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LETTER TO THE EDITORS

Paroxysmal central positional nystagmus responsive to clonazepam

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Dear Sirs,

Central positional nystagmus (CPN) is defined as a nystagmus generated by a change in head position with respect to gravity due to lesions involving the brainstem or cerebellum [1]. It can be classified into paroxysmal and persistent forms according to its temporal characteristics. Paroxysmal CPN mostly manifests as downbeat nystagmus (DBN) after lying down or straight head hanging (SHH), and apogeotropic nystagmus when the head is turned to either side while supine [2]. Previous studies have systematically investigated the characteristics and possible mechanisms of paroxysmal CPN [3, 4], but its treatment has received little attention. We report a patient with paroxysmal downbeat CPN responsive to clonazepam (CZP).

A 58-year-old man with hypertension and diabetes mellitus presented with sudden unconsciousness due to intraventricular hemorrhage (IVH) in both lateral, third and fourth ventricles (Fig. 1). His consciousness gradually improved after performing burr hole trephination, but he suffered from brief vertigo episodes while lying down or getting out of bed. An examination showed vigorous DBN that lasted for a few seconds during SHH and both Dix-Hallpike maneuvers, which changed to paroxysmal upbeat nystagmus when uprighting, and mild apogeotropic nystagmus during the supine head roll test. Paroxysmal DBN did not respond to repeated canalith repositioning maneuvers for benign paroxysmal positional vertigo involving the anterior semicircular canals. The patient was suggested as having paroxysmal CPN due to IVH, and pharmacotherapy was attempted to relieve symptoms. Positional nystagmus was recorded before treatment using video-oculography (VOG, SLMED, Seoul, South Korea). The intensity of DBN during SHH initially peaked without latency. The maximal slow phase velocity (SPV) of the nystagmus was 33˚/s, and its duration and time constant (TC) were 14 and 7 s, respectively (Fig. 2A). The

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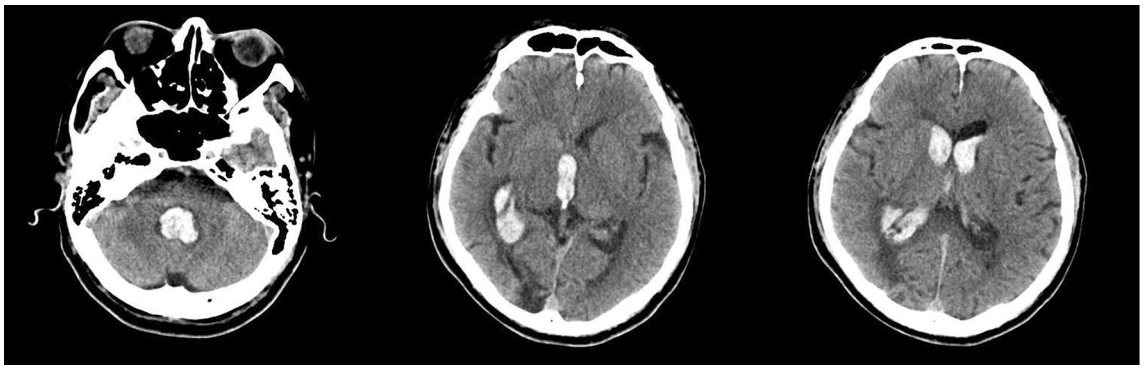

Fig. 1 Computed tomography of the brain shows intraventricular hemorrhage in the third, fourth, and lateral ventricles

initial trial with baclofen at 20 mg/day for 1 week failed due to their intolerance to the drug. We then applied CZP at 1 mg/day, and the positional vertigo of the patient began to gradually improve. Two-month follow-up VOG demonstrated resolution of the paroxysmal downbeat CPN and apogeotropic nystagmus (Fig. 2A). The patient remained symptom free while using CZP for 6 months. However, his positional vertigo became worse after CZP cessation, and the downbeat CPN intensity returned to its pretreatment level (Fig. 2A). After resuming CZP consumption, the maximal SPV of downbeat CPN decreased again from 32°/s to 6°/s. Since positional vertigo and downbeat CPN were exacerbated whenever CZP ceased or was reduced (Fig. 2B), the patient has been maintained on pharmacotherapy using CZP.

Paroxysmal CPN has been reported in lesions involving the brainstem or cerebellum, but the nodulus and uvula were the most-involved structures [1]. In previous studies, paroxysmal CPN primarily occurred in the planes of semicircular canals inhibited during the positioning, and the characteristics suggested canal-driven signals regarding the latency and TC of the evoked nystagmus [3, 4]. These findings lead to the hypothesis that lesions in the nodulus and uvula disinhibit the irregular vestibular afferents and cause a prominent post-acceleratory secondary response during positioning that manifests as paroxysmal CPN. Paroxysmal downbeat CPN in our patient had no latency with a TC of 7 s, similar to the findings of previous studies [3, 4]. Although a lesion was not present in the nodulus or uvula, IVH within the fourth ventricle might result in reciprocal connection impairment between the vestibular nuclei and vestibulocerebellum, which might, in turn, cause paroxysmal downbeat CPN via transient over-activation of the anterior canals on both sides during positioning.

CZP enhances the activity of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) in the central nervous system. CZP is known to alleviate DBN by compensating for the loss of inhibitory input from the cerebellum to the vestibular nuclei [5, 6]. Similarly, the paroxysmal downbeat CPN of our patient might have been attenuated by CZP through enhancement of inhibitory GABAergic

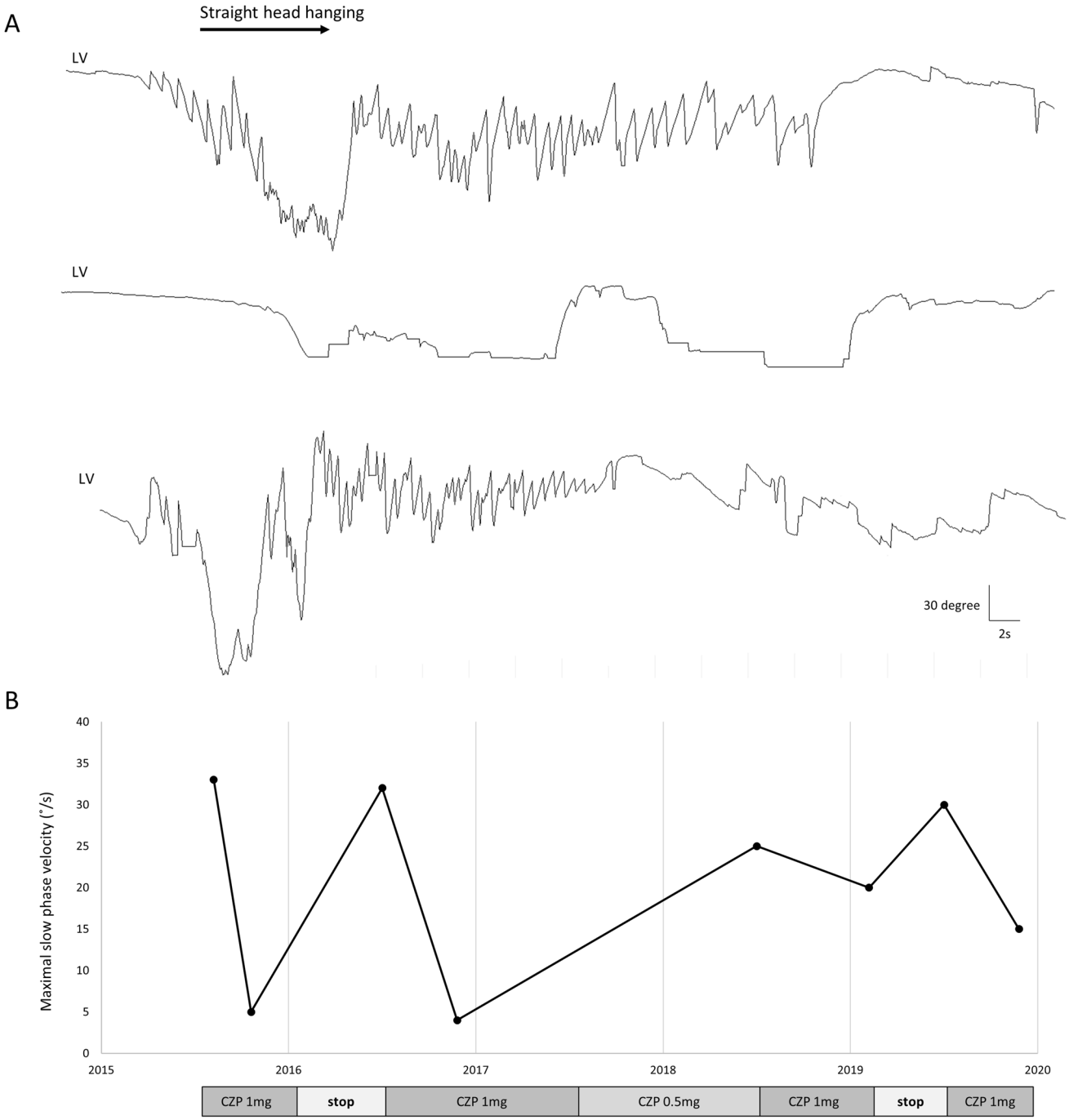

Fig. 2 **A** Before treatment, vertical eye movement recording using video-oculography showed paroxysmal downbeat nystagmus (pDBN) with a maximal slow phase velocity (SPV) of 33°/s during straight head hanging (upper panel). After the clonazepam (CZP) trial at 1 mg/day for 2 months, the pDBN was almost resolved during positioning (middle panel). After CZP cessation, the pDBN intensity returned to its pre-treatment level (lower panel). **B** Graph illustrating the maximal SPV of the pDBN during positioning according to CZP dosage. The maximal SPV increased whenever CZP ceased or was reduced. LV vertical position of the left eye

synaptic transmission between the vestibulocerebellum and vestibular nuclei, and stabilization of the exaggerated post-acceleratory secondary response during positioning. The effect of CZP needs to be determined in a study involving a large CPN patient cohort.

Declarations

Conflicts of interest We have no disclosure of any competing interest.

Ethical approval All experiments followed the tenets of the Declaration of Helsinki and this study was approved by the institutional review board of Pusan National University Yangsan Hosptial.

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