Concurrent Periodic Alternating Gaze Deviation and Periodic Alternating Nystagmus in Brainstem Glioma

Dear Editor,

A 20-year-old man presented with recurrent vomiting and back pain radiating to both lower limbs followed by an altered sensorium. Two years earlier, magnetic resonance imaging (MRI) brain had detected an enhancing lesion involving the posterior aspect of third ventricle. He underwent an endoscopic third ventriculostomy and biopsy that revealed a diffuse midline glioma (WHO grade IV). Thereafter, he underwent concurrent chemo-radiation. On admission, computed tomography (CT) brain showed a nodular lesion measuring 15 mm × 14 mm in the posterior third ventricle with obstructive hydrocephalus. A ventriculoperitoneal shunt (VP shunt) was immediately placed. However, he continued to remain drowsy even after 3 days. Electroencephalography (EEG) showed generalized slowing without any features to suggest nonconvulsive seizures. On examination, he had a Glasgow coma scale (GCS) score of 10/15 (E3V2M5) with bilateral spasticity and extensor plantar responses.

He exhibited large-amplitude nystagmus, with fast phases in the opposite direction of gaze deviation that decreased in intensity and velocity followed by a slow eye deviation and persistent gaze to the contralateral side. This was followed by a slow conjugate eye deviation to the opposite side and reversal of nystagmus. Vestibulo-ocular reflex testing with fast head rotations did not overcome the gaze deviation. There were no spontaneous saccades (Video). These eye movements were suggestive of periodic alternating gaze (PAG) deviation with periodic alternating nystagmus (PAN). During the PAG to the left, incomplete adduction was noticed in the right eye suggestive of a right-sided internuclear ophthalmoplegia (INO).

MRI brain showed new hyperintensities in the posterior midbrain, pons, cerebellar folia, vermis and both cerebellar peduncles with nodular multifocal leptomeningeal enhancement suggestive of leptomeningeal metastases [Figure 1].

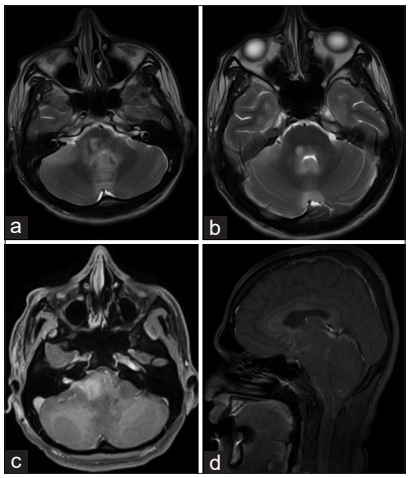

Figure 1: Panel A and B; T2-weighted axial MR images. Shows hyperintensities in the pontine tegmentum (region of the vestibular nuclei; yellow arrow), middle cerebellar peduncle, nodulus and uvula. Panel C: Axial T1 contrast scan enhancement along the cisternal segments of bilateral (right > left) 7th–8th nerve complexes and the pons (right > left). Panel D; Sagittal T1 contrast image- showing leptomeningeal enhancement around the lower brainstem and pineal region with enlargement of the cerebellum and a tight posterior fossa

Due to financial constraints, he was discharged after a few days without any further improvement.

PAG is an involuntary continuous cyclic horizontal sustained conjugate deviation of the eyes, which alternates sides with a cycle of 1–2 min.[1] PAN is a spontaneous horizontal nystagmus that periodically reverses every 1–2 min, with fast phases alternating between left and right sides, separated by null phases. Although they are not often seen together, PAG and PAN share a similar time constant and a common pathological mechanism (instability of the velocity-storage mechanism [VSM]).[2]

During angular acceleration, the semi-circular canals (SCCs) (peripheral vestibular apparatus [PVA]) sense sustained angular acceleration only for 3–5 s and sends an angular velocity signal to the central vestibular apparatus (CVA). For the CVA to continue to sense angular acceleration beyond these 3–5 s period, a central VSM is necessary. The VSM boosts the time constant of the PVA by 3–5 times to 15–25 s. The VSM utilizes inputs from the SCC, otolith organs, and visual (optokinetic) information to align the axis of eye velocity toward the spatial vertical even when the head orientation is the off-vertical axis.[3] The VSM also plays a role in assisting postural stability by modifying the vestibulospinal system activity.[4]

Corrective horizontal eye movements are provided by neurons in the vestibular nuclei, regardless of the head orientation in space. Approximately 65% of these neurons have asymmetrical responses and are more sensitive to contralateral than ipsilateral rotation. These directionally orientated neurons on either side of the brainstem respond to rotation in one direction and also code for rotational velocity-storage signals only in that direction. Although they are clustered in contralateral parts of the brainstem in "Vestibular-only" (VO) and vestibular-pause-saccade (VPS) neurons of the superior and medial vestibular nuclei, they are interconnected forming a bilateral model of VSM.[5]

The cerebellar uvula and nodulus also play an important role by transmitting otolith graviceptive and orientation information to the VSM. Thus, lesions here can cause central apogeotropic

or geotropic nystagmus or PAN. Damage to the VSM or loss of visual inputs makes the VSM unstable and increases gain in the vestibulo-ocular reflex, activating the intrinsic properties of the VSM and lead to PAG or PAN.[6] PAN can be generated by an unstable VSM only if the brainstem horizontal saccadic generators (PPRF) are intact. PAG can be considered a variant of PAN with only slow phase movements causing gaze deviation without corrective fast-phase eye movements (nystagmus). This occurs when there is concomitant dysfunction of the PPRF (brainstem saccadic generator) and only the slow phase of the rotational correction induced by the VSM occurs without corrective fast phases.[7] Our patient had brainstem infiltration of the vestibular nuclear complex, its interconnections and the cerebellar nodulus and uvula without involvement of the PPRF, resulting in concomitant PAG and PAN with a time-cycle of 45 s to 1 min.

Although the underlying mechanisms of PAG and PAN are similar, concurrent PAG and PAN are uncommon and have been reported only twice before, with recurrent cerebellar medulloblastoma and posterior reversible encephalopathy syndrome (PRES).[8,9]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Boby V. Maramattom

Department of Neurology, Aster Medcity, Kochi, Kerala, India

Address for correspondence: Dr. Boby V. Maramattom, Department of Neurology, Aster Medcity, Kochi - 682 027, Kerala, India.
E-mail: bobvarkey@gmail.com

References

1. Goldberg RT, Gonzalez C, Breinin GM, Reuben RN. Periodic alternating gaze deviation with dissociation of head movement. Arch Ophthalmol 1965;73:324-30.
2. Leigh RJ, Robinson DA, Zee DS. A hypothetical explanation for periodic alternating nystagmus: Instability in the optokinetic-vestibular system. Ann N Y Acad Sci 1981;374:619-35.
3. Yakushin SB, Raphan T, Cohen B. Coding of velocity storage in the vestibular nuclei. Front Neurol 2017;8:386.
4. Versino M, Romani A, Callieco R, Alfonsi E, Beltrami G, Manfrin M, *et al*. Periodic alternating nystagmus and vestibulo-spinal system facilitating activity. Clin Neurophysiol 2000;111:1337-9.
5. Raphan T. Vestibular, locomotor, and vestibulo-autonomic research: 50 years of collaboration with Bernard Cohen. J Neurophysiol 2020;123:329-45.
6. Leigh RJ, Robinson DA, Zee DS. A hypothetical explanation for periodic alternating nystagmus: Instability in the optokinetic-vestibular system. Ann N Y Acad Sci 1981;374:619-35.
7. Climans SA, Tyndel FJ, Mason WP, Lang AE. Periodic alternating gaze deviation due to paraneoplastic cerebellar degeneration. Mov Disord Clin Pract 2021. doi: 10.1002/mdc3.13249.
8. Mackay DD, Zepeda Garcia R, Galetta SL, Prasad S. Periodic alternating gaze deviation and nystagmus in posterior reversible encephalopathy syndrome. Neurol Clin Pract 2014;4:482-5.
9. Kennard C, Barger G, Hoyt WF. The association of periodic alternating nystagmus with periodic alternating gaze. A case report. J Clin Neuroophthalmol 1981;1:191-3.

Submitted: 04-Apr-2021 **Accepted:** 14-Jun-2021 **Published:** 14-Oct-2021

DOI: 10.4103/aian.AIAN_290_21