Neurological Sciences
https://doi.org/10.1007/s10072-020-04627-8

LETTER TO THE EDITOR

Levodopa-responsive Holmes head titubation caused by midbrain cavernoma hemorrhage

Sofia Maldonado Slootjes[1] · Thierry Lejeune[2] · Thierry Duprez[3] · Tévi Morel Lawson[4] · André Peeters[1]

Received: 17 June 2020 / Accepted: 21 July 2020
© Fondazione Società Italiana di Neurologia 2020

Dear Editor,

Herein we report a patient with a rare delayed-onset Holmes head titubation after midbrain cavernoma hemorrhage that dramatically responded to levodopa treatment. To our knowledge, the levodopa responsiveness of a Holmes head titubation has not yet been reported with accompanying video footage.

A 40-year-old woman known for severe cerebral cavernomatosis complicated by persistent post-hemorrhage left facial palsy presented with sudden-onset cerebellar ataxia and left oculomotor nerve III palsy. Brain magnetic resonance imaging (MRI) demonstrated acute bleeding within a cavernoma of the left cerebral peduncle (Fig. 1) matching clinical symptoms. Three weeks later, an invalidating Holmes head titubation appeared progressively. It consisted of a large-amplitude, low-frequency oscillation predominantly along a "yes-yes" axis with a superimposed "no-no" component (see Video). It was attenuated by lateral rotation of the head and disappeared during sleep. It was exacerbated when standing upright, which caused major instability and falls. The movement disorder resulted in a dramatic loss of autonomy in daily life activities. The patient was started on immediate-release levodopa 50 mg with benserazide 12.5 mg three times a day. The dose was rapidly increased to levodopa 100 mg plus benserazide 25 mg three times a day when no adverse events were reported by the patient. The next day, the Holmes titubation had already improved, allowing the patient to resume her rehabilitation, which resulted in a marked increase in quality of life. At 3-month follow-up, no residual tremor was observed under levodopa treatment. Progressive tapering of levodopa was successful, with no reappearance of the head titubation. Follow-up MRI showed regression of the cavernoma bleeding as expected. No hypertrophic olivary degeneration was noted at the time.

Holmes tremor (or titubation when affecting the head or trunk) consists of an arrhythmic, low-frequency (< 5 Hz) oscillation with rest, posture, and intention components [1, 2]. Because of these characteristics, this movement disorder can be severely disabling. It usually affects one upper limb, but may be observed bilaterally, on the lower limbs, head, or trunk. It is due to the disruption of both dopaminergic nigrostriatal and cerebellothalamic pathways, and thus may arise after lesions within the brainstem, the cerebellum, or the thalamus [2]. As it generally occurs several weeks or months after stroke, it is thought to arise from aberrant neuroplasticity [3]. Symptomatic treatment is often challenging. Many medications, including levodopa, have been used with varying degrees of response, which might be explained by a heterogeneous involvement of the two affected pathways among different patients [4, 5]. Other methods for symptom management have been proposed, including botulinum toxin injections, stereotaxic thalamotomy and deep brain stimulation. The latter technique most commonly targets the ventral intermediate thalamic nucleus [5]. Interestingly, the head titubation of our patient had completely subsided at 3-month follow-up, which might be explained by hemorrhage regression and further neuroplastic changes with correcting effects. Hence, invasive techniques should only be considered for patients suffering from a persistent Holmes tremor with unsatisfactory response to pharmacological treatment.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s10072-020-04627-8) contains supplementary material, which is available to authorized users.

✉ André Peeters
andre.peeters@uclouvain.be

[1] Department of Neurology, Cliniques universitaires Saint-Luc, Avenue Hippocrate 10, 1200 Brussels, Belgium

[2] Department of Physical medicine and Rehabilitation, Cliniques universitaires Saint-Luc, Avenue Hippocrate 10, 1200 Brussels, Belgium

[3] Department of Radiology, Cliniques universitaires Saint-Luc, Avenue Hippocrate 10, 1200 Brussels, Belgium

[4] Department of Neurosurgery, Cliniques universitaires Saint-Luc, Avenue Hippocrate 10, 1200 Brussels, Belgium

Published online: 27 July 2020

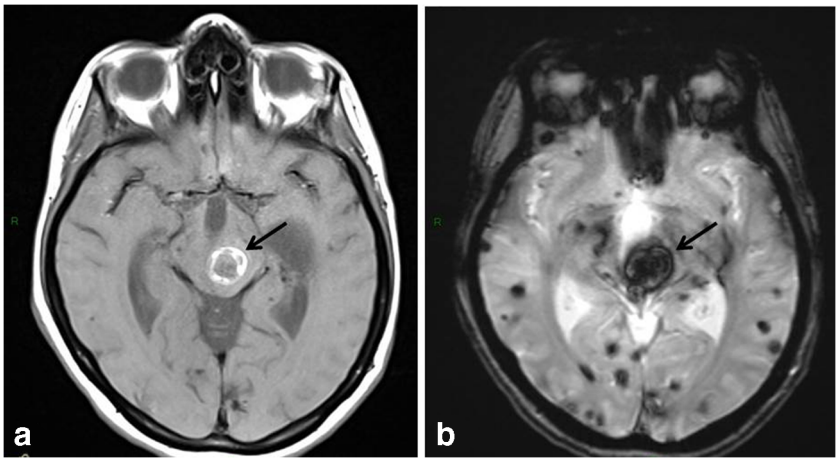

Fig. 1 **a** Unenhanced transverse T1-weighted view showing acute hematoma within the left part of the tegmentum (arrow) disclosing central hypointensity due to deoxyhemoglobin and hyperintense peripheral rim due to methemoglobin. **b** Axial transverse T2*-weighted view revealing numerous additional cavernomas

In conclusion, our video-illustrated case report highlights the debilitating aspect of Holmes tremor and supports the efficacy of levodopa for symptom management. Clinicians should be able to recognize this unusual movement disorder as proper treatment may dramatically improve quality of life.

Acknowledgments The authors wish to thank Ana Teresa Mota and Marta Miguel Mota for their technical support.

Authors' contribution All authors contributed to the patient's care. Video footage was collected by Sofia Maldonado Slootjes. The first draft of the manuscript was written by Sofia Maldonado Slootjes and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval Not applicable.

Informed consent Informed consent for publication of their clinical details and clinical images was obtained from the patient.

References

1. Bhatia KP, Bain P, Bajaj N, Elble RJ, Hallett M, Louis ED, Raethjen J, Stamelou M, Testa CM, Deuschl G (2018) Consensus statement on the classification of tremors. From the task force on tremor of the International Parkinson and Movement Disorder Society. Mov Disord 33:75–87. https://doi.org/10.1002/mds.27121
2. Seidel S, Kasprian G, Leutmezer F, Prayer D, Auff E (2009) Disruption of nigrostriatal and cerebellothalamic pathways in dopamine responsive Holmes' tremor. J Neurol Neurosurg Psychiatry 80: 921–923. https://doi.org/10.1136/jnnp.2008.146324
3. Ueno T, Nishijima H, Arai A, Tomiyama M (2016) Acute hemorrhagic cerebellar infarction presenting with isolated head titubation. J Neurol Sci 372:456–458. https://doi.org/10.1016/j.jns.2016.10.047
4. Akkus DE, Diramali AB (2006) Postischemic delayed Holmes' tremor responding to low-dose cabergoline. Mov Disord 21:733–734. https://doi.org/10.1002/mds.20862
5. Raina GB, Cersosimo MG, Folgar SS, Giugni JC, Calandra C, Paviolo JP, Tkachuk VA, Zuñiga Ramirez C, Tschopp AL, Calvo DS, Pellene LA, Uribe Roca MC, Velez M, Giannaula RJ, Fernandez Pardal MM, Micheli FE (2016) Holmes tremor. Clinical description, lesion localization, and treatment in a series of 29 cases. Neurology 86(10):931–938. https://doi.org/10.1212/WNL.0000000000002440

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.