Journal of Otology 18 (2023) 246–249

Contents lists available at ScienceDirect

Journal of Otology

journal homepage: www.journals.elsevier.com/journal-of-otology/

Acute isolated vertigo with vertical up-beating nystagmus: A rare case of nucleus intercalatus of Staderini ischemia

Francesco Comacchio [a, *], Giacomo Talenti [b], Renzo Manara [b], Chiara Briani [c]

[a] Otolaryngology Unit, University Hospital Sant'Antonio Padova, Via Facciolati 71, 35127, Padova, Italy
[b] Neuroradiology Unit, University Hospital Padova, Via Giustiniani 2, 35128, Padova, Italy
[c] Neurology Unit, University Hospital Padova, Via Giustiniani 2, 35128, Padova, Italy

ARTICLE INFO

Article history:
Received 14 July 2023
Received in revised form
28 August 2023
Accepted 7 September 2023

Handling Editor: Ms. Ivy Gao

Keywords:
Vertigo
Up-beating nystagmus
Intercalatus nucleus Staderini
Vertebral artery occlusion
Brainstem ischemia

ABSTRACT

The role of intercalatus nucleus of Staderini (INS), the most caudal of the perihypoglossal nuclei, is much debated. Last research seems to suggest that this nucleus plays a role as a vertical eyes movements integrator. The few clinical reports present in the literature that describe isolated lesions of the INS have described patients presenting in acute with up-beating vertical spontaneous nystagmus. Isolated acute lesion of INS is, in fact, much rare, and, without other neurological signs, is exceptional. We present a case of acute isolated vertigo with no other neurological signs or symptoms, due to INS ischemia provoked by vertebral artery stenosis. The patient presented with spontaneous vertical up-beating nystagmus that showed at videonystagmographic recording, a clear exponential decay of angular slow-phase velocity, that is considered a typical sign of neural integrator impairment. This case seems to represent a further confirm that INS is part, as a vertical-to-position neural integrator, of the neural circuit controlling the vertical eyes movements.

1. Introduction

Primary position up-beating nystagmus (PPUN) is a relatively rare clinical sign and a type of central nystagmus frequently associated with lesions ranging from the thalamus rostrally to the lower medulla, caudally (Kim et al., 2006). It is usually transient and less common than downbeat nystagmus. Possible causes may include spinocerebellar degeneration, Wernicke's encephalopathy, multiple sclerosis, brainstem infarction, brainstem tumor, trauma, and meningitis. PPUN has also been described during organophosphate poisoning, amitriptyline, and tobacco intoxication (Osborne and Vivian, 2004; Sibony et al., 1987). In all these cases, however, PPUN is not the only clinical sign of the pathology; other neurological symptoms are often associated. The pathophysiological explanation may be that the lesion debilitates inhibition of the flocculovestibular inhibitory pathway on the superior vestibular nuclei, which causes hypoactivity of the superior recti muscles. That leads to the slow drifting of the globes downward and the corrective saccadic movement upward (Janssen et al., 1998). Different varieties of up-beating nystagmus have been described according to the velocity of the slow phase (SPV) of the nystagmus-namely, linear or exponentially decaying, and these types of PPUN seem to reflect different pathophysiological mechanisms or different sites of lesion. A nystagmus with constant slow phase velocity is thought to be caused by an imbalance of vertical vestibulo-ocular reflex, while the presence of a slow phase decay seems to reflect an involvement of the vertical eye movement integrator. The interstitial nucleus of Cajal in the midbrain has been considered the main integrator of the vertical eye movements, as the nucleus prepositus hypoglossi represents the horizontal eye's movement integrator. PPUN as a unique clinical sign presenting with an acute isolated vertigo is very rare. Previous reports with isolated PPUN and no other neurological signs with MRI detection of small lesions in restricted areas of the dorsal medulla have refocused attention on the intercalatus nucleus of Staderini (INS) as another site of possible vertical eye movements integrator (Janssen et al., 1998; Hirose et al., 1998). We here described a rare case of a very restricted lesion of the dorsal medulla attributable to the INS in a patient presenting an acute isolated vertigo and a video-nystagmographic recording of a PPUN with a clear SPV decay.

* Corresponding author.
E-mail address: francesco.comacchio@aopd.veneto.it (F. Comacchio).
Peer review under responsibility of PLA General Hospital Department of Otolaryngology Head and Neck Surgery.

https://doi.org/10.1016/j.joto.2023.09.001

2. Case report

A 66-year-old man woke up in the middle of the night with severe dizziness, postural instability, and nausea with vomiting. No headache was reported. His past medical history was unremarkable, except for benign prostatic hyperplasia. His vital signs were normal except for high blood pressure (180/90 mmHg). Brain Computed Tomography (CT) showed no bleeding or hyperacute signs of ischemia. The otoneurological examination revealed spontaneous, irregular vertical up-beating nystagmus in all positions of gaze, poorly inhibited by fixation (videos 1-3). The neurologist confirmed the clinical-semeiological pattern. No ophtalmoplegia, diplopia, skew deviation, or cerebellar signs were present. The patient was admitted to the Neurology department for a suspected ischemic stroke and started on single antiplatelet agent IV for three days before switching to oral therapy. No cardiac symptoms were reported, and the ECG was unremarkable. 24 h of Holter ECG revealed no evidence of atrial fibrillation with numerous supraventricular ectopic beats, and brief runs of atrial tachycardia. His symptoms resolved completely within 24 h of admission, and he remained asymptomatic thereafter. Blood pressure gradually improved with oral agents. He then underwent contrast-enhanced encephalic MRI, intracranial ultrasonographic study, and vestibular reassessment a few days later. Brain MRI showed a small area with diffusion signal restriction on the dorsal medulla compatible with a recent ischemic lesion in the proximity of the INS and multiple chronic lacunar spots in the right cerebellar hemisphere and left basal ganglia. Intracranial MR arterial imaging revealed a hypoplastic left vertebral artery and severe focal stenosis at the pre-junctional area (Fig. 1). The left posterior communicating artery was also hypoplastic. The intracranial ultrasound study was normal. A vestibular videonystagmographic assessment 36 h later, revealed a slight improvement of the initial vertical, up-beating nystagmus that was non-exhaustible and poorly suppressed by fixation, increasing in upward and in supine position. A clear decay of SPV was recorded (Fig. 2). No abnormalities in optokinetic nystagmus, saccadic, or horizontal smooth pursuit movements were noted. An impairment of vertical smooth pursuit was observed, while vestibular caloric tests were also normal.

Supplementary video related to this article can be found at https://doi.org/10.1016/j.joto.2023.09.001

3. Discussion

The perihypoglossal nuclei (PHN) are located within the dorsal medulla and the flocculus. They are composed of the prepositus nucleus of the hypoglossus, the INS, and the nucleus of Roller. Experimental anatomical studies have shown that the perihypoglossal nuclei receive afferent connections from the cerebellum, from the cerebral cortex, and higher levels of the brain stem, and from the spinal cord. On the other hand, the same nuclei project to the cerebellum (Saito et al., 2010). It has long been known that the INS receives afferent projections, particularly from the medial and descending vestibular nuclei and from the prepositus nucleus of hypoglossus of both sides (Mergner et al., 1977).

Few cases of intercalated nucleus lesions characterized by the presence of up-beating nystagmus have been described in the literature. Munro et al. (1993) described a case of an infarct on the left side of the medulla, caudal and ventral to the vestibular nuclei, possibly involving the most caudal of the perihypoglossal nuclei, the INS. In their case, the patient presented with a PPUN with slow-phase decay. The lesion involved the central nuclei of the medulla oblongata, the medullary part of the fifth nerve nucleus, the inferior tip of the nucleus ambiguous, and the spinothalamic tract and the patient presented many other neurological symptoms. Hirose et al. (1998) reported another case of lateral medullary ischemia in a patient with sudden onset of vertigo, nausea, vomiting, and weakness of the right arm. The lesion was caudal to the vestibular nuclei and to the most rostral of the perihypoglossal nuclei, the INS. Also in their case, a PPUN with slow phase decay was recorded. The first case of an acute isolated PPUN with no other neurological symptoms or signs was reported by Janssen et al. (1998). A focal paramedian lesion in the caudal medulla was found on MRI, encompassing the INS but not the more central region. In this case, a linear PPUN was noted with disappearing in supine position, and the authors stated that their findings argue against the possible role of INS as neural integrator of vertical eye movements (Larner et al., 1998). A more large lesion with PPUN involving also the INS was described by Adamec et al. (2012). Finally, a PPUN was described by Choi et al. (2011) in a case of caudal medulla cavernoma and by Meling et al. (2020) after removal of a brainstem cavernoma with hemorrage. The authors hypothesized a lesion of the INS and Roller nucleus, but in this case, the pattern of the SPV of vertical

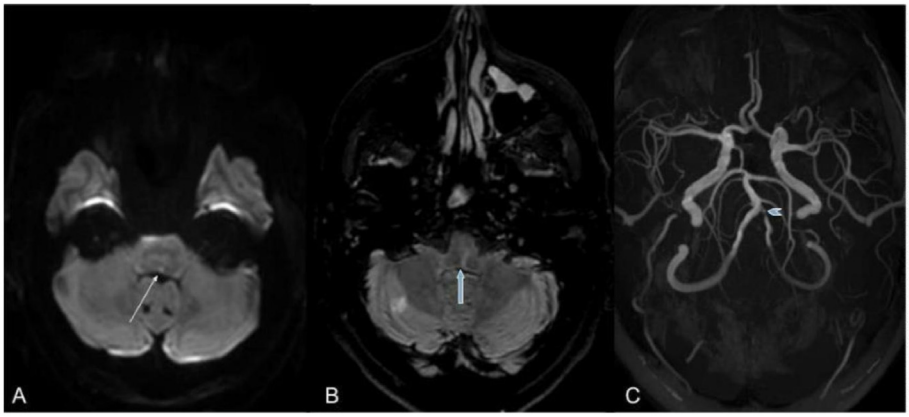

Fig. 1. A. Diffusion-Weighted Image (DWI) shows a small spot of restricted diffusion (thin arrow) in the dorsal medulla. B. Axial Flair image demonstrates a linear hyperintensity (thick arrow) in the same region, compatible as a location with the Staderini nucleus; a chronic ischemic lesion is also seen in the right cerebellar hemisphere. In C, a focal stenosis (arrowed) is noted in the distal V4 segment of the left vertebral artery at Time of Flight (ToF) MR Angiography.

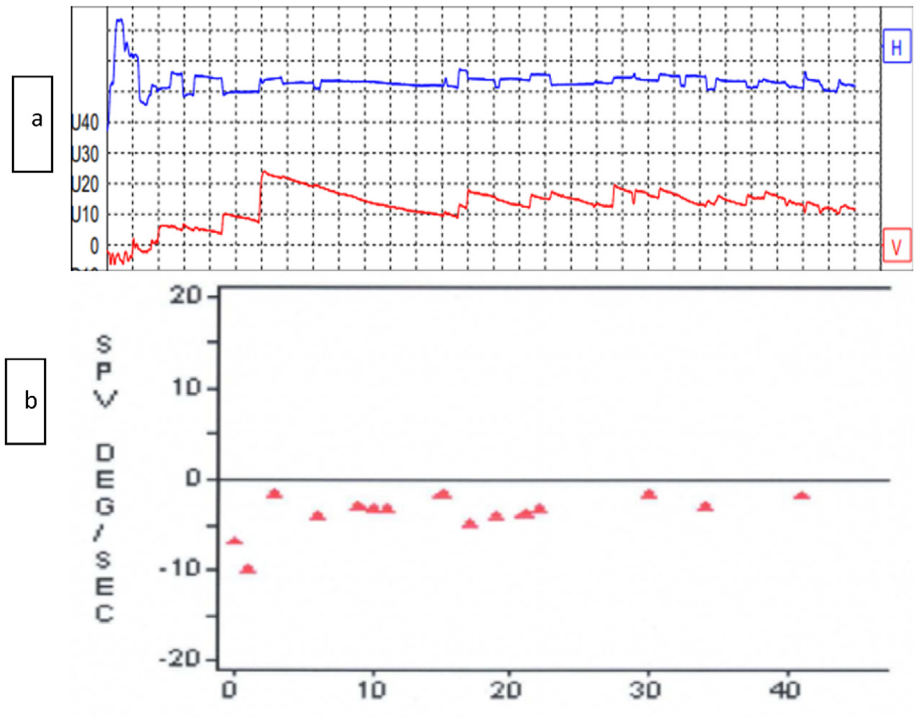

Fig. 2. Videonystagmographic recording of up-beating vertical nystagmus (a) with clear decay of angular slow-phase velocity, plotted in picture b.

nystagmus was not described. Our case is very similar to that described by Munro et al. (1993), but with a more restricted area of lesion corresponding to INS. The decay of SPV is clearly exponential and seems to confirm the role of INS as neural integrator. Our patient, with a clear ischemic lesion and such a precisely localized lesion at the level of the INS adds to the few cases already reported in the literature, going to reinforce the hypothesis that this nucleus may be part of the neural integrator of vertical gaze control center (Munro, 1999). Specialists dedicated to the evaluation and treatment of vertigo patient must therefore consider, in the case of a patient with only clinical findings of up-beating nystagmus, a lesion located in this anatomical area.

4. Conclusions

Our report of an acute isolated vertigo, presenting with spontaneous vertical up-beating nystagmus with exponential decay of angular SPV and a restricted lesion of INS, represents a clinical confirmation of the possible role of this nucleus as part of the neural integrator circuit controlling the eye's vertical movements.

Patient consent for publication

Informed patient consent was obtained.

Author's contributions

Francesco Comacchio was involved in the study design, analysis of the data, interpretation and writing the manuscript. Renzo Manara and Giacomo Talenti were involved in the study design, analysis of the data, and interpretation. Chiara Briani was involved in the study design, analysis of the data interpretation and reviewing the manuscript.

Declaration of competing interest

The authors declare that they have no conflict of interest. This study has no grant or funding.

Acknowledgment

This article has been written in memoriam, and with the valuable contribute of Francesco Berti, MD, resident in Neurology, recently passed away.

References

Adamec, I., Gabelic, T., Krbot, M., Ozretic, D., Milivojevic, I., Habek, M., 2012. Primary position upbeat nystagmus. J. Clin. Neurosci. 19 (1), 161–162. https://doi.org/10.1016/j.jocn.2011.05.028.

Choi, H., Kim, C.H., Lee, K.Y., Lee, Y.J., Koh, S.H., 2011. A probable cavernoma in the medulla oblongata presenting only as upbeat nystagmus. J. Clin. Neurosci. 18 (11), 1567–1569. https://doi.org/10.1016/j.jocn.2011.02.043.

Hirose, G., Ogasawara, T., Shirakawa, T., Kawada, J., Kataoka, S., Yoshioka, A., Halmagyi, G.M., 1998. Primary position upbeat nystagmus due to unilateral medial medullary infarction. Ann. Neurol. 43, 403–406. https://doi.org/10.1002/ana.410430323.

Janssen, J.C., Larner, A.J., Morris, H., Bronstein, A.M., Farmer, S.F., 1998. Upbeat nystagmus: clinicoanatomical correlation. J. Neurol. Neurosurg. Psychiatry 65, 380–381. https://doi.org/10.1136/jnnp.65.3.380.

Kim, J.S., Yoon, B., Choi, K.D., Oh, S.Y., Park, S.H., Kim, B.K., 2006. Upbeat nystagmus: clinicoanatomical correlations in 15 patients. J. Clin. Neurol. 2 (1), 58–65. https://doi.org/10.3988/jcn.2006.2.1.58. Epub 2006 mar 20.

Larner, A.J., Bronstein, A.M., Farmer, S.F., 1998. Role of the nucleus intercalatus in upbeat nystagmus. Ann. Neurol. 44 (5), 840. https://doi.org/10.1002/ana.410440523.

Meling, T.R., Nouri, A., May, A., Guinand, N., Vargas, M.I., Destrieux, C., 2020. Upbeat nystagmus after brain stem cavernoma resection: a rare case of nucleus intercalatus/nucleus of Roller injury. J. Neurol. 267, 2865–2870. https://doi.org/10.1007/s00415-020-09891-4.

Mergner, T., Pompeiano, O., Corvaja, N., 1977. Vestibular projections to the nucleus intercalatus of Staderini mapped by retrograde transport of horseradish peroxidase. Neurosci. Lett. 5 (6), 309–313. https://doi.org/10.1016/0304-3940(77)90105-7.

Munro, N.A., 1999. The role of the nucleus intercalatus in vertical gaze holding. J. Neurol. Neurosurg. Psychiatry 66 (4), 552–553. https://doi.org/10.1136/jnnp.66.4.552.

Munro, N.A., Gaymard, B., Rivaud, S., Majdalami, A., Pierrot-Deseilligny, C., 1993. Upbeat nystagmus in a patient with a small medullary infarct. J. Neurol. Neurosurg. Psychiatry 56 (10), 1126–1128. https://doi.org/10.1136/jnnp.56.10.1126.
Osborne, S.F., Vivian, A.J., 2004. Primary position upbeat nystagmus associated with amitriptyline use. Eye 18, 106. https://doi.org/10.1038/sj.eye.6700529.
Saito, T., Aizawa, H., Sawada, J., Katayama, T., Hasebe, N., 2010. Lesion of the nucleus intercalatus in primary position upbeat nystagmus. Arch. Neurol. 67 (11), 1403–1404. https://doi.org/10.1001/archneurol.2010.285.
Sibony, P.A., Evinger, C., Manning, K.A., 1987. Tobacco-induced primary-position upbeat nystagmus. Ann. Neurol. 21 (1), 53–58. https://doi.org/10.1002/ana.410210110.