Duazary / Vol. 20, No. 2 – 2023 / 139 - 144
DOI: https://doi.org/10.21676/2389783X.5376

Presentation of clinical cases

Post-traumatic hypertrophic olivary degeneration associated with Holmes tremor: Clinical-imaging correlation

Degeneración olivar hipertrófica postraumática asociada a temblor de Holmes: correlación clínico- imagenológica

Edinson Montero-Cruz [1], Alejandra Mendoza-Ospina [2], Jorge Andrés Aldana-Bocanegra [3], Juan Manuel Montaño-Lozada [4], Edgard Eliud Castillo-Támara [5]

1. Universidad del Sinú. Cartagena, Colombia. Correo: edisonmontero429@gmail.com - http://orcid.org/0000-0003-4063-7981
2. Universidad Central del Valle del Cauca. Tuluá, Colombia. Correo: malmeos@hotmail.com - http://orcid.org/0000-0001-9089-6872
3. Universidad Pontificia Javeriana. Cali, Colombia. Correo: jaldana01@hotmail.com - http://orcid.org/0000-0002-7170-8140
4. Universidad del Sinú. Cartagena, Colombia. Correo: juanmanuelmontano6@gmail.com - http://orcid.org/0000-0002-9747-2498
5. Universidad Sinú. Cartagena, Colombia. Correo edgardeliud@gmail.com - http://orcid.org/0000-0001-8084-8586

How to cite this article: Montero-Cruz E, Mendoza-Ospina MA, Aldana-Bocanegra JA, Montaño-Lozada JM, Castillo-Támara EE. Degeneración olivar hipertrófica postraumática asociada a temblor de Holmes: correlación clínico- imagenológica. Duazary. 2023; 20 (2): 139-144. https://doi.org/10.21676/2389783X.5376

Received on March 20, 2023
Accepted on June 28, 2023
Posted online en June 30, 2023

ABSTRACT

Hypertrophic olivary degeneration is a disease secondary to damage to the neuronal circuit of the Guillain Mollaret Triangle, generating symptoms as varied as Holmes tremor. This article describes the case of a 52-year-old man with a history of head trauma in 2016, without mediate sequelae, who progressively presented tremors associated five years later with headache requiring emergency assistance, where studies were carried out, and pharmacological therapy was instituted. Finally, it is concluded that post-traumatic lesions in the Guillain Mollaret Triangle can generate movement disorders secondary to hypertrophic olivary degeneration as sequelae, an entity that is rarely diagnosed.

Keywords: Hypertrophic olivary degeneration; Midbrain hemorrhage; Inferior olivary nucleus; Holmes tremor; Head trauma; Guillain mollaret triangle.

RESUMEN

La degeneración olivar hipertrófica, es una enfermedad secundaria al daño en el circuito neuronal del Triángulo de Guillain Mollaret lo que genera síntomas tan variados como el temblor de Holmes. El presente artículo describe el caso de un hombre de 52 años, con antecedente de trauma craneoencefálico en 2016, sin secuelas mediatas, quien de manera progresiva presentó temblor, y se asoció cinco años después a cefalea lo que requirió asistencia a urgencias, allí realizaron estudios e instauraron terapia farmacológica. Finalmente se concluye, que lesiones postraumáticas en el Triángulo de Guillain Mollaret, pueden generar como secuelas trastornos del movimiento secundarios a degeneración olivar hipertrófica, una entidad poco diagnosticada.

Palabras clave: degeneración olivar hipertrófica; hemorragia mesencefálica; núcleo olivar inferior; temblor de Holmes; trauma craneoencefálico; triangulo de Guillain Mollaret.

INTRODUCTION

Hypertrophic olivary degeneration (HOD) is a rare disease of unknown incidence, resulting from damage to the neuronal circuit that relates ipsilaterally to the red nucleus and inferior olivary nucleus with the contralateral dentate nucleus, comprising the Guillain Mollaret Triangle (TMG). 1,2 See (Figure 1. The lesion causes synaptic degeneration of the inferior olivary nucleus, which loses its afferent inhibition of the circuit, becoming hypertrophic due to the resulting neuronal hyperactivity. Its most frequent causes correspond to unilateral or bilateral noxa in the brainstem or cerebellum, such as hemorrhage, ischemia, neoplasia, or trauma, which can be identified in the Brain Magnetic Resonance (BMR). HOD implies great variability of clinical presentations, from asymptomatic pictures to palatal tremor, ocular myoclonus, dystonia, dentato-rubral, or Holmes tremor (TH)[3–9].

This work aimed to describe the clinical and imaging manifestations of a man with movement disorder associated with HOD.

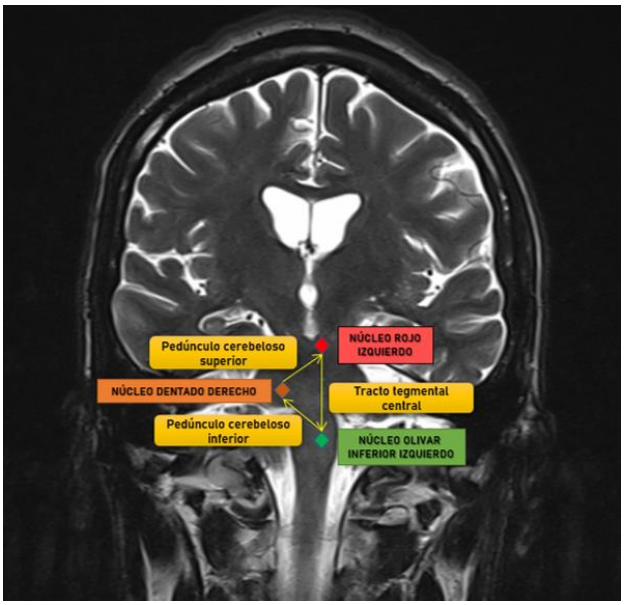

Figure 1. Schematic representation of the TGM with its nuclei and connection pathways in CMR in a Coronal cut in T2, taken in the Case Patient.

CLINICAL CASE

A 52-year-old male from Cali-Valle del Cauca-Colombia, with no significant clinical history until 2016, who, under a state of intoxication, fell from the stairs at an undetermined height, with subsequent severe head trauma (TCE) and injury diffuse axonal pathology, required management in an intensive care unit, prolonged orotracheal intubation and tracheostomy, without the need for neurosurgical management. He gradually recovered one month after the event without presenting apparent mediate sequelae.

After six months of the TBI, he refers to the progressive appearance of a distal to proximal tremor at rest with a frequency of 4 to 6 Hz, low amplitude, symmetrical, predominantly left in the upper limbs, gradually worsening with the anti-gravity posture and intention. No neurological medical approach was reported until April 2021, when he consulted the emergency department for a clinical picture of two days of evolution consisting of a left hemicranial headache without irradiation, progressive increase in intensity, without Valsalva effect, associated with decreased visual acuity: dysarthria, and worsening tremor pattern.

The anamnesis describes arterial hypertension managed with amlodipine 5 mg orally (PO) every 24 hours and losartan 50 mg PO every 12 hours; ex-smoker since 2016 and occasional consumption of alcohol until drunkenness.

Myotendinous reflexes in the lower limbs and standard in the upper limbs, he presented abnormal movements: tremor in the upper limbs, predominantly on the left, at rest with increased changes in posture and intention to move, taxis was not evaluable, without rigidity or bradykinesia, slightly ataxic gait—no alteration in other systems.

Simple brain tomography revealed incidental findings of a diffuse increase in density in the left suprasellar and parasellar region without hemorrhage, ischemia, or hydrocephalus. Serum studies: complete blood count, renal function, ionogram, blood glucose, coagulation times, prolactin, morning serum cortisol, morning ACTH, TSH, LH, FSH, and typical arterial blood gases, with GH (14.2 ng/ mL) increased, and somatomedin C (887 ng/ mL) increased. Simple cranial magnetic resonance imaging revealed a 14x10 mm macropituitary adenoma, foci of microhemorrhages in the frontal and left parietal region at a subcortical level, probably sequelae of diffuse axonal injury and

old hemorrhage in the left midbrain at the level of the tectum and tegmentum on T2 weighting in both coronal and axial section (Figure 2). In addition to hyperintensity in the left inferior olivary nucleus and hypointensity ipsilateral periaqueductal (Figure 3).

Neurosurgery performed surgical management by transsphenoidal route without complications. On the other hand, after the evolution since 2016, he presented a progression of abnormal movements that limited his daily activities, and neuroimaging lesions were evidenced in the TGM. For that reason, the TH neurology service considered it secondary to post-traumatic HOD, not fulfilling parkinsonism criteria; pharmacological treatment with biperiden 2 mg PO every 24 hours was started, and a therapeutic trial with levodopa/ carbidopa 25 mg/250 mg po titrated, half a tablet four times a day, obtaining progressive clinical improvement with subsequent post-surgical outpatient controls for neurosurgery and neurology.

Statement on ethical aspects

In the present case, the patient signed an informed consent to authorize the publication, guaranteeing confidentiality, privacy, and anonymity.

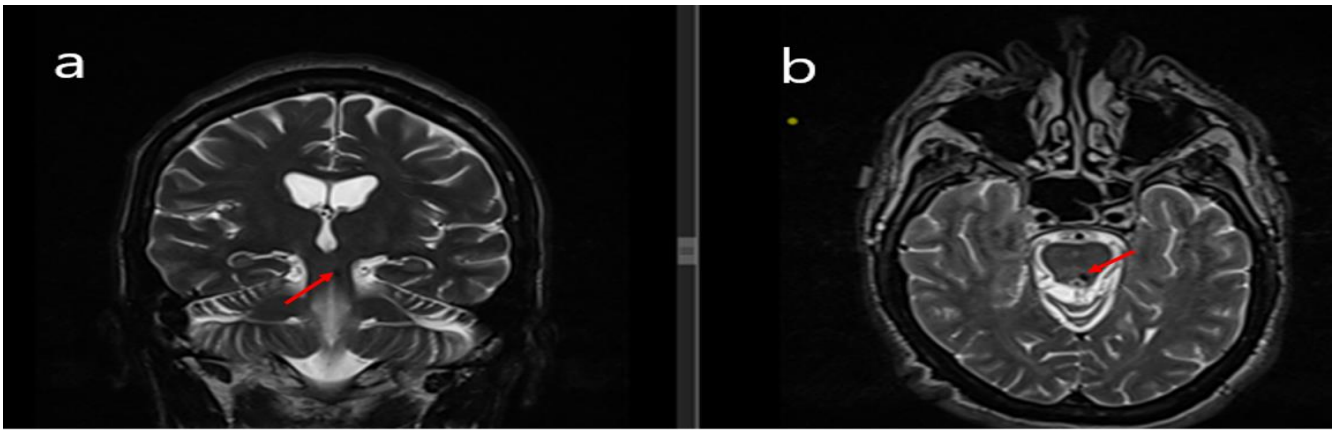

Figure 2. CMR on T2 Coronal (a) and axial (b) section showing mesencephalic hypointense at the level of the tectum and left tegmentum (Red Arrow).

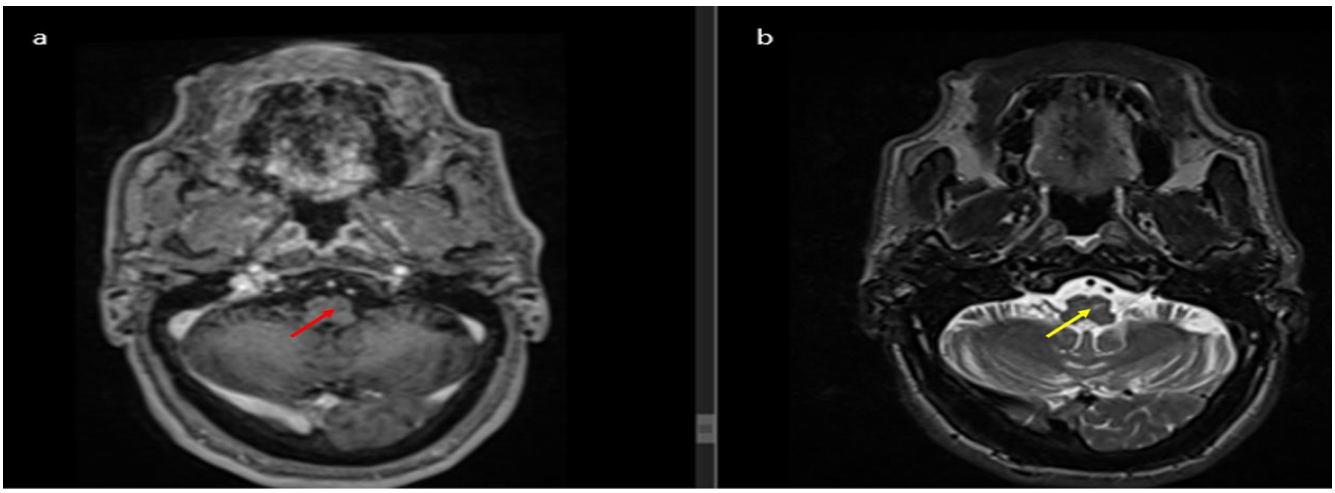

Figure 3. CMR at the level of the medulla oblongata, axial section. a) T1 sequence with mild hypointensity in the left inferior olive (Red Arrow), b) T2 sequence with hyperintensity in the left inferior olive (Yellow Arrow).

DISCUSSION

HOD, as a clinical condition of low prevalence, is more frequent in male adults; among the leading causes include cerebrovascular attack (CVA), TCE, toxins and neoplasms, entities that generate partial lesions between the connections of the components of the TGM (excluding lesions of the olivodentate tract as these lead to cerebellar atrophy), causing transsynaptic degeneration and interruption of

afferent input to the inferior olivary nucleus, generating loss of inhibition within the circuit and subsequently prolonged nuclear hypertrophy, which in the long term culminating in nuclear atrophy, all of the above can be correlated with the post-traumatic etiology of HOD described in the present case and is related to the findings of reviews and case series established in the literature, who together describe clinical imaging correlation as diagnostic criteria [10–14], as will be described below.

Regarding the characteristic neuroimaging signs of HOD, up to now, no definitive Gold Standard diagnostic consensus has been described [13,15], so most authors propose CMR as part of the arsenal to define the radiological criteria, which are usually defined as a pattern of unilateral and ipsilateral imaging damage to the causative noxa located predominantly in the brainstem on T2 sequences, specifically in the course of the central tegmental tract of the TGM, with increased inferior olivary hyperintensity on T2 or FLAIR, as a result of hypertrophy nuclear that is usually revealed 4 to 6 months after the establishment of the etiological agent [8,12,14,16–18]. Several of these aspects previously mentioned in the literature, are coupled to the case in the description since the cranial magnetic resonance of the patient showed disruption of the TGM, given by the association of a hypointense midbrain lesion on T2 of the hemorrhagic type ipsilaterally distanced from the hyperintense inferior olivary nucleus affected by HOD, in the same imaging sequence.

Although the clinical presentation of HOD corresponds to a complex movement disorder with various underlying causes and presentations, clinical suspicion criteria can help identify this pathology, such as palatal tremor, ocular myoclonus with nystagmus, or as appropriate. In this case, debut with LT [4,19,20] makes it necessary to rule out structural damage, identify the etiology and offer the best treatment to affected patients. Even though reports of HT associated with HOD due to damage to the dento-rubro-olivar pathway are scarce [5,21], the possibility that the diagnosis of this condition is being overlooked is not ruled out, as commented in a recent review of 2023 [22]on the clinical syndromes associated with injuries in the TGM.

A fundamental contribution of this clinical case to the literature is the semiological description of a rarely diagnosed entity, such as LT. The patient in question met the definition criteria for this movement disorder, established in the latest consensus on the Classification of tremors of 2018[23] (1. Onset at rest, postural and intentional, 2. Proximal and distal rhythmic muscle contraction, 3. Low frequency (<5 Hz)). From the IPMDS (International Parkinson and Movement Disorder Society). Pyrgelis *et al*[24] proposed that the diagnosis should be based mainly on a careful clinical examination, together with neurophysiological and imaging studies, proposing cranial magnetic resonance imaging as the test of choice for initial evaluation. He also describes how this tremor is frequently associated with additional neurological signs, which in the corresponding case were dysarthria and alterations in gait and balance.

Regarding the therapeutic approach of HT associated with HOD, the main objective is to improve the quality of life of patients; since there is currently no cure for this disorder, the options to improve symptoms usually include levetiracetam, levodopa/ carbidopa and other non-pharmacological measures such as deep brain stimulation [24], interventions which have shown benefits in treated patients. In the present case, there was a progressive favorable response to an alternative readily available in our environment, such as levodopa/carbidopa, controlling a large part of the tremor and the patient's functionality. Finally, the prognosis of HOD depends on the causative agent, so some cases reveal marked progressive disability, such as those related to stroke [22], while others, such as the present case, remain stable over time with symptomatic treatment.

CONCLUSIONS

From functional neuroanatomy, it is vital to consider that post-traumatic lesions in the Guillain Mollaret Triangle can generate movement disorders secondary to HOD as sequelae, a rarely diagnosed entity, the knowledge of which could avoid erroneous diagnoses and prevent unnecessary interventions in affected patients.

DECLARATION ON CONFLICTS OF INTEREST

The authors declare that they have no interest conflict.

AUTHORS' CONTRIBUTION

First author: Writing the manuscript and structuring the case.

Second author: Reviewing medical board of the case, and review, analysis.
Third author: Reviewing medical case board, and review, analysis.
Fourth author: Reviewing case medical board, manuscript writing, and review analysis.
Fifth author: Reviewing the analysis, review, and final approval.

REFERENCES

1. Font R, Ramos J, Torales O, Moreno S, Bondía J, Martí M. Degeneración olivar hipertrófica: formas de presentación en resonancia magnética. Seram. 2021; 1(1): 1-21.

2. Murdoch S, Shah P, Jampana R. The Guillain–Mollaret triangle in action. Pract Neurol. 2016;16(3):243-246. https://doi.org/10.1136/practneurol-2015-001142

3. Behzadi F, Fiester PJ, Rao D. Bilateral hypertrophic olivary degeneration following brainstem insult: A retrospective review and examination of causative pathology. Neurosci Insights. 2021; 16:7. https://doi.org/10.1177/26331055211007445

4. Wang H, Wang Y, Wang R, Li Y, Wang P, Li J, et al. Hypertrophic olivary degeneration: A comprehensive review focusing on etiology. Brain Res. 2019; 1718:53-63. https://doi.org/10.1016/j.brainres.2019.04.024

5. Dogan SN. Hypertrophic Olivary Degeneration and Holmes Tremor: Case Report and Review of the Literature. World Neurosurg. 2020; 137:286-290. https://doi.org/10.1016/j.wneu.2020.02.068

6. Demaerel R, Demaerel P, van Loon J, Decramer T. Limb ataxia after double hit in the Guillain–Mollaret triangle. Acta Neurol Belg. 2020;120(3):771-773. https://doi.org/10.1007/s13760-020-01313-6

7. Fleet JL, Calver R, Perera GC, Deng Z. Palato-pharyngo-laryngeal myoclonus with recurrent retrograde feeding tube migration after cerebellar hemorrhagic stroke: A case report and review of hypertrophic olivary degeneration. BMC Neurol. 2020;20(1):1-5. https://doi.org/10.1186/s12883-020-01800-6

8. Wang YL, Gao Y, He PP, Yin J, Dong R, Li X, et al. A meta-analysis of case studies and clinical characteristics of hypertrophic olivary degeneration secondary to brainstem infarction. J Integr Neurosci. 2020;19(3):507-511. https://doi.org/10.31083/j.jin.2020.03.1238

9. Lycett M, Cui CK, Dragicevich D, Harris R, Ng K. Hypertrophic olivary degeneration associated with bilateral vocal cord adductor dystonia. BMC Neurol. 2023; 23(1): 1-4. https://doi.org/10.1186/s12883-023-03123-8

10. Bulleid L, Hughes T, Leach P. Mollaret's triangle: An important neuroanatomical territory for all clinicians. Surg Neurol Int. 2021;12(94): 1-3. https://doi.org/10.25259/SNI_625_2020

11. Zhou J, Liu Y, Ali Shah SZ. Hypertrophic olivary degeneration following cerebral trauma managed with rehabilitation — A case report. J Pak Med Assoc. 2021;71(4):1252-1254. https://doi.org/10.47391/JPMA.1124

12. Schaller MA, Steidl E, Shrestha M, Deichmann R, Steinmetz H, Seiler A, et al. Multicenter prospective analysis of hypertrophic olivary degeneration following infratentorial stroke (hod-is): evaluation of disease epidemiology, clinical presentation, and mr-imaging aspects. Front Neurol. 2021; 12:1124. https://doi.org/10.3389/fneur.2021.675123

13. Steidl E, Rauch M, Hattingen E, Breuer S, Rudiger J, Grapengeter M, et al. Qualitative and quantitative detectability of hypertrophic olivary degeneration in T2, FLAIR, PD, and DTI: A prospective MRI study. Front Neurol. 2022;13: 950191. https://doi.org/10.3389/fneur.2022.950191

14. Onen MR, Moore K, Cikla U, Ucer M, Schmidt B, Field A, et al. Hypertrophic olivary degeneration: neurosurgical perspective and literature review. World Neurosurg. 2018;112: e763-e771. https://doi.org/10.1016/j.wneu.2018.01.150

15. Elnekiedy A, Naguib N, Hamed W, Mekky J, Mamdouh Hassan HH. MRI and neurological

presentation of hypertrophic olivary degeneration. Egypt J Radiol Nucl M. 2016;47(3):1019-1029. https://doi.org/10.1016/j.ejrnm.2016.04.019

16. Zheng B, Wang J, Huang XQ, Chen Z, Gu GF, Luo XJ. Bilateral Hypertrophic Olivary Degeneration after Pontine Hemorrhage: A Case Report. World J Clin Cases. 2022;10(1):289-295. https://doi.org/10.12998/wjcc.v10.i1.289

17. De Lima Raeder MT, Reis EP, Campos BM, Zamilute IAG, Junior MCF, Reis F. Transaxonal degenerations of cerebellar connections: the value of anatomical knowledge. Arq Neuropsiquiatr. 2020;78(5):301-306. https://doi.org/10.1590/0004-282x20200021

18. Radu RA, Ionita LM, Terecoasa EO, Marinescu AN, Tiu C. Hypertrophic olivary degeneration after brainstem haemorrhage – A case report. Rom J Neurol. 2019;18(1):45-50. https://doi.org/10.37897/RJN.2019.1.8

19. Kakei S, Manto M, Tanaka H, Mitoma H. Pathophysiology of cerebellar tremor: The forward model-related tremor and the inferior olive oscillation-related tremor. Front Neurol. 2021; 12:954. https://doi.org/10.3389/fneur.2021.694653

20. Özdemir M, Turan A, Pelin R, Dilli A. Hypertrophic olivary degeneration: A case report. Indian J Radiol Imaging. 2019; 29:435-437. https://doi.org/10.4103/ijri.IJRI_412_18

21. Cosentino C, Velez M, Nuñez Y, Palomino H, Quispe D, Flores M, et al. Bilateral hypertrophic olivary degeneration and holmes tremor without palatal tremor: an unusual association. Tremor Other Hyperkinet Mov. 2016; 6:400. https://doi.org/10.5334/tohm.302

22. Ogut E, Armagan K, Tufekci D. The Guillain-Mollaret triangle: A key player in motor coordination and control with implications for neurological disorders. Neurosurg Rev. 2023; 46:181. https://doi.org/10.1007/s10143-023-02086-1

23. Bhatia KP, Bain P, Bajaj N, Elble RJ, Hallet M, Louis ED, et al. Consensus Statement on the classification of tremors. from the task force on tremor of the International Parkinson and movement disorder society. MDS. 2018;33(1):75-87. https://doi.org/10.1002/mds.27121

24. Pyrgelis ES, Agapiou E, Angelopoulou E. Holmes tremor: an updated review. Neurol Sci. 2022;43(12):6731-6740. https://doi.org/10.1007/s10072-022-06352-w