection via a lateral suboccipital craniotomy,2-4,7,8 posterior fusion, or conservative management.5 Most of our 12 patients with hypoglossal palsy caused by CCJ JAC chose conservative management because the hemiglossal palsy was clinically tolerable and considered likely irreversible. Four patients with CCJ JAC underwent surgery. Two patients with cyst resection had no change in hypoglossal palsy, though suboccipital headache decreased for 1 patient. For 2 patients who underwent occipital-C2 fusion, postoperative MRI showed that the JACs either resolved or decreased in size, though neither patient reported improvement in hypoglossal palsy symptoms or suboccipital headache. The CCJ JAC decreased size or resolution after occipital-C2 fusion supports the theory that spinal instability strongly contributes to synovial cyst formation because increased motion causes synovial inflammation and secondary fluid production.

Retro-Odontoid Fibrous Pseudotumor

Retro-odontoid soft tissue masses causing cervicomedullary compression can result from numerous diseases, including rheumatoid arthritis15 and calcium pyrophosphate deposition disease.16 Some investigators have theorized that in noninflammatory ROFP, also known as degenerative pseudopannus, soft tissue masses composed of benign fibrous granulation tissue form in response to chronic atlantoaxial subluxation.17,18 Other investigators have reported ROFP formation in patients without overt atlantoaxial subluxation19,20 and proposed that altered biomechanics attributable to adjacent segment ankyloses cause repeated transverse ligament injury with resulting hypertrophy. None of our 4 patients with ROFP had a systemic arthritic condition. Two had previously undergone surgical cervical fixation, with resulting altered biomechanics likely contributing to chronic, excessive atlantoaxial stress.

Although most of the previously reported patients with ROFP were men, most patients in our series were women. Our mean patient age of 82 years (range, 70–87 years) is higher than previously reported by Chikuda et al19 (mean, 72 years) and Kakutani et al20 (mean, 76 years). The most common clinical manifestation of ROFP is myelopathy secondary to ventral cervicomedullary compression.18-20 To the best of our knowledge, ROFP has not been previously reported as a cause of hypoglossal palsy. Of interest, none of our 4 patients with CCJ ROFP hypoglossal palsy had myelopathy on neurologic examination, though imaging showed ventral cervicomedullary compression in 2 of the 4 patients.

ROFPs in our series showed variable MR imaging characteristics on T1- (hypointense, 2/3; isointense, 1/3) and T2-weighted (hypointense, 2/3; mixed iso-hypointense, 1/3) sequences. Most ROFPs have been reported as iso-hypointense on T1-weighted images and hypointense on T2-weighted images,17,19 consistent with a predominant fibrous composition. Alternatively, some ROFPs have been described on T2-weighted images as an admixture of iso-hypointensity,18,20 perhaps reflecting a larger component of vascular granulation tissue. ROFP enhancement, variably described as “absent” and “present” in previous reports,18,20 was seen in 3 of our 4 patients. Prior studies have shown that CCJ pseudotumor mass volume can decrease after direct resection,17 occipital-cervical fusion,18,19 or C1 laminectomy,20 with secondary myelopathy commonly improved after either surgical approach.18-20

Atlan-to-Occipital Osteoephyles

Hypoglossal palsy secondary to atlanto-occipital osteophyes has been previously described in single-case reports.5,10 In our 2 patients with hypoglossal palsy secondary to C1-occipital osteophyes, osteophyte encroachment and secondary hypoglossal canal wall erosions were observed at the external ostium. This external canal encroachment is in contrast to ROFPs and CCJ JACs, which encroach on the internal ostium, and commonly extended within and/or through the hypoglossal canal. One of our 2 patients with C1-occipital osteophyes had underlying congenital C2–C3 vertebral body nonsegmentation. Both patients were treated conservatively because unilateral hypoglossal palsy is reasonably well tolerated, requires complex surgery with substantial morbidity, and is unlikely to regress postoperatively.

Improving CCJDD Lesion Recognition and Differentiating JACs from Hypoglossal Schwannomas

In our series, CCJDD lesions causing hypoglossal palsy were often undiagnosed at initial imaging interpretation because of percep-
tual or interpretive errors. Among the 18 patients, perceptual errors—in which the underlying CCJ lesion was not described in the initial imaging interpretation despite radiologist notation of ipsilateral hemiglossal atrophy—were found in 4 patients (2 of 12 patients with JACs; 1 of 3 with ROFPs; 1 of 2 with osteophytes). Interpretive errors—in which the lesion was described in the initial imaging report, yet was not correctly specified within the differential diagnosis—occurred in 6 of the 12 patients with CCJ JAC. Therefore, hypoglossal palsy causative JAC was correctly included in the initial radiology report in only 33% (4/12) of our patients with JAC. The underlying lesion was correctly included in the initial radiology report’s differential diagnosis in 3 of 4 ROFP cases and 1 of 2 cases of hypoglossal canal osteophyte encroachment.

Diverse MR imaging and CT techniques used at outside institutions and our tertiary medical centers during this 10-year retrospective period were seldom optimized for evaluation of twelfth cranial nerve pathologies. Contrast-enhanced CT is the most common initial imaging study for evaluating patients with hypoglossal palsy. Helical acquisition from the posterior fossa to the hyoid bone allows evaluation from the medullary hypoglossal nuclei to the end-organ intrinsic tongue, styloglossus, hyoglossus, and genioglossus muscles. Demonstration of hypoglossal canal encroachment by CCJDD lesions can be aided by small field of view, thin-section (≤2 mm) axial, coronal, and sagittal soft tissue and bone reconstructions centered at the hypoglossal canal. Oblique reformations parallel to the hypoglossal canal can be helpful in assessing intracranial extension and bony erosion. In our series, CCJ JACs, the most common CCJDD lesion to cause hypoglossal palsy, were more conspicuous on MR imaging than CT. A dedicated posterior fossa–skull base MR imaging protocol, including thin-section (≤3 mm), small field of view sequences, should be used to evaluate patients with hypoglossal palsy in whom initial enhanced neck CT is unrewarding or in whom hemiglossal atrophy is noted on routine MR imaging. Besides postcontrast T1-weighted images, T2-weighted sequences are particularly helpful in evaluating CCJ degenerative lesions. Their inclusion in all 3 planes, ideally as a high-resolution volumetric sequence, is strongly recommended.

Among our 12 patients with CCJ JACs, cystic hypoglossal schwannoma was listed within the report differential 5 times. Differentiating CCJ JACs from “cystic” hypoglossal schwannomas is challenging. In a series of 44 surgically treated hypoglossal schwannomas, Nonaka et al found clinical presentations similar to CCJ JACs, with a female predominance, mean patient age of 45.8 years, and symptoms including ipsilateral tongue atrophy (92%), headache (61%), and dysphagia (32%). Hypoglossal schwannomas can be characterized as intracranial (31.5%), extracranial (18.5%), with secondary hypoglossal canal enlargement reported in up to 83%. So-called cystic hypoglossal schwannomas are uncommon, with cystic foci most often developing within large tumors with necrosis or spontaneous intratumoral hemorrhage. In a previous cystic hypoglossal schwanna case report, preoperative MR imaging showed peripheral enhancement surrounding cystic regions, whereas the tumor solid component enhanced uniformly. Thus, hypoglossal schwannomas and CCJ JACs share identical clinical presentations, might extend into and remodel the hypoglossal canal, and appear T1 hypointense and T2 hyperintense on MR imaging. However, an extradural location at the premedullary cistern, contiguity with the atlanto-occipital or atlantoaxial joints, lobular projections inconsistent with the hypoglossal nerve course, and thin peripheral contrast enhancement without solid enhancing component are helpful in distinguishing CCJ JACs from cystic hypoglossal schwannomas. This distinction is imperative because CCJ JAC misdiagnosis as a hypoglossal schwannoma can result in mistreatment and potential morbidity of stereotactic radiosurgery or an unwarranted intradural surgical approach with possible cranial nerve injury.

The present study has several limitations. It is a retrospective review of a rare entity and is limited as such. Based on our method for identifying patients for review, the potential exists for missing cases in which the neuroradiologist did not include “hypoglossal palsy” or “tongue atrophy” in the radiology report. A referral bias might be present because our institution is a tertiary care center. In addition, at our large referral center, many patients had limited or no long-term follow-up after their initial evaluation. Most patients were conservatively treated, limiting surgical confirmation.

CONCLUSIONS

Though degenerative disease at the craniocervical junction is commonly seen on imaging studies, it has been rarely reported as a cause of hypoglossal palsy. JACs were a more common CCJDD causative lesion than ROFPs and osteophytes. CCJDD should be added to the list of potential hypoglossal palsy causes, and familiarity with each type of CCJ degenerative lesion and its characteristic imaging appearance should improve the diagnosis and treatment of these disorders.

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