Hypertrophic olivary degeneration after surgical removal of cavernous malformations of the brain stem: Report of four cases and review of the literature

Mark Hornyak, MD,[1] Anne G. Osborn, MD,[2] and William T. Couldwell, MD, PhD[1]

Departments of [1]Neurosurgery and [2]Radiology, University of Utah, Salt Lake City, Utah

Corresponding author: William T. Couldwell, MD

Department of Neurosurgery

University of Utah

175 North Medical Drive East

Salt Lake City, UT 84132

Phone: 801-581-6908

Fax: 801-581-4385

Email: william.couldwell@hsc.utah.edu

UU IR Author Manuscript

Abstract

Background: Hypertrophic olivary degeneration (HOD) is a pathological phenomenon that occurs after injury to the dentato-olivary pathway. Its hallmarks include hypertrophy of the olive with increased T2 signal intensity on magnetic resonance imaging, and often manifests with palatal tremor and oscillopsia clinically.

Method: We report the cases of four patients who developed delayed HOD after surgical resection of pontine lesions.

Findings: We discuss the anatomical and pathological details of this disease and review the few other reported cases of HOD after resection of lesions within the brainstem.

Conclusions: HOD should be recognized as a possible complication of surgery within the brainstem and must be diagnosed promptly so that patients can be appropriately counseled and symptoms can be treated.

Keywords: hypertrophic olivary degeneration; surgery; cavernous malformation; brainstem

Running header: HOD and cavernomas of the brainstem

UU IR Author Manuscript

Introduction

Hypertrophic olivary degeneration (HOD) is a rare phenomenon that occurs after an insult to the dentato-rubro-olivary pathway of the brain stem. As the name implies, it is a degenerative disorder that initially causes hypertrophy, and thus enlargement, of the inferior olivary nucleus. The first description of this process is attributed to Oppenheim (19). In 1889, he described the pathological enlargement of the inferior olivary nucleus in postmortem examination. Later, HOD was associated anatomically with lesions of the central tegmental tract and dentate nucleus and also clinically with palatal tremor.

Insults to this pathway are most commonly caused by vascular pathology but can include trauma, tumor, demyelinating or degenerative diseases, and surgical manipulation, as well as hemorrhage or infarct. We describe four patients who presented with symptomatic pontine cavernous malformations that were treated with microsurgical resection. Three of these four patients developed delayed palatal tremor postoperatively, and HOD was noted on subsequent MR imaging in all four cases. We examine the anatomical and pathological details of this disease and review other cases of HOD after resection of cavernomas of the brainstem that have been reported in the literature.

Case Reports

Case 1

This 45-year-old man had a 9-year history of symptoms from a brainstem cavernous malformation. His symptoms began with sudden-onset diplopia. Clinical evaluation at that time revealed a pontine cavernoma, but his symptoms resolved, and surgery was

UU IR Author Manuscript

postponed. He presented 9 years later with sudden-onset horizontal diplopia and sensory changes on the right side of his body, as well as some weakness of his right arm. Examination revealed bilateral abducent weakness, right-sided pronator drift, and hyperreflexia with diminished vibratory sensation. Magnetic resonance (MR) imaging was repeated, and a 12-mm left-sided cavernoma, located in the paramedian dorsal tegmentum of the caudal pons, presenting to the ventricular surface, was again visualized (Figure 1A). It was calcified on computed tomography (CT) images.

The patient underwent microsurgical resection of the brainstem cavernous malformation via a midline suboccipital craniectomy with a transvermian approach to the inferior fourth ventricle. The cavernoma was visualized and the brainstem was entered via a midline incision into the lesion. The cavernoma was removed without difficulty, but the patient had a worsened weakness of his left abducent and facial nerves (House-Brackman 3/6) postoperatively. He also developed a mild right hemiparesis with some gait disturbance. Immediate postoperative imaging showed only unremarkable postoperative changes in the resection bed. Evaluation of the pathological specimen confirmed a diagnosis of cavernous malformation. The patient was discharged to rehabilitation on postoperative day four, and then to home eleven days later.

The patient's neurological deficits showed steady improvement, but approximately four months after his surgery, he complained of vertical oscillopsia of his left eye, and he was noted to have some palatal tremor. Repeat MR imaging revealed evolution of the postoperative changes (Figure 1B) and HOD, as demonstrated by an enlarged left inferior

UU IR Author Manuscript

olive with abnormal T2 hyperintensity (Figure 1C). The patient's symptoms were controlled with benzodiazepines and carbamazepine. At the last follow-up examination, 3 years after surgery, his symptoms are well controlled, but he continues to have mild facial weakness and horizontal diplopia. MR imaging at his most recent follow-up examination again showed only resolution of postoperative changes with persistent T2 hyperintensity of his left inferior olivary nucleus.

Case 2

This 50-year-old woman presented one month after a sudden onset of diplopia. Radiographic evaluation showed a 14-mm cavernous malformation in the left dorsal rostral paramedian pons adjacent to the superior cerebellar peduncle with extension into the midbrain, distorting the ventricular surface (Figure 2A). Examination revealed minimal left trochlear nerve weakness and some sensory changes throughout her right face. The patient elected to have the lesion surgically removed. She underwent midline suboccipital craniectomy and transvermian approach to the fourth ventricle. The cavernoma was visualized as discoloration of the ependyma rostral to the facial nucleus, which was mapped electrophysiologically. The cavernoma was entered with a paramedian incision 5 mm to the left of midline, above the facial colliculus. The cavernous malformation was surrounded by hemorrhage of differing ages and it was removed uneventfully. A venous angioma was noted adjacent to the cavernous malformation in the resection cavity but was not disturbed. The patient did well postoperatively, although she had some worsened diplopia and vertigo. Both of these symptoms improved without intervention. Immediate postoperative MR imaging

UU IR Author Manuscript

revealed only postoperative changes in the resection cavity, and pathological evaluation confirmed the diagnosis of cavernous angioma. The patient was discharged home on postoperative day five.

The patient continued to have some dizziness, but 17 months after her operation, she complained of worsening of her vision and was noted to have bilateral vertical ocular oscillations and palatal tremor. Repeat MR imaging showed only unremarkable postoperative changes and HOD on the left (Figure 2B,C). Her symptoms were controlled with benzodiazepines, and she remains in good condition 2 years after her operation.

Case 3

This 53-year-old man with a history of alcohol abuse presented acutely with the sudden onset of decreased hearing, horizontal diplopia, perioral dysesthesia, and gait ataxia. Emergent CT scanning revealed a large hemorrhage within the fourth ventricle and early obstructive hydrocephalus. An external ventricular drain was placed and MR imaging was performed. These images showed an 8mm abnormality in the midline floor of the fourth ventricle at the pontomesencephalic junction, consistent with vascular malformation or tumor. Formal cerebral angiography failed to reveal any abnormality. The following day, the patient had an acute deterioration with loss of consciousness requiring endotracheal intubation. Repeat CT demonstrated increased hemorrhage with mass effect upon the brainstem. The patient was taken emergently to the operating room for a midline suboccipital craniotomy and transvermian approach to the fourth ventricle.

UU IR Author Manuscript

The intraventricular clot was evacuated and an abnormality in the midline of the floor of the fourth ventricle was biopsied. The abnormal tissue was grossly vascular in nature, but the final pathologic report revealed no abnormal tissue; although it cannot be confirmed, the lesion was presumed to be a cavernous malformation. Postoperatively the patient made a fair recovery. He was discharged from the hospital 4 weeks later with significant diplopia and severe ataxia of his trunk. By six months after his operation his diplopia had resolved, and his ataxia had improved to the point he could ambulate with a cane. His MR images at that time demonstrated the site of the lesion in the midline of the pontomesencephalic junction (Figure 3A) and radiographic HOD (Figure 3 B,C), but he never demonstrated oculopalatal myoclonus. The patient continued to improve, but was lost to follow-up one year after his surgery; he was still suffering from ataxia.

Case 4

This 47-year-old woman with a known history of multiple cerebral cavernous malformations presented with an acute change in mental status after several days of headache and right upper extremity numbness. On neurological examination, she was opening her eyes only to voice but following commends. Her right pupil was 3 mm and reactive, while her left pupil was 5 mm and sluggishly reactive. She had limited upward gaze on the right, and complete ophthalmoplegia on the left. Her strength was normal on the left, but she demonstrated extensor posturing on the right. Emergent CT of the head revealed a 2.5-cm mesencephalic hemorrhage as the cause of her Weber syndrome. Her neurological condition declined initially but improved after placement of an external ventricular drain. MR imaging was performed, which also demonstrated hemorrhage

UU IR Author Manuscript

within the mesencephalon eccentric to the left, with extension into the left thalamus and cerebral peduncle, resulting in significant mass effect and effacement of the prepontine and interpeduncular cisterns, consistent with a cavernous malformation (Figure 4A). When the patient's clinical condition had stabilized, she underwent evacuation of the hematoma and resection of the cavernoma. The lesion was removed via a frontal craniotomy and a transcallosal approach. Intraoperatively, the hematoma was seen at the surface of the midbrain and a cavernous malformation was found and resected from the wall of the clot cavity. Postoperatively, the patient was neurologically unchanged, following commands and withdrawing the right upper extremity. Tracheostomy and feeding tubes were placed, and the patient was discharged to a skilled nursing facility after a one-month hospitalization. After six weeks, she showed improvement but seemed to have a Parinaud syndrome. She remained awake, and her pupils remained asymmetrical but were both reactive to light yet not accommodation. She had nystagmus and limitations of upgaze bilaterally, and her left ocular movements were improved. Her strength was improved on the right. She had no oculopalatal tremor. MR imaging performed at that time was unremarkable (Figure 4B). Six months after her hemorrhage, her ophthalmologic and neurological examination was remarkably improved. She was fully oriented and had improved eye movements with stereopsis. She continued to have diminished elevation of both eyes and limitations of movement of the left. Her right-sided strength improved remarkably, but she developed palatal tremor on the left. MR imaging demonstrated bilateral HOD (Figure 4C). One year later, her condition remains essentially unchanged, with only improvement in her motor function. Her oculopalatal tremor has improved with the administration of clonazepam.

UU IR Author Manuscript

Discussion

Cavernous malformations are the most common surgically treated lesion in the brainstem. The pons is the most common location for cavernomas of the brain stem, with 39% occurring within the pons and another 30% involving the pons (6, 21). The natural history of these lesions favors surgical excision (6, 29), but even in the best surgical hands, morbidity rates up to 10% can be expected (5, 21). Morbidity after resection of a cavernous malformation of the brainstem usually involves a worsening of preoperative deficits but can also include new deficit. Delayed deficits may also be seen, as with some patients whose deficits are associated with HOD.

The pathological hallmark of HOD is hypertrophy rather than atrophy in response to neurological insult to the dentato-rubro-olivary pathway. Pathological changes within the olive have been described to occur in six stages (9). The first is a stage of no noticeable change immediately after an insult, but in the second stage the amiculum degenerates, and then olivary neuronal hypertrophy is noted approximately three weeks after the insult. This third stage is followed by glial hypertrophy adding to olivary enlargement (4th stage), and then by pseudohypertrophy, which develops as neurons degenerate but large gemistocytic astrocytes persist (5th stage). Finally, the olivary nucleus atrophies more than a year after the injury (6th stage) (9). Hypertrophic neurons have an enlarged dendritic tree and still respond to afferent input (24). Ultrastructural analysis with electron microscopy shows increased neuronal size due to neurofilamentous proliferation and cytoplasmic vacuolization through the formation of rough endoplasmic reticulum

vesicles. Glial cells demonstrate a marked proliferation of mitochondria (17), and the olive may have increased metabolic activity as demonstrated on positron emission tomography (4). Radiographic changes correlate with the pathological findings. MR images show prolongation of T2 relaxation at approximately three weeks after an insult. Olivary enlargement is noted as early as six months after injury and persists for up to four years, while hyperintense T2 signal may persist indefinitely (10). This hypertrophic variant of degeneration is not unique to the inferior olivary nucleus. Similar hypertrophy has been seen in the dorsal root ganglion and in the dentate nucleus (1). The proposed mechanism of this change is transsynaptic degeneration (7, 14, 16, 27), which has also been described in other areas of the brain, including the lateral geniculate body and fornix (8). It is believed that the loss of a functional synapse leads to anterograde degeneration and atrophy; however, the inferior olivary nucleus shows hypertrophy of both neurons and glia. This may be due to the increase in spiny dendrites and mitochondria, respectively, to maintain active connections (17).

Anatomically, HOD and palatal tremor have been associated with injury to the dentate nucleus, the superior cerebellar peduncle, or the central tegmental tract (Figure 5). In 1931, Guillain and Mollaret described the dentato-rubro-olivary pathway and associated disruptions of this pathway with oculopalatal tremor and HOD (11). This pathway, also known as the triangle of Guillain and Mollaret, connects the dentate nucleus of the cerebellum, the red nucleus of the mesencephalon, and the inferior olivary nucleus of the medulla. Fibers originating in the dentate nucleus ascend to the contralateral red nucleus in the superior cerebellar peduncle. These axons decussate within the brachium

UU IR Author Manuscript

conjunctivum and synapse in the red nucleus. From the red nucleus, fibers descend in the central tegmental tract to enter the inferior olivary nucleus. The central tegmental tract contains many connections within the brainstem, especially to the reticular system but appears to be the major input to the inferior olive. The olive then sends fibers to the contralateral dentate nucleus via the inferior cerebellar peduncle, crossing midline at the level of the olive, completing the "triangle." Lesions that disrupt this pathway, deafferentiating the olive (dentato-rubral or rubro-olivary pathways), can lead to HOD, whereas disruption of efferent fibers from the olive (olivo-dentate) are less likely to cause HOD (7, 9, 14, 18, 28). This, again, is an example of transsynaptic degeneration, the proposed mechanism for HOD.

A number of causes for disruption of these pathways have been described. The most common factor that may contribute to this disruption is cerebrovascular disease (infarction or hemorrhage) (2, 3, 10, 14-16, 22), but other potential factors include traumatic head injury (2), tumor (14, 23), degenerative neurological disease (12), and surgical manipulation (27). Cavernous angiomas of the brainstem have been reported previously as the cause of HOD (14, 16), but the incidence of HOD after such an insult is unknown. Kitajima et al. (15) reported radiographic HOD in eight patients with brainstem hemorrhage and another three after cerebellar hemorrhage. Krings et al. (16) reported four cases of HOD caused by pontine hemorrhages, presumably caused by cavernous malformations. No surgical intervention was undertaken in these patients. Controlled cerebellar hemispherectomy in cats produced variable effects on the inferior olive (24). In 100 patients harboring cavernous malformations of the brainstem, 86 of

UU IR Author Manuscript

whom underwent surgical resection, Porter et al. (21) did not report any cases of HOD pre- or postoperatively. The incidence of palatal tremor, the clinical hallmark of HOD, is also variable. In three autopsy series, one of three (1), two of three (7), and two of 29 (14) cases (14%) of confirmed HOD demonstrated palatal myoclonus. Thus the incidence of HOD after brainstem injury is unknown and the occurrence of palatal tremor with HOD is variable.

Three cases of HOD after surgical resection of pontine cavernoma have been reported previously (13, 20, 26). All of the reported cases (including ours) involve symptomatic cavernous malformations in the pons that were resected. All seven patients developed HOD postoperatively, diagnosed between 3 and 17 months after their surgeries. In all cases, including the cases presented here, the HOD was attributed to disruption of the central tegmental tract. Four of the seven cases had only unilateral HOD, ipsilateral to the lesion and resection. Tsui et al. (26) reported bilateral HOD after involvement of both the ipsilateral central tegmental tract as well as the adjacent ipsilateral superior cerebellar peduncle, which would disrupt the ipsilateral central tegmental tract, and the dentato-rubral fibers ascending to the contralateral red nucleus; this is the presumed mechaninism in Patient 3, as his pontine insult was in the midline. However, the incidence of palatal myoclonus or tremor is variable, occurring unpredictably in association with HOD, and occurring in four of the seven surgical cases reported. The myoclonus associated with HOD has been successfully treated with benzodiazepines, carbamazepine, and 5-hydroxytryptophan (18). One refractory case has been treated with deep brain stimulation (25).

UU IR Author Manuscript

Thus, when hypertrophy and signal change are seen within the inferior olivary nucleus on MR imaging more than three weeks after surgical resection of a brainstem lesion, HOD should be suspected rather than a second neurological disease such as stroke or tumor. Whenever these changes are seen on MR images, a simple but careful examination of the pharynx, larynx, and eyes should be performed. When HOD is considered in the differential diagnosis, patients can be counseled appropriately, and medical management can be initiated.

Conclusion

Hypertrophic olivary degeneration is a unique pathological entity that occurs variably after injury to the brainstem. Specifically, injury to the dentato-rubro-olivary pathway can result in HOD pathologically or radiographically, and may present with or without palatal myoclonus. In patients who develop these findings after having undergone resection of a lesion of the brainstem that may have affected these pathways, HOD should be considered. Radiographic abnormalities usually progress predictably. It is important not to mistake HOD for a new ischemic event, degenerative disease, or malignancy. If HOD is suspected, symptoms can be treated medically. It is important to consider HOD as a potential complication of surgical resection of cavernous malformations of the brainstem, when counseling patients about treatment options.

UU IR Author Manuscript

References

1. Aberfeld DC (1966) The hypertrophic degeneration of the olives. Acta Neurol Scand 42:296-306

2. Anderson JR, Treip CS (1973) Hypertrophic olivary degeneration and Purkinje cell degeneration in a case of long-standing head injury. J Neurol Neurosurg Psychiatry 36:826-832

3. Conforto AB, Smid J, Marie SK, Ciriaco JG, Santoro PP, Leite Cda C, Mansur LL, Scaff M (2005) Bilateral olivary hypertrophy after unilateral cerebellar infarction. Arq Neuropsiquiatr 63:321-323

4. Dubinsky RM, Hallett M, Di Chiro G, Fulham M, Schwankhaus J (1991) Increased glucose metabolism in the medulla of patients with palatal myoclonus. Neurology 41:557-562

5. Ferroli P, Sinisi M, Franzini A, Giombini S, Solero CL, Broggi G (2005) Brainstem cavernomas: long-term results of microsurgical resection in 52 patients. Neurosurgery 56:1203-1212; discussion 1212-1214

6. Fritschi JA, Reulen HJ, Spetzler RF, Zabramski JM (1994) Cavernous malformations of the brain stem. A review of 139 cases. Acta Neurochir (Wien) 130:35-46

7. Gautier JC, Blackwood W (1961) Enlargement of the inferior olivary nucleus in association with lesions of the central tegmental tract or dentate nucleus. Brain 84:341-361

8. Gay AJ, Silberberg DH (1964) Histochemical Correlates of Transynaptic Degeneration. Studies in the Monkey Lateral Geniculate Nucleus. Arch Neurol 10:85-90

UU IR Author Manuscript

9. Goto N, Kaneko M (1981) Olivary enlargement: chronological and morphometric analyses. Acta Neuropathol (Berl) 54:275-282

10. Goyal M, Versnick E, Tuite P, Cyr JS, Kucharczyk W, Montanera W, Willinsky R, Mikulis D (2000) Hypertrophic olivary degeneration: metaanalysis of the temporal evolution of MR findings. AJNR Am J Neuroradiol 21:1073-1077

11. Guillain G, Mollaret P (1931) Deus de myoclonies synchrones et rhythmees velopharyngolaryngo-oculo-diaphragmatiques. Rev. Neurol 12:545-546

12. Hanihara T, Amano N, Takahashi T, Itoh Y, Yagishita S (1998) Hypertrophy of the inferior olivary nucleus in patients with progressive supranuclear palsy. Eur Neurol 39:97-102

13. Harter DH, Davis A (2004) Hypertrophic olivary degeneration after resection of a pontine cavernoma. Case illustration. J Neurosurg 100:717

14. Jellinger K (1973) Hypertrophy of the inferior olives. Report on 29 cases. Z Neurol 205:153-174

15. Kitajima M, Korogi Y, Shimomura O, Sakamoto Y, Hirai T, Miyayama H, Takahashi M (1994) Hypertrophic olivary degeneration: MR imaging and pathologic findings. Radiology 192:539-543

16. Krings T, Foltys H, Meister IG, Reul J (2003) Hypertrophic olivary degeneration following pontine haemorrhage: hypertensive crisis or cavernous haemangioma bleeding? J Neurol Neurosurg Psychiatry 74:797-799

17. Kurachi M, Nakamura I, Katsukawa K, Kobayashi K, Sano Y, Isaki K, Yamaguchi N (1985) Olivary hypertrophy in a case with palatal myoclonus: light- and electron-microscopic study. Folia Psychiatr Neurol Jpn 39:543-550

UU IR Author Manuscript

18. Lapresle J (1986) Palatal myoclonus. Adv Neurol 43:265-273

19. Oppenheim H (1887) Über Olivendegeneration bei Atheromatese der basalen Hirnarterien. Berl Klin Wschr 34:638-639

20. Phatouros CC, McConachie NS (1998) Hypertrophic olivary degeneration: case report in a child. Pediatr Radiol 28:830-831

21. Porter RW, Detwiler PW, Spetzler RF, Lawton MT, Baskin JJ, Derksen PT, Zabramski JM (1999) Cavernous malformations of the brainstem: experience with 100 patients. J Neurosurg 90:50-58

22. Revel MP, Mann M, Brugieres P, Poirier J, Gaston A (1991) MR appearance of hypertrophic olivary degeneration after contralateral cerebellar hemorrhage. AJNR Am J Neuroradiol 12:71-72

23. Robin JJ, Alcala H (1975) Olivary hypertrophy without palatal myoclonus associated with a metastatic lesion to the pontine tegmentum. Neurology 25:771-775

24. Ruigrok TJ, de Zeeuw CI, Voogd J (1990) Hypertrophy of inferior olivary neurons: a degenerative, regenerative or plasticity phenomenon. Eur J Morphol 28:224-239

25. Shepherd GM, Tauboll E, Bakke SJ, Nyberg-Hansen R (1997) Midbrain tremor and hypertrophic olivary degeneration after pontine hemorrhage. Mov Disord 12:432-437

26. Tsui EY, Cheung YK, Mok CK, Yuen MK, Chan JH (1999) Hypertrophic olivary degeneration following surgical excision of brainstem cavernous hemangioma: a case report. Clin Imaging 23:215-217

UU IR Author Manuscript

27. Uchino A, Hasuo K, Uchida K, Matsumoto S, Tsukamoto Y, Ohno M, Masuda K (1993) Olivary degeneration after cerebellar or brain stem haemorrhage: MRI. Neuroradiology 35:335-338

28. Zarranz JJ, Fontan A, Forcadas I (1990) MR imaging of presumed olivary hypertrophy in palatal myoclonus. AJNR Am J Neuroradiol 11:1164

29. Zimmerman RS, Spetzler RF, Lee KS, Zabramski JM, Hargraves RW (1991) Cavernous malformations of the brain stem. J Neurosurg 75:32-39

UU IR Author Manuscript

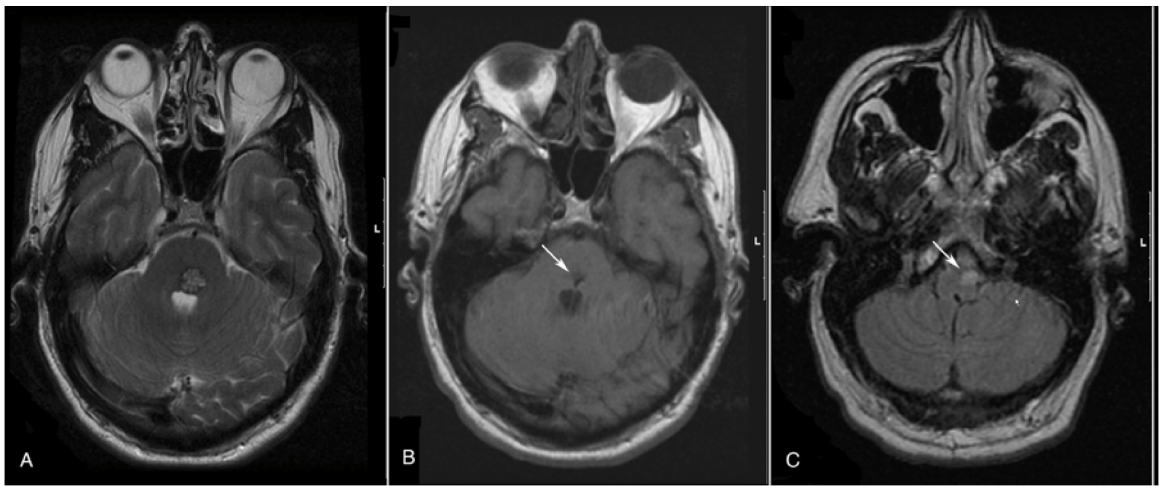

Figure 1: MR imaging scans of Patient 1. (A) Axial T2-weighted, preoperative MR image demonstrates the location of the cavernous malformation in the left dorsal pons. (B) Axial, unenhanced T1-weighted MR image obtained four months following resection demonstrates the unremarkable postoperative changes at the operative site (arrow). (C) Postoperative axial FLAIR MR image shows increased signal intensity in the left lateral medulla with an enlarged of the olivery nucleus (arrow) compared to the contralateral side; left unilateral HOD.

UU IR Author Manuscript

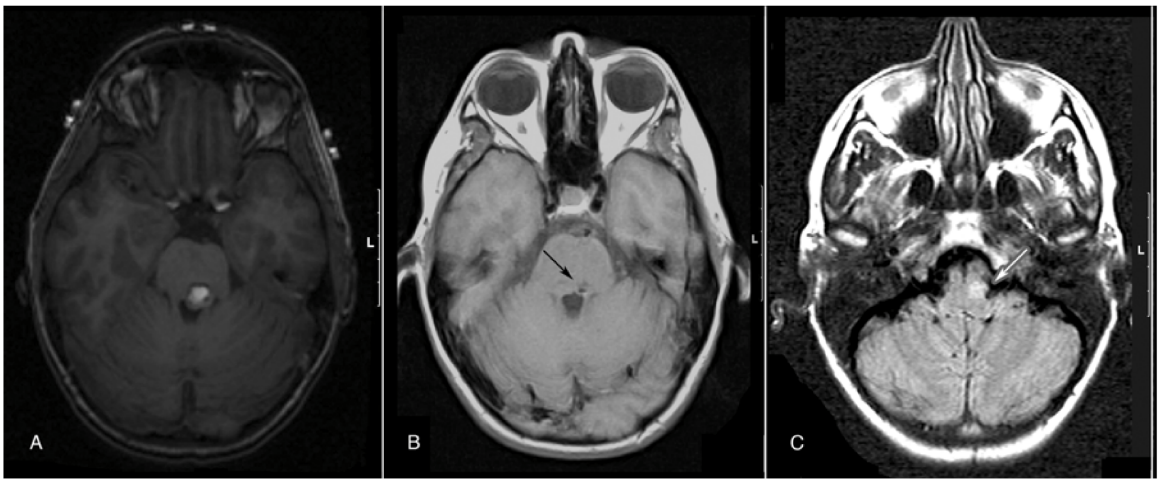

Figure 2: MR imaging scans of patient 2. (A) Axial, unenhanced, fat-suppressed T1-weighted MR image demonstraties preoperative location of cavernous malformation with in the left dorsal pons. (B) Axial, unenhanced T1-weighted MR image obtained 17 months postoperatively demonstrates the unremarkable changes in the resection bed (arrow). (C) Postoperative axial FLAIR MR image shows increased signal intensity in the left lateral medulla with an enlarged of the olivery nucleus (arrow) compared to the contralateral side; left, unilateral HOD.

UU IR Author Manuscript

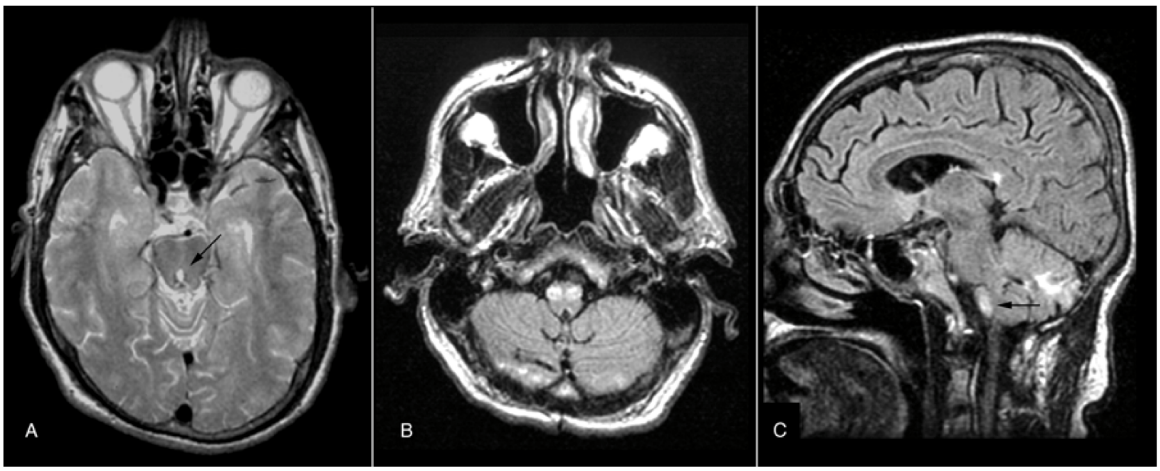

Figure 3: MR imaging of patient 3. (A) Axial, T2-weighted MR image obtained 6 months postoperatively demonstrates the unremarkable postoperative changes in the brainstem. The resection cavity is located in the midline at the pontomesencephalic junction (arrow). (B) Postoperative axial FLAIR MR image shows increased signal intensity within the lateral aspect of both sides of the medulla with enlargement of both inferior olivary nuclei; bilateral HOD. (C) Postoperative sagital FLAIR MR image demonstrates the increased signal intensity and enlargement of the inferior olive within the ventral medulla (arrow).

UU IR Author Manuscript

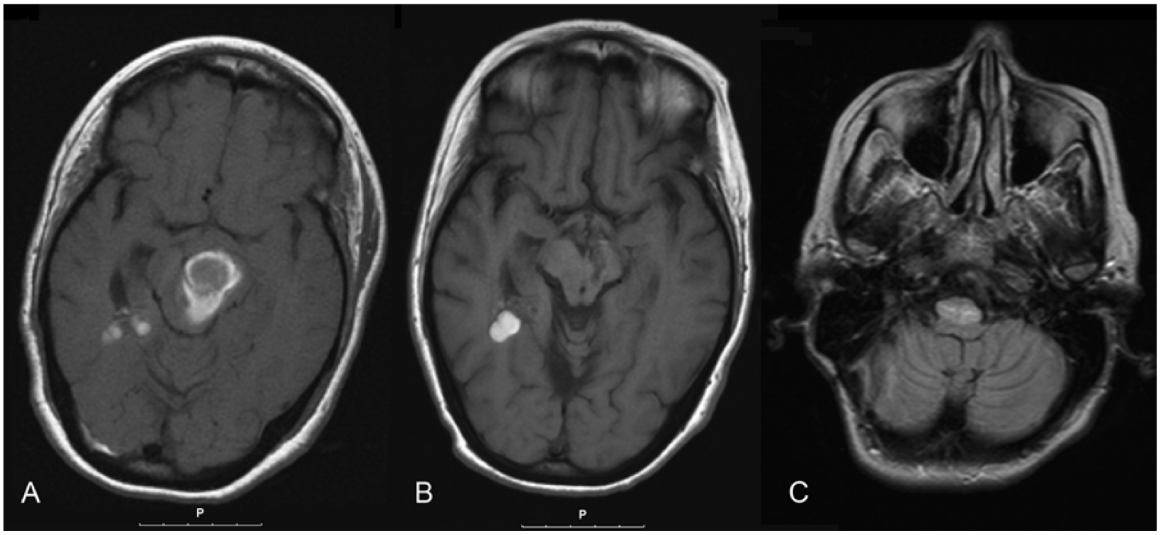

Figure 4: MR imaging of patient 4. (A) Axial, unenhanced T1-weighted MR image demonstrates preoperative location of cavernous malformation within the left mesencephalon. (B) Axial, unenhanced T1-weighted MR image obtained 6 months postoperatively demonstrates the unremarkable changes in the resection bed and improvement of mass effect. (C) Postoperative axial FLAIR MR image obtained 18 months after intervention shows increased signal intensity within the lateral aspect of both sides of the medulla with enlargement of both inferior olivary nuclei; bilateral HOD.

UU IR Author Manuscript

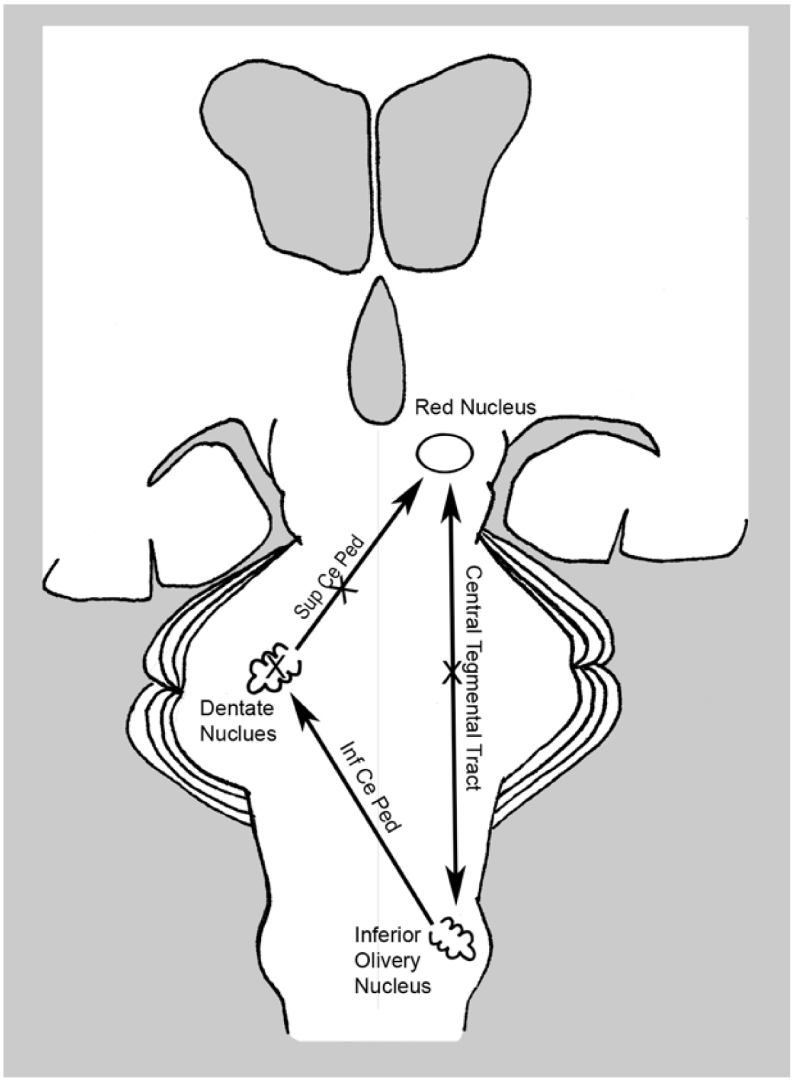

Figure 5: Illustration of the brainstem pathways involved in HOD. The triangle of Guillain and Mollaret is depicted. Injury to the central tegmental tract or the superior cerebellar peduncle (Sup Ce Ped), as demonstrated with the "X," are likely to cause HOD. Injury to the inferior cerebellar peduncle (Inf Ce Ped) is less likely to lead to HOD.

UU IR Author Manuscript

Table 1: Summary of seven cases of HOD that developed after surgical resection of pontine cavernoma

Patient/Author	Age/Gender	Size of Lesion	Time to Diagnosis of HOD (months)	Palatal Tremor
Phatouros and McConachie (1998)(20)	14/F	25 mm	13	N
Tsui et al. (1999)(26)	43/F	NA	7	Y
Harter and Davis (2004)(13)	32/M	20 mm	3	N
Patient 1	44/M	12 mm	4	Y
Patient 2	50/F	14 mm	17	Y
Patient 3	53/M	8 mm	6	N
Patient 4	47/F	25 mm	6	Y

UU IR Author Manuscript