OPEN ACCESS Freely available online

Tremor and Other Hyperkinetic Movements

Case Reports

Bilateral Hypertrophic Olivary Degeneration and Holmes Tremor without Palatal Tremor: An Unusual Association

Carlos Cosentino,* Miriam Velez, Yesenia Nuñez, Henry Palomino, Darko Quispe, Martha Flores & Luis Torres

Departamento de Enfermedades Neurodegenerativas, Instituto Nacional de Ciencias Neurológicas, Lima, Peru

Abstract

Background: Lesions in the Guillain–Mollaret triangle or dentate-rubro-olivary pathway may lead to hypertrophic olivary degeneration (HOD), a secondary trans-synaptic degeneration of the inferior olivary nucleus. HOD is usually associated with palatal tremor and rarely with Holmes tremor. Bilateral HOD is a very unusual condition and very few cases are reported.

Case Report: We report here two cases of bilateral HOD after two different vascular lesions located at the decussation of superior cerebellar peduncles, thus impairing both central tegmental tracts and interrupting bilaterally the dentate-rubral-olivary pathway. Interestingly, both developed bilateral Holmes tremor but not palatal tremor.

Discussion: Lesions in some of the components in the Guillain–Mollaret triangle may develop Holmes tremor with HOD and without palatal tremor. Magnetic resonance imaging is an invaluable tool in these cases. Better understanding of the pathways in this loop is needed.

Keywords: Holmes tremor, olivary nucleus, Guillain–Mollaret triangle

Citation: Cosentino C, Velez M, Nunez Y, et al. Bilateral hypertrophic olivary degeneration and Holmes tremor without palatal tremor: an unusual association. Tremor Other Hyperkinet Mov. 2016; 6. doi: 10.7916/D87944SS

*To whom correspondence should be addressed. E-mail: ccosentinoe@gmail.com

Editor: Elan D. Louis, Yale University, USA

Received: April 19, 2016 **Accepted:** June 7, 2016 **Published:** July 14, 2106

Funding: None.

Financial Disclosures: None.

Conflict of Interest: The authors report no conflict of interest.

Ethics Statement: This study was considered exempted from review by the Institutional Ethics Committee.

Introduction

Lesions in the dentate-rubro-olivary pathway may lead to hypertrophic olivary degeneration (HOD), a secondary trans-synaptic degeneration of the inferior olivary nucleus. Lesions causing pathway interruption are usually unilateral and include hemorrhage, ischemia, and demyelination. HOD is usually associated with palatal tremor and rarely with Holmes tremor. Even if anatomical pathways are well studied, the pathophysiology of movement disorders associated with HOD is poorly understood.

We report here two unusual cases of midbrain vascular lesions at the level of the commissure of Wernekinck associated with Holmes tremor and bilateral HOD without palatal tremor.

Case report

Case 1

A year before admission to another center, a 60-year-old male with poorly controlled arterial hypertension presented a clinical picture compatible with a severe midbrain hemorrhage causing obstructive hydrocephalus. He was discharged some months later with diplopia, mild quadriparesis, and action tremor of the upper limbs. Four months before admission to our service he complained of cephalic tremor and persistent diplopia. On admission, we found bilateral paresis of the third and fourth cranial nerves with marked anisocoria. He also had dysarthria and head tremor (3 Hz) at rest, as well as a postural tremor

and marked Holmes tremor in the upper extremities. No palatal tremor was observed.

Magnetic resonance imaging (MRI) revealed a small anteromedial hypointensity in the midbrain in T2 compatible with hemosiderin and bilateral enlarged hyperintensities in the region of both inferior olivary nuclei (Figure 1a,b). Levodopa/carbidopa was tried at a dose of 500 mg/day with marked and sustained improvement in the amplitude of the head and upper extremities tremor. Family members did not allow the patient to be videotaped.

Case 2

A 69-year-old female, diabetic for 20 years, suffered a midbrain infarction 4 months before admission with left palpebral ptosis and diplopia, unsteady gait, dysarthria, right hemiparesis and hypoesthesia,

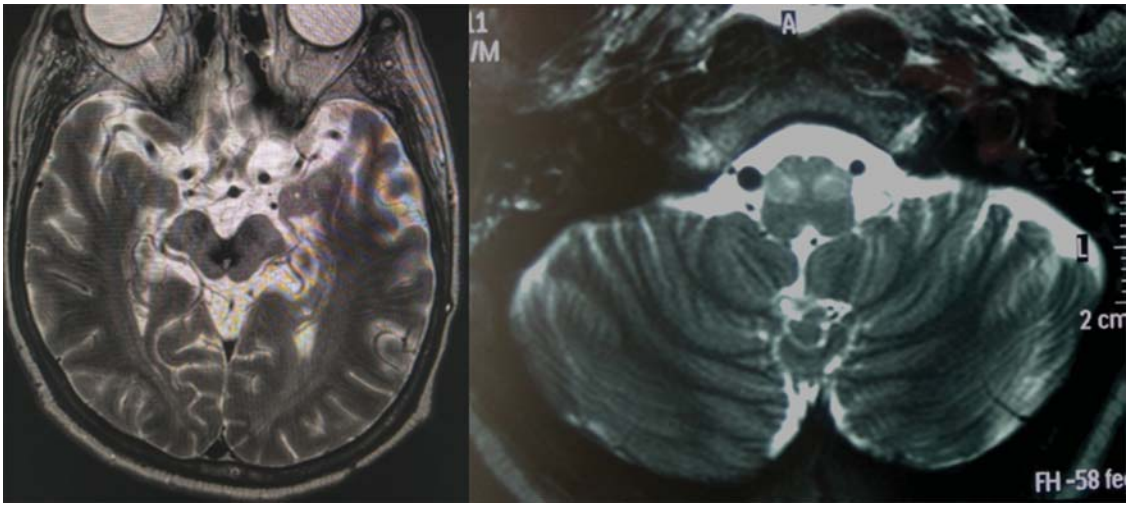

Figure 1. **(a,b) Midbrain hemorrhage and bilateral hypertrophic olivary degeneration.**

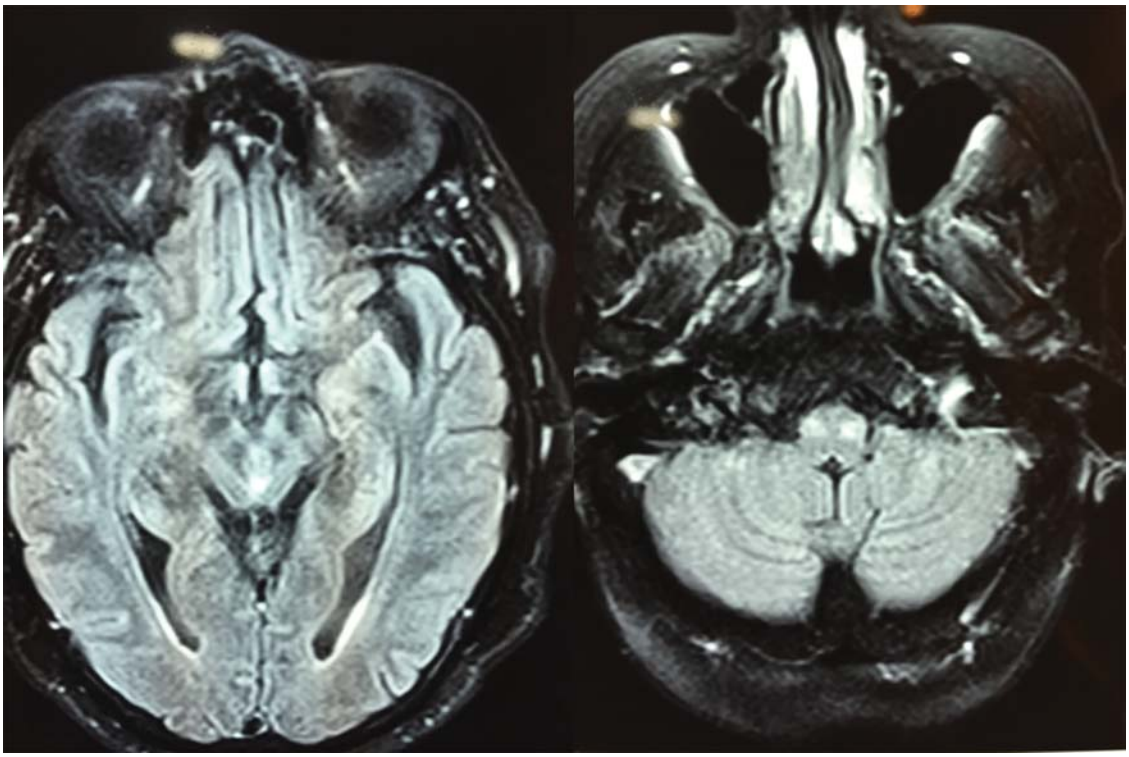

Figure 2. **(a,b) Midbrain ischemia and bilateral hypertrophic olivary degeneration.**

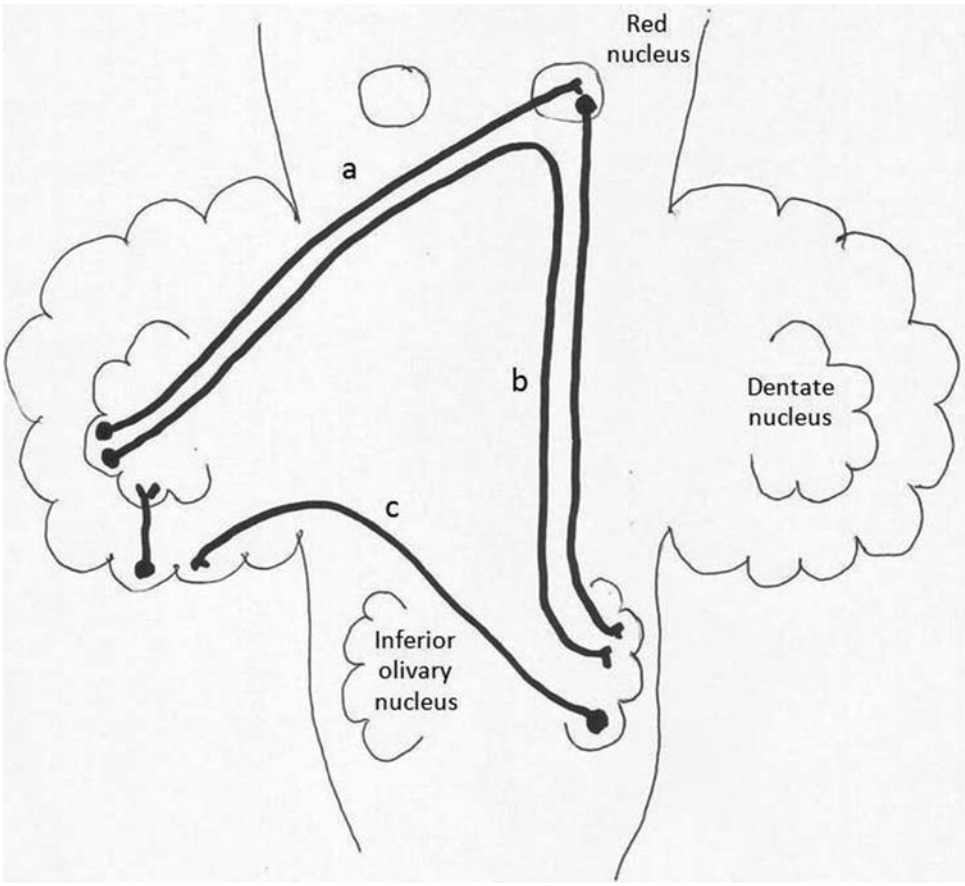

Figure 3. Guillain–Mollaret Triangle. (a) Dentate-rubral tract; (b). Dentate-rubral-olivary tract; (c) olivo-dentate tract.

and bilateral upper limbs dysmetria. A week later, MRI showed ischemic lesion in the medial region of midbrain and bilateral hyperintensities in the inferior olive nucleus.

Two weeks after the vascular event, she developed head tremor while lying down, which increased in amplitude when seated. Holmes tremor in the upper extremities and moderate gait disturbances as well as bilateral internuclear ophthalmoplegia were also present. No palatal tremor was observed.

MRI performed 4 months after the event revealed a T2-anteromedial hyperintensity in the midbrain compatible with infarction and enlargement of both inferior olivary nuclei with hyperintensity on T2W images (Figure 2a,b). A very mild response was achieved with levodopa. Family members did not allow the patient to be videotaped.

Discussion

The inferior olive nucleus receives its major input from the contralateral dentate nucleus of the cerebellum passing into the brainstem by way of the superior cerebellar peduncle or brachium conjunctivum crossing the midline at the caudal midbrain (commissure of Wernekinck), then synapse occurs in the contralateral red nucleus and descends within the central tegmental tract to enter into the inferior olive nucleus. This disynaptic pathway is parallel to a monosynaptic one that does not enter the red nucleus. The efferent fibers from the inferior olive nucleus cross the midline, forming the largest component of the inferior cerebellar peduncle. They first synapse in the cerebellar cortex via the olivocerebellar tract and the Purkinje cells of the cerebellar cortex project to the dentate nucleus, thus the inferior olive nucleus does not project directly to the dentate nucleus. The triangle comprising connections among the inferior olive nucleus, the red nucleus, and the contralateral dentate nucleus is referred to as the Guillain–Mollaret triangle (Figure 3).[1]

HOD is caused by lesions in the dentatorubral or central tegmental tracts. Disruption of these pathways leads to functional deafferentation of the inferior olive nucleus, so HOD is considered to be the result of trans-synaptic degeneration. Lesions of the superior cerebellar peduncle can also result in contralateral HOD, whereas primary lesions of the central tegmental tract cause ipsilateral HOD. Bilateral HOD can occur if the primary lesion involves both of the aforementioned structures or if a midline lesion is located in the brachium conjunctivum, impairing both the right and the left dentate olivary fibers as they cross.[2]

The clinical manifestations of any lesion in the Guillain–Mollaret triangle can be quite diverse. Classically, the clinical presentation

associated with HOD is palatal tremor.[3] Palatal tremor usually develops many months after the primary lesion, although not all patients with HOD develop this symptom.[4] At the same time, the incidence of HOD after brainstem injury is unknown, and the occurrence of palatal tremor with HOD is also variable. Although unusual, other movement disorders can also occur in association with HOD presenting as Holmes tremor or ocular myoclonus.[5]

Descriptions of Holmes tremor associated with HOD are scarce.[6–11] Upper brainstem lesions are more frequent than lower brainstem ones. It is most likely that disruption of the disynaptic dentate-rubro-olivary tract degeneration is associated with tremor and disruption of the monosynaptic dentate-olivary tract is associated with HOD. The convergence of both components makes the combination of Holmes tremor and HOD after upper brainstem damage plausible and even likely.

HOD is considered unique because the degenerating olive initially becomes hypertrophic rather than atrophic.[12] Over time, the olive undergoes atrophy. These changes can be followed by MRI, and characteristic phases have been identified[13] Even though the imaging characteristics of HOD resolve, the clinical hallmarks such as palatal tremor persist.[14]

The patients we describe here had bilateral HOD after two different vascular lesions, ischemia and hemorrhage, located at the decussation of the superior cerebellar peduncles, thus impairing both central tegmental tracts and interrupting bilaterally the dentate-rubral-olivary pathway. Interestingly, both developed bilateral Holmes tremor but not palatal tremor. To our knowledge the association of lesions in the commissure of Wernekinck with bilateral Holmes tremor and bilateral HOD has not been reported.[15] We can infer that both monosynaptic and disynaptic components of the dentate-rubro-olivary pathway were interrupted. Further clinical and imaging studies are needed to better understand the role of lesions in these pathways in the pathogenesis of Holmes tremor associated with HOD.

References

1. Guillain G, Mollaret P. Deux cas de myoclonies synchrones et rhythmes vélopharyngo-laringo-oculo-diaphragmatiques. *Rev Neurol* 1931;2:545–566.

2. Trelles JO. L'hypertrophie des olives bulbaires. Thèse de médicine, Paris, 1935.

3. Trelles JO. Les myoclonies vélo-palatines: considération anatomiques et physiologiques. *Rev Neurol* 1968;119:165–171.

4. Jellinger K. Hypertrophy of the inferior olives: report on 29 cases. *J Neurol* 1973;205:153–174. doi: 10.1007/BF00316018.

5. Deuschl G, Bain P, Brin M. Consensus statement of the movement disorder society on tremor. Ad hoc scientific committee. *Mov Disord* 1998; 13(Suppl. 3):2–23. doi: 10.1002/mds.870131303.

6. Yang YW, Chang FC, Tsai CH, et al. Clinical and magnetic resonance imaging manifestations of Holmes tremor. *Acta Neurol Taiwan* 2005;14:9–15.

7. Shepherd G, Tauboll E, Jacob Bakke S, Nyberg-Hansen R. Midbrain tremor and hypertrophic olivary degeneration after pontine hemorrhage. *Mov Disord* 1997;12:432–437. doi: 10.1002/mds.870120327.

8. Kipfer S, Frigeriro S. Post-ischemic stroke Holmes' tremor of the upper limb. *Mov Disord* 2013;28:1347. doi: 10.1002/mds.25621.

9. Kim MK, Cho BP, Park SH, Yoon DY. Holmes' tremor associated with bilateral hypertrophic olivary degeneration following brainstem hemorrhage: a case report. *J Cerebrovasc Endovasc Neurosurg* 2014;16:299–302. doi: 10.7461/jcen. 2014.16.3.299.

10. Rieder CR, Rebouças RG, Ferreira MP. Holmes tremor in association with bilateral hypertrophic olivary degeneration and palatal tremor chronological considerations, case report. *Arq Neuropsiquiatr* 2003;61:473–477. doi: 10.1590/S0004-282X2003000300028.

11. Samie MR, Selhorst JB, Koller WC. Post-traumatic midbrain tremors. *Neurology* 1990;40:62–66. doi: 10.1212/WNL.40.1.62.

12. Goto N, Kanenko M. Olivary enlargement: chronological and morphometric analyses. *Acta Neuropathol* 1981;54:275–282. doi: 10.1007/BF00697000.

13. Goyal M, Versnick E, Tuite P, et al. Hypertrophic olivary degeneration: meta-analysis of the temporal evolution of MRI findings. *Am J Neuroradiol* 2000; 21:1073–1037. doi: 10.1093/brain/awf126.

14. Nishie M, Yoshida Y, Hirata Y, Matsunaga M. Generation of symptomatic palatal tremor is not correlated with inferior olivary hypertrophy. *Brain* 2002;125:1348–1357.

15. Liu H, Qiao L, He Z. Wernekink commissure syndrome: a rare midbrain syndrome. *Neurol Sci* 2012;33:1419–1421. doi: 10.1007/s10072-012-0966-4.