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ORIGINAL ARTICLE

Dorsolateral pontine lesions produce distinct ocular motor abnormalities with anatomical correlations

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Abstract

Background and Purpose: The dorsolateral portion of the caudal pons contains the vestibular nucleus (VN) and inferior cerebellar peduncle (ICP) that play important roles in conveying and processing vestibular and ocular motor signals. This study aimed to characterize ocular motor abnormalities along with their anatomical correlations in dorsolateral pons (DLP) lesions.

Methods: We analyzed clinical features, and results of neuro-otological evaluations and neuroimaging of 18 patients with unilateral DLP lesions (17 with DLP infarction and 1 with cavernous malformation) from among 506 patients with pontine infarction in a stroke registry.

Results: Most of the patients ($n = 16$) presented with isolated acute vestibular syndrome (AVS). The involved structures within the DLP were the ICP in four patients and the VN in the remaining 14. The unilateral ICP lesions were associated with consistent abnormalities in vestibular and ocular motor tests, including ipsilesional nystagmus without gaze-evoked nystagmus (GEN), and normal head impulse tests (HITs) and caloric response. In contrast, lesions of the VN were associated with a broader range of eye-movement abnormalities, including ipsi- or contralesional nystagmus with GEN, positive HITs, normal or abnormal caloric responses, and fixation nystagmus. Initial diffusion-weighted magnetic resonance imaging (within 48 h) was falsely negative in 41% ($n = 7$) of the DLP infarction cases.

Conclusions: This study demonstrates that unilateral DLP lesions frequently present with isolated AVS and diverse ocular motor abnormalities. These characteristics may be due to the complex involvement of afferent or efferent fibers to and from the VN.

KEYWORDS
acute vestibular syndrome, dorsolateral pontine infarction, inferior cerebellar peduncle, vestibular nucleus

Hyun Sung Kim and Jae-Hwan Choi contributed equally to this work.

INTRODUCTION

The dorsolateral portion of the caudal pons contains the vestibular nucleus (VN) and inferior cerebellar peduncle (ICP) that play important roles in conveying and processing vestibular and ocular motor signals [1, 2]. Dorsolateral pons (DLP) is supplied by the anterior inferior cerebellar artery [3], and the lesions involving the DLP commonly give rise to acute vestibular syndrome (AVS) along with diverse ocular motor findings [4].

Previous reports have described abnormal ocular motor findings that occur in circumscribed lesions of the VN or ICP within the DLP [5–10]. Lesions of the VN produce combined peripheral and central vestibular signs including contralesional spontaneous nystagmus (SN), direction-changing gaze-evoked nystagmus (GEN), abnormal head impulse tests (HITs), caloric paresis, and ipsiversive ocular tilt reaction (OTR) [5–8]. In contrast, an ICP lesion results in ipsilesional SN without GEN, normal HITs and caloric tests, and contraversive OTR [9, 10].

The VN and ICP are located in close proximity to the DLP [1, 2]. The VN subdivides into four major nuclei, and has complex connections to surrounding structures including the contralateral VN, nucleus prepositus hypoglossi (NPH), and vestibulocerebellum [11]. Therefore, DLP lesions may present with a broader range of eye-movement abnormalities beyond the previously reported dichotomized findings [4–10].

The aim of this study was to characterize abnormal ocular motor findings associated with DLP lesions to help differentiate them from AVS resulting from benign peripheral vestibulopathy, and identify their anatomical correlations.

METHODS

Subjects

This study included 17 patients with DLP infarction from among the 506 patients with pontine infarctions in the stroke registry of Pusan National University Yangsan Hospital from 2013 to 2023. One additional patient with cavernous malformation in the DLP was also included in the analyses. These 18 patients included 14 males and 4 females with an age ranging from 38 to 80 years (62 ± 12 years, mean ± SD). The interval from symptom onset to evaluation ranged from 0 to 6 days (median, 1.5 days). All patients received full neurological and neuro-otological evaluations including HINTS plus (Head Impulse, Nystagmus, Test of Skew, and acute hearing loss detected by finger rubbing), which were performed by one of the authors (J-HC) [12]. This study was conducted in accordance with the Declaration of Helsinki and approved by the institutional review board of Pusan National University Yangsan Hospital (55-2024-030). Informed consent to participate in this study was obtained from each participant.

Ocular motor function tests

Video-oculography (SLMED) at a sampling rate of 120 Hz was used to record SN with and without fixation, GEN with horizontal target displacements of ±30°, positional nystagmus, saccades, and smooth pursuit. Patients also underwent bithermal caloric tests, video HITs, and measurements of skew deviation, ocular torsion, and subjective visual vertical (SVV). The detailed methods and normative data of each test have been reported previously [9, 13]. Canal paresis (CP) was defined as a response difference of >25% between the ears according to Jongkee's formula [14]. If the summated maximum slow-phase velocity of the nystagmus was <20°/s under four stimulation conditions, the caloric response was considered bilateral vestibular hypofunction [13]. In video-HITs, the vestibulo-ocular reflex (VOR) gain was calculated as the ratio of the area under the entire eye-velocity response relative to the area under the entire head-velocity response stimulus. Corrective catch-up saccades (CSs) were defined as saccades in the direction opposite to head rotation whose acceleration peaked before (covert) or after (overt) the head stopped moving. We defined an impaired HIT response when the mean VOR gains exceeded the mean ± 2SD obtained from healthy controls (normal gains for the horizontal canals (HCs) = 0.89–1.02, for the anterior canals (ACs) = 0.80–1.18, for the posterior canals (PCs) = 0.88–1.09), and when there were corrective CSs [13]. The SVV tilt was considered abnormal when it exceeded normal values of healthy controls (−3.0°–3.0° in both eyes, where a negative value indicates a counterclockwise rotation) [9]. The ocular torsion was considered pathological when the eye showed any intorsion (<0°) or extorsion exceeding 12.6° [9].

Lesion analysis

All patients received stroke-protocol magnetic resonance imaging (MRI), including axial T2-weighted image, fluid-attenuated inversion recovery image, diffusion-weighted image (DWI, section thickness = 4 mm), and angiography using a 3.0-T (n = 15) or 1.5-T (n = 3) unit. In patients with negative early DWI, we performed repeat DWI within 1 week from the symptom onset. The lesions on MRI were analyzed using an anatomical template. The caudal pons was subdivided into upper and lower portions based on the shape of the fourth ventricle in the axial plane. The upper portion was determined when the fourth ventricle resembled the shape of a "Kaiser Wilhelm helmet" in axial imaging (Figure 1) [15]. This unique appearance was formed by the nodulus posteriorly and the anterolateral protuberance by the facial colliculi. The lower portion was defined when the tonsil was visible adjacent to the nodulus in the fourth ventricle.

Since the VN and ICP are located in close proximity within the DLP, we determined which structures were involved in MRI using the anatomical diagrams in *Neuroanatomy: Text and Atlas*, as described previously [1, 6, 9, 10]. The involvement of each structure was assessed independently by two of the authors (HSK and EHO) who were blinded to all clinical data. If there were any disagreements between the two, we made a final decision on consensus by all of the authors. Vestibular and ocular motor findings along with their anatomical correlations were identified by performing lesion analysis using MRIcron software. DWI and T2-weighted MRI lesions of each patient were mapped onto slices of a T1-weighted template MRI scan, and overlap images were then obtained according to the

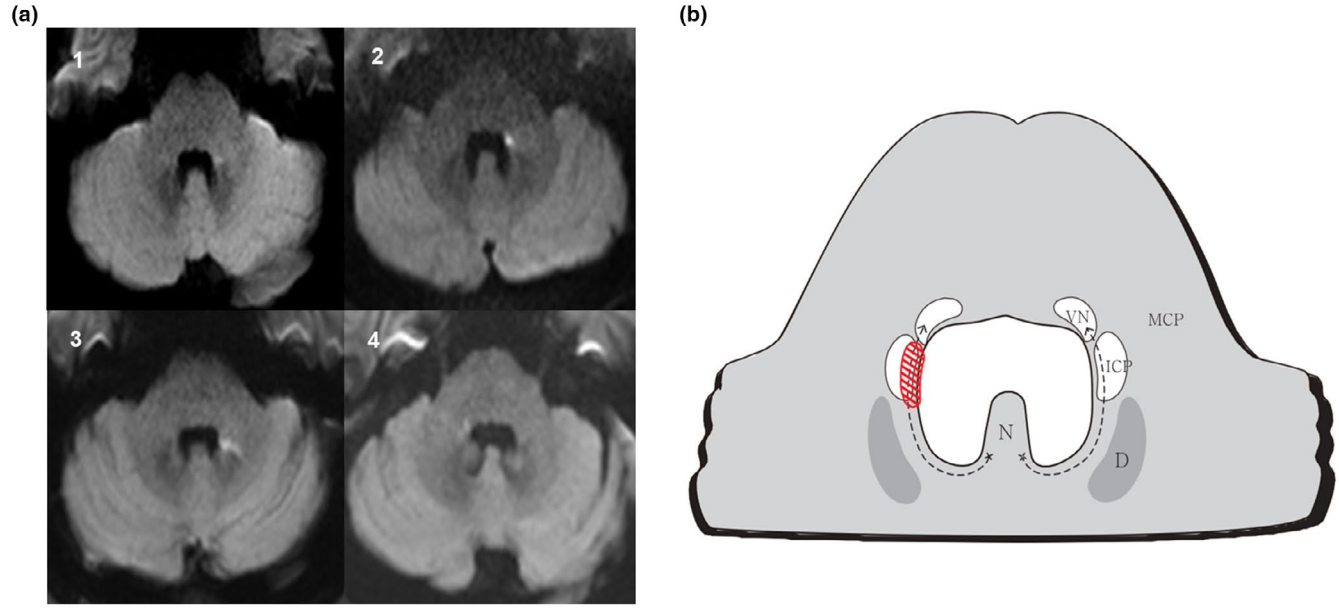

FIGURE 1 Magnetic resonance imaging (MRI) findings and schematic illustration of the neural structures involved in patients with ICP lesions. (a) Diffusion-weighted MRI showing acute infarctions restricted to the unilateral ICP around the lateral wall of the fourth ventricle at the level of the upper DLP in four patients (patients 1–4). (b) The upper portion of the DLP is determined when the fourth ventricle resembles the shape of a "Kaiser Wilhelm helmet." The lesions may involve inhibitory fibers (dashed lines) traveling to the VN from the nodulus. D, dentate nucleus; DLP, dorsolateral pons; ICP, inferior cerebellar peduncle; MCP, middle cerebellar peduncle; N, nodulus; VN, vestibular nucleus.

involved structures using lesion density plots. We flipped the regions of interest in patients with left-sided lesions so that they could be aligned with those on the right side.

RESULTS

Clinical characteristics

Sixteen of the 18 patients (89%) presented with isolated AVS, while the remaining two had accompanying neurological signs including ipsilesional sudden sensorineural heading loss (patient 5) or abducens nerve palsy (patient 7). All patients had at least one central vestibular sign, such as normal HITs, direction-changing GEN, or skew deviation. Twelve of the 18 patients (67%) exhibited a peripheral vestibular sign including abnormal HITs or CP.

The lesion was located in the upper ($n=6$) or lower ($n=12$) portion of the DLP. Initial DWI (within 48 hours) produced false-negative findings in 41% ($n=7$) of the DLP infarction cases. However, all of these seven patients were suspected to have central lesions based on dangerous HINTS plus examinations.

Abnormal ocular motor findings with anatomical correlations

Patients with DLP lesions showed distinct ocular motor abnormalities with anatomical correlations (Table 1).

ICP lesions

Four patients (patients 1–4, 22%) had lesions restricted to the unilateral ICP around the lateral wall of the fourth ventricle in the upper DLP (Figure 1a). Abnormal ocular motor findings in these patients included ipsilesional SN without direction-changing GEN, normal HITs and caloric responses (Figure 2), and contraversive SVV tilt/OTR. These findings were consistent with those reported previously for ICP lesions [9, 10]. The patients showed mainly ipsilesional horizontal nystagmus with ($n=3$) or without ($n=1$) vertical components. Two patients (patients 2 and 4) exhibited apogeotropic positional nystagmus after turning their head to either side while supine. All patients in this group had normal caloric tests and bedside HITs ($n=1$) or video HITs ($n=3$), but exhibited contraversive SVV tilt with skew deviation ($n=2$) or ocular torsion ($n=3$). Three patients showed hypometric saccades and impaired horizontal smooth pursuits unilaterally ($n=1$) or bilaterally ($n=2$).

VN lesions

The remaining 14 patients had unilateral lesions of the VN on the floor of the fourth ventricle in the upper ($n=2$) or lower ($n=12$) DLP (Figure 3a). Four patients (patients 5–8) showed typical ocular motor abnormalities by involvement of the VN such as contralesional SN, direction-changing GEN, abnormal HITs, or CP (Figure 4) [4–8]. The video HITs revealed decreased VOR gains for the HCs on both sides

TABLE 1 Abnormal ocular motor finding in patients with dorsolateral pontine lesions.

Patient ID	Sex/age	Lesion side & level	SN with and without fixation	GEN	HITs	Caloric paresis (%)	Skew deviation	Ocular torsion	SVV tilt (°)	Saccade	SP impairment
ICP lesion											
1	M/38	L, upper	Ipsilesional (L)	(–)	NL	(–)	Contraversive (R)	Contraversive (R)	Contraversive (+7.1)	B, hypometria	L
2	M/48	L, upper	Ipsilesional (L, U)	(–)	NL	(–)	(–)	(–)	Contraversive (+14.2)	B, hypometria	B, L > R
3	M/53	L, upper	Ipsilesional (L, U)[b]	(–)	NL	(–)	(–)	Contraversive (R)	Contraversive (+3.1)	NL	NL
4	M/73	R, upper	Ipsilesional (R, U)[b]	(–)	NL (bedside)	(–)	Contraversive (L)	Contraversive (L)	Contraversive (−27.9)	B, hypometria	B
VN lesion											
Typical pattern											
5	F/78	R, lower	Contralesional (L, U, CCW)[a]	L > R	Impaired, B HCs (R > L), PCs, and ACs	B	Ipsiversive (R)	Ipsiversive (R)	Ipsiversive (+10.5)	B, hypometria	B
6	M/62	L, lower	Contralesional (R, U, CW)	R > L	Impaired, B HCs (L > R) and PCs	L (72.2)	(–)	NP	Ipsiversive (−3.1)	NL	NL
7	M/61	R, upper	Contralesional (L)[b]	L > R	Impaired, B HCs (R > L) and R PC	B	(–)	(–)	(–)	NL	B
8	M/68	R, lower	Contralesional (L)	L > R	Impaired, B HCs (R > L) and PCs	R (38.1)	(–)	NP	(–)	NL	B
Atypical pattern											
9	M/55	R, upper	Contralesional (L, U, CCW)	R > L	Impaired, B HCs (R > L)	R (27.1)	(–)	NP	NP	NL	B
10	M/66	R, lower	Contralesional (L, CCW)	(–)	Impaired, B HCs (R > L) and ACs	R (40.8)	Ipsiversive (R)	Ipsiversive (R)	Ipsiversive (+7.0)	NP	NP
11	F/78	L, lower	Contralesional (R, CW)	(–)	NL (bedside)	(–)	(–)	Ipsiversive (L)	Ipsiversive (−8.0)	NL	B
12	M/55	R, lower	Ipsilesional (R, U, CW)	R > L	NL (bedside)	(–)	Ipsiversive (R)	Ipsiversive (R)	Ipsiversive (+4.4)	NL	B, R > L
13	M/67	L, lower	Ipsilesional (L, D, CCW)[a]	L > R	Impaired, B HCs (R > L) and PCs	B	(–)	NP	Ipsiversive (−6.1)	L, slowing	B
14	F/80	R, lower	Ipsilesional (R, U, CW)	R > L	Impaired, B HCs (L > R), PCs, and ACs	(–)	Contraversive (L)	Contraversive (L)	Contraversive (−10.4)	NL	B
15	F/65	R, lower	Ipsilesional (R, D)[b]	R > L	Impaired, B HCs (L > R) and PCs	(–)	(–)	(–)	(–)	NL	B

TABLE 1 (Continued)

Patient ID	Sex/age	Lesion side & level	SN with and without fixation	GEN	HITs	Caloric paresis (%)	Skew deviation	Ocular torsion	SVV tilt (°)	Saccade	SP impairment
16	M/49	R, lower	U&CCW	L > R	Impaired, B HCs (L > R)	(–)	Ipsiversive (R)	Ipsiversive (R)	Ipsiversive (+5.4)	NL	B
17	M/71	L, lower	U & CW	R > L	Impaired, L HC and B PCs	NP	Ipsiversive (L)	Ipsiversive (L)	Ipsiversive (–10.3)	NL	B
18	M/55	R, lower	U & CCW[a]	R > L	Impaired, B HC (R > L)	(–)	(–)	NP	Contraversive (–5.7)	B, hypometria	B

Abbreviations: AC, anterior semicircular canal; B, bilateral; CW, clockwise from the patient's perspective; CCW, counterclockwise from the patient's perspective; D, downbeat; F, female; GEN, gaze-evoked nystagmus; HC, horizontal semicircular canal; HIT, head impulse test; ICP, inferior cerebellar peduncle; L, left; LB, left-beat; M, male; NL, normal; NP, not performed; PC, posterior semicircular canal; R, right; RB, right-beat; SN, spontaneous nystagmus; SP, smooth pursuit; SVV, subjective visual vertical; UB, upbeat; VN, vestibular nucleus.

[a]Fixation nystagmus.

[b]The nystagmus was present only in darkness.

with the involvement of the PCs ($n=4$) or ACs ($n=1$). Bithermal caloric tests documented ipsilesional ($n=2$) or bilateral ($n=2$) CP. The other three patients (patients 9–11) also had contralesional SN, but showed some atypical features including ipsilesional strong GEN ($n=1$) or the absence of GEN ($n=2$). Two patients had decreased VOR gains for HCs and/or ACs with ipsilesional CP, but the remaining patient showed normal HITs and caloric responses.

Another four patients (patients 12–15) presented with mainly ipsilesional horizontal nystagmus with direction-changing GEN. The results of caloric tests and HITs were variable: normal ($n=1$) or abnormal ($n=1$) VOR function in both tests, or abnormal HITs with normal caloric responses ($n=2$, Figure 5). The VOR gains on video HITs were mainly decreased bilaterally for the HCs and PCs.

The last three patients (patients 16–18) showed dissociative vertical-torsional nystagmus, which was characterized by contraversive torsional nystagmus with larger upbeat components in the contralesional eye (Figure 6). They also had direction-changing GEN and abnormal HITs but normal caloric responses. The VOR gains were decreased bilaterally or ipsilesionally for the HCs with or without the involvement of the PCs.

Most patients showed augmentation of SN in darkness, but three patients (patients 5, 13, and 18) exhibited fixation nystagmus, which was present during visual fixation but absent or markedly decreased in darkness (Figure 4a).

The abnormal SVV tilt/OTR present in ten patients was either ipsiversive ($n=8$) or contraversive ($n=2$). Saccades were abnormal in three patients, comprising hypometric saccades ($n=2$) and ipsilesional saccadic slowing ($n=1$), and horizontal smooth pursuit was impaired bilaterally in 12 patients.

Lesions mapping analysis

Lesion mapping analysis revealed that the ICP lesions were located on the lateral wall of the fourth ventricle in the upper DLP, whereas the VN lesions were mainly on the floor of the fourth ventricle in the lower DLP (Figure 7). The distribution of VN lesions did not differ between patients with typical and atypical ocular motor abnormalities.

DISCUSSION

The main findings of this study can be summarized as follows: (1) DLP lesions frequently present with isolated AVS, (2) DLP lesions produce both central and peripheral vestibular signs, but all show at least one central vestibular sign, and (3) DLP lesions can manifest as distinct ocular motor abnormalities with anatomical correlations.

Identifying acute strokes as a cause of AVS can be challenging since accompanying focal neurological signs are present in only around 27% of AVS patients [16]. It has been reported that initial DWI can fail to detect strokes in 4%–20% of cases of posterior circulation stroke within 2 days from symptom onset [16–20]. The present study found that most patients with DLP lesions had isolated

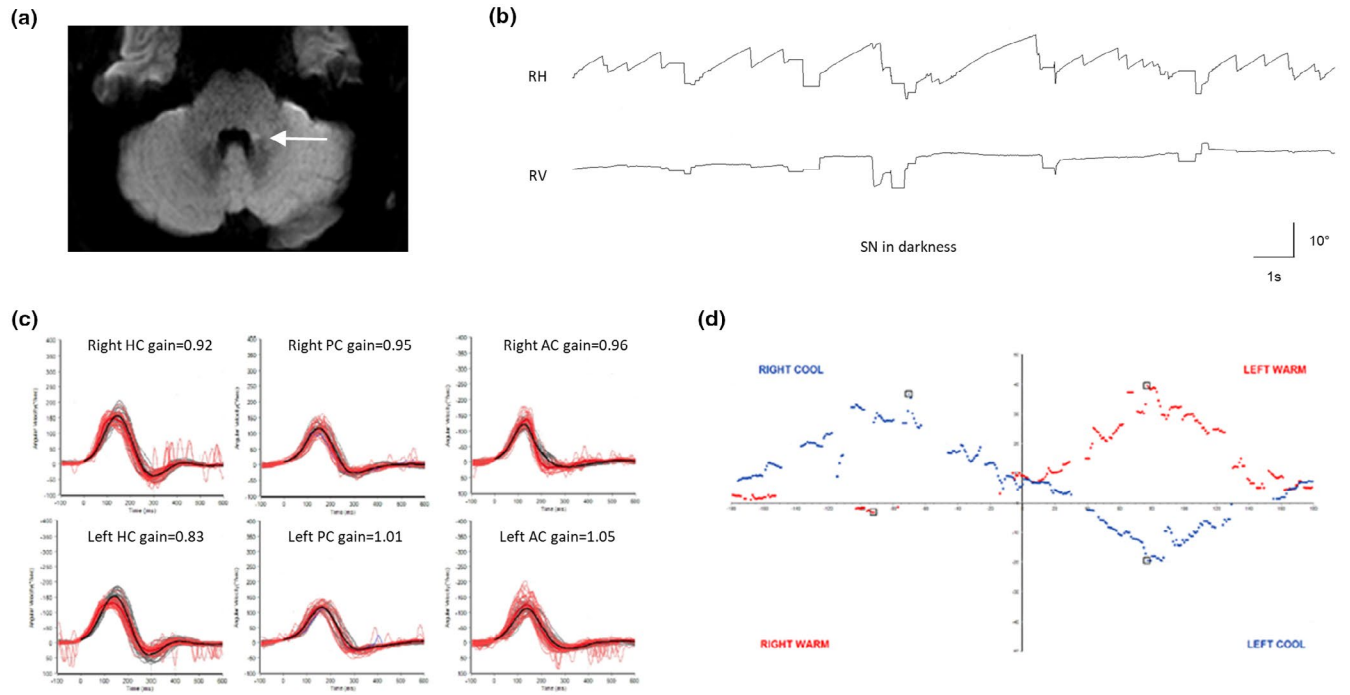

FIGURE 2 Ocular motor findings in patient 1. Diffusion-weighted magnetic resonance imaging showing an acute infarction confined to the left ICP at the upper DLP (a, arrow). Video-oculography shows spontaneous left-beating nystagmus without visual fixation (b), but normal video head impulse tests (c) and bithermal caloric tests (d). AC, anterior semicircular canal; DLP, dorsolateral pons; HC, horizontal semicircular canal; ICP, inferior cerebellar peduncle; PC, posterior semicircular canal; RH, horizontal position of right eye; RV, vertical position of right eye; SN, spontaneous nystagmus.

AVS without accompanying neurological signs. Moreover, initial DWI produced false-negative findings in approximately 40% of cases, which is more frequent than the rates of 4%–20% reported for other posterior circulation strokes [16–20]. In a previous study, three ocular motor signs (normal horizontal HIT, direction-changing GEN, and skew deviation) plus acute hearing loss (HINTS plus) were more sensitive than early DWI for detecting acute strokes in AVS [12, 17]. In contrast, abnormal HITs in association with unidirectional horizontal-torsional nystagmus and no skew deviation were the signature signs of acute unilateral peripheral vestibulopathy (Table S1). Although most of our patients with DLP lesions had peripheral vestibular signs such as abnormal HITs or CP, all patients presented at least one central vestibular sign of HINTS-plus examination: normal HITs, direction-changing GEN, or skew deviation. Furthermore, either fixation nystagmus or vertical-torsional nystagmus was also central vestibular sign suggesting the presence of posterior circulation stroke.

Eye movement abnormalities with anatomical correlation

Previous studies found that abnormal ocular motor findings in DLP lesions may be attributed to the involvement of the ICP or VN [4–10]. Although both of these structures are located in the rostral medulla as well as the DLP, the selective involvement of the ICP or VN may be more common in DLP lesions [4–10, 18], which can help us to better understand ocular motor signs and their anatomical correlations. About 20% of our patients had lesions restricted to the unilateral ICP around the lateral wall of the fourth ventricle. The lesions were mainly located in the upper portion of the DLP, implying that isolated involvement of the ICP might be not common in the lower DLP due to the simultaneous involvement of other vestibular structures. The ICP contains afferent and efferent fibers to and from the vestibulocerebellum that primarily integrate proprioceptive and vestibular information [1, 2]. The inhibitory fibers from the nodulus to the VN pass through the ICP [21]. Therefore, a unilateral ICP lesion may increase the tonic resting activity of the ipsilesional VN due to the loss of cerebellar inhibition (Figure 1b). This can lead to ipsilesional SN, normal HITs, central positional nystagmus, and contraversive OTR or SVV tilt. These findings are quite different from those seen in lesions involving the middle cerebellar peduncle which frequently produce abnormal HITs or CP, GEN, and bilateral impairments of horizontal smooth pursuit [22]. Instead, the findings are consistent with those reported in lesions of the unilateral nodulus, suggesting that both ICP and nodular lesions share similar ocular motor abnormalities by the involvement of inhibitory cerebellar fibers traveling to the VN [4, 23, 24].

Lesions of the VN typically showed features of both central and peripheral vestibulopathies because the VN serves as a final destination for peripheral vestibular signals, but is also involved in the neural integration for horizontal eye motion [5, 6, 11, 18].

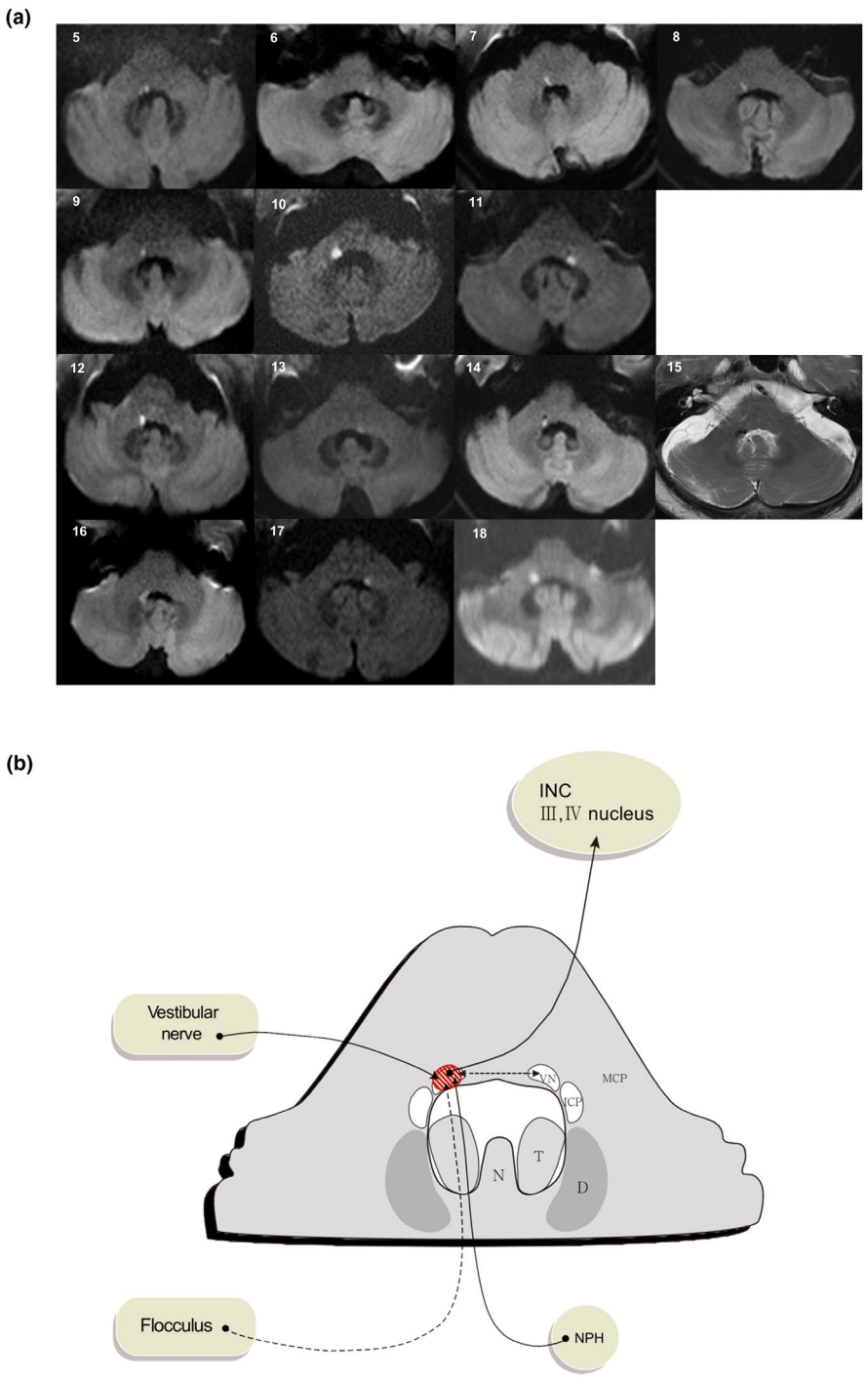

FIGURE 3 Magnetic resonance imaging (MRI) findings and schematic illustration of the neural structures involved in patients with VN lesions. (a) Diffusion-weighted MRI showing acute infarctions confined to the unilateral VN in the upper ($n=2$, patients 7 and 9) or lower ($n=12$) portion of the DLP. The remaining patient (patient 15) has a cavernous malformation in the right DLP. (b) The lower portion of the DLP is defined when the tonsil is visible adjacent to the nodulus in the fourth ventricle. The VN receives excitatory projections (solid lines) from the ipsilateral vestibular nerve and contralateral NPH, while it also receives inhibitory projections (dashed lines) from the contralateral VN and ipsilateral vestibulocerebellum such as the flocculus. The graviceptive utricular and vertical vestibulo-ocular reflex pathways project to the contralateral INC and third/fourth nuclei from the VN. The lesions may involve afferent or efferent fibers to and from the VN. D, dentate nucleus; DLP, dorsolateral pons; ICP, inferior cerebellar peduncle; INC, interstitial nucleus of Cajal; MCP, middle cerebellar peduncle; N, nodulus; NPH, nucleus prepositus hypoglossi; T, tonsil; VN, vestibular nucleus.

The contralesional horizontal-torsional nystagmus, positive ipsilesional HITs and ipsilesional CP were consistent with unilateral peripheral vestibulopathy, while direction-changing GEN indicates the involvement of central vestibular structures such as the neural integrator [6]. However, the VN divides into four major subnuclei at the caudal pons and rostral medulla, and has complex connections to the surrounding structures including the contralateral VN, NPH, and vestibulocerebellum (Figure 3b) [11]. Therefore, lesions involving the VN may present with a broader range of ocular motor abnormalities rather than the above-mentioned typical features. As expected, our study demonstrated that atypical ocular motor findings were more commonly observed in conjunction with VN lesions, such as the absence of GEN, normal or discordant VOR functions, ipsilesional SN, vertical-torsional nystagmus, and fixation nystagmus. Although these findings may depend on the time from symptom onset, the absence of GEN or normal VOR function can be explained by partial or incomplete involvement of the VN. Alternatively, it is possible that both the VN and ICP are involved in patients with atypical ocular motor findings. However, the ICP acts as a bridge between the VN and vestibulocerebellum and mainly comprises afferent and efferent fibers to and from the VN [1, 2, 9, 10]. Thus, even if both structures were invaded, the ICP signs

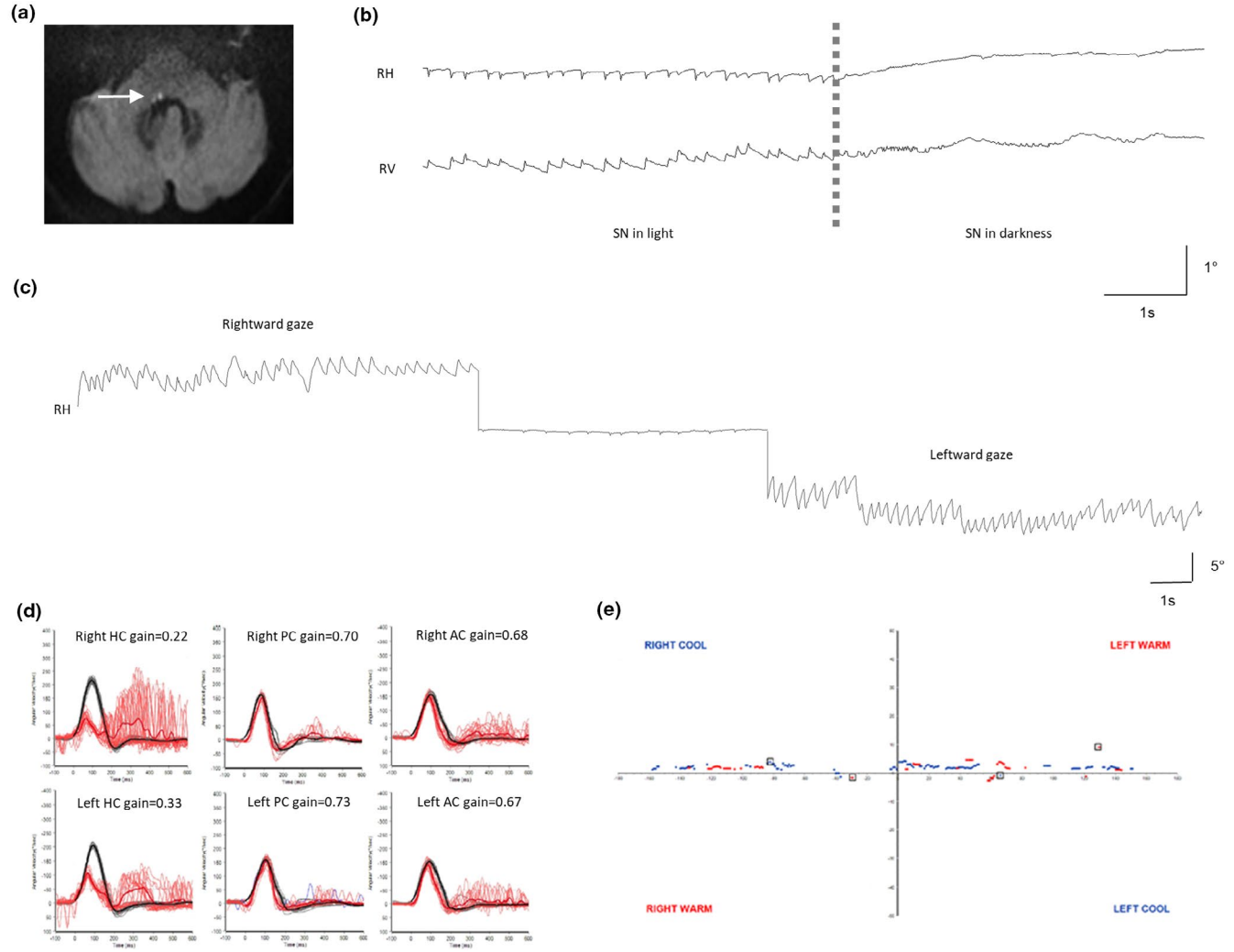

FIGURE 4 Ocular motor findings in patient 5. Diffusion-weighted magnetic resonance imaging reveals an acute infarction confined to the right VN at the lower DLP (a, arrow). Video-oculography shows spontaneous left-beating nystagmus with upbeat components with visual fixation, which markedly decreases in darkness (b). The spontaneous left-beating nystagmus increases during leftward gaze and changes into right-beating nystagmus during rightward gaze (c). Video-head impulse tests show decreased vestibulo-ocular reflex gains with corrective catch-up saccades in all bilateral semicircular canals (d), and the responses to bithermal caloric tests were minimal in both ears (e). AC, anterior semicircular canal; DLP, dorsolateral pons; HC, horizontal semicircular canal; PC, posterior semicircular canal; RH, horizontal position of right eye; RV, vertical position of right eye; SN, spontaneous nystagmus; VN, vestibular nucleus.

may be concealed by involvement of the VN. The lesion mapping analysis additionally revealed that the MRI lesions in atypical subtypes were located more medially than were typical ICP lesions, suggesting involvement of the VN.

The SN appearing with VN lesions is usually directed away from the lesion side due to asymmetrically reduced VOR gains, more marked for the ipsilesional canals. However, some patients in our study had SN beating to the lesion side. Ipsilesional SN has previously been reported in a patient with a tiny infarction restricted to the superior VN [7]. Experimental inactivation of the superior and rostral medial vestibular nuclei also induced nystagmus beating toward the lesions [25]. In contrast, the lesions in our patients were located in the lower DLP, which was below the superior VN. The VN receives excitatory projections from the ipsilateral vestibular nerve and contralateral NPH, and inhibitory projections from the ipsilateral vestibulocerebellum such as the flocculus (Figure 3b) [11, 26]. An imbalance between excitatory and inhibitory projections to the VN may determine the direction of the SN [7]. Thus, the dominant involvement of inhibitory fibers originating from the ipsilateral vestibulocerebellum could induce ipsilesional SN when VN lesions are present. Indeed, patients with isolated unilateral floccular or nodular infarction showed ipsilesional SN by involvement of inhibitory cerebellar fibers traveling to the VN [23, 24, 27, 28].

Remarkably, we observed dissociative vertical-torsional nystagmus in conjunction with VN lesions, which presents as conjugate torsional nystagmus with disparate vertical components. This pattern is commonly observed in internuclear ophthalmoplegia involving the medial longitudinal fasciculus [29]. Our patients exhibited contraversive torsional nystagmus with larger upbeat components in

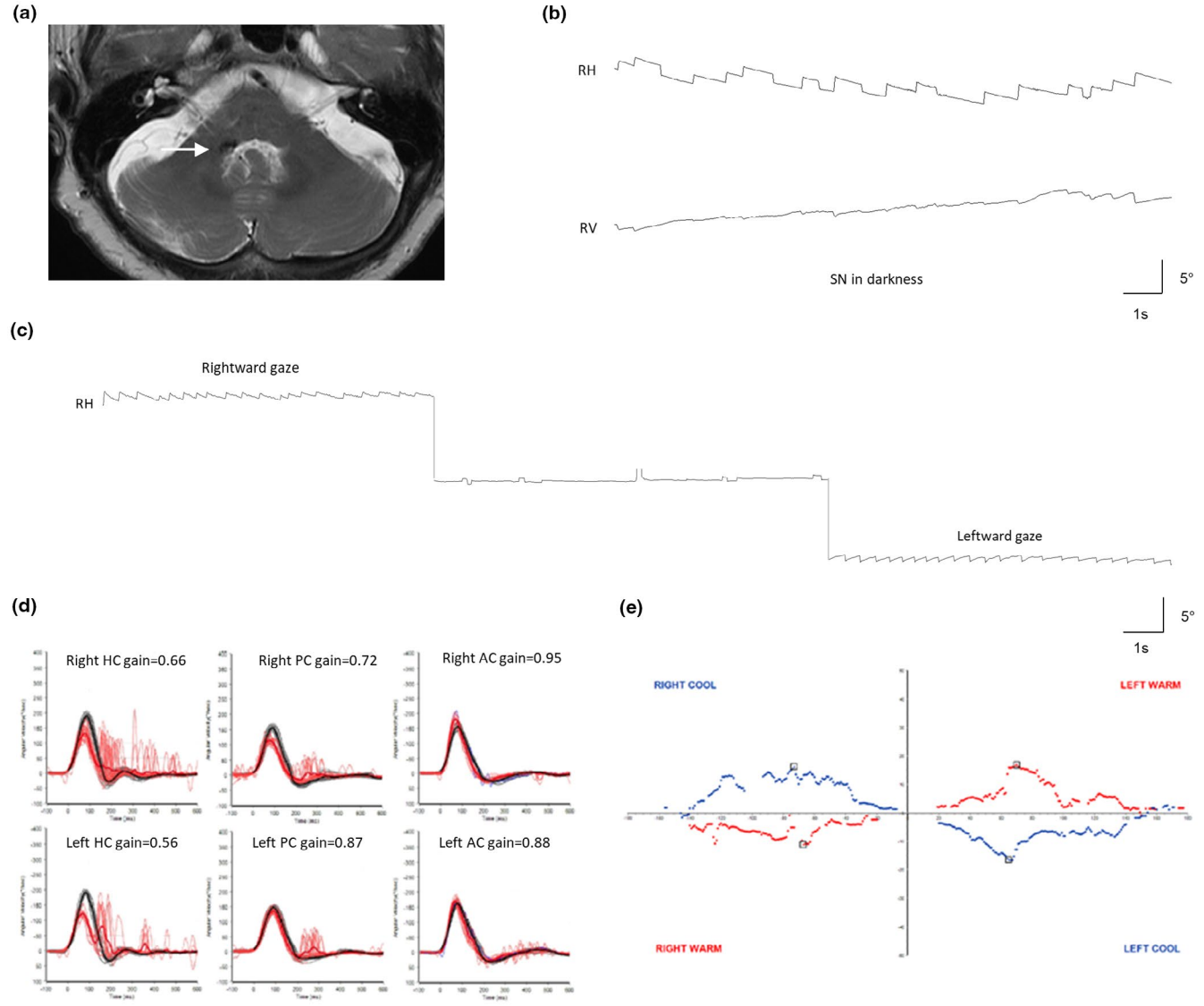

FIGURE 5 Ocular motor findings in patient 15. T2-weighted magnetic resonance imaging shows a cavernous malformation in the right VN at the lower DLP (a, arrow). Eye-movement recordings reveal spontaneous right-beating nystagmus without visual fixation (b), horizontal gaze-evoked nystagmus (c), decreased vestibulo-ocular reflex gains for both HCs and PCs during video-head impulse tests (d), and normal caloric responses (e). AC, anterior semicircular canal; DLP, dorsolateral pons; HC, horizontal semicircular canal; PC, posterior semicircular canal; RH, horizontal position of right eye; RV, vertical position of right eye; SN, spontaneous nystagmus; VN, vestibular nucleus.

the contralesional eye. This type of nystagmus has been attributed to the disruption of the utriculo-ocular reflex or VOR pathways from the vertical canals [29]. Given the torsional components in the opposite direction of the OTR or SVV tilt and normal VOR responses from ACs in our patients, dissociative vertical-torsional nystagmus in conjunction with VN lesions may be ascribed to disruption of the graviceptive utricular pathway rather than to vertical VOR dysfunction [30, 31].

Most patients with DLP lesions showed augmentation of SN in darkness, but some with involvement of the VN exhibited fixation nystagmus that appeared or increased markedly with fixation. This is associated with lesions involving the cerebellar nuclei or the fibers projecting from the cerebellum to the brainstem [32]. According to a mathematical model, fixation nystagmus reflects an imbalance in the central zone due to abnormal functioning of the cerebellar circuits that normally optimize the interaction between visual following (pursuit) and the VOR during attempted fixation [33]. Our patients with fixation nystagmus also showed impairments of both smooth pursuit and the VOR, suggesting the involvement of the cerebellar circuits responsible for interactions between the visual and vestibular systems.

Study limitation

This study had a few potential limitations. We included only a small number of patients from a single center. Because a focal lesion restricted to the unilateral DLP is not common, further studies

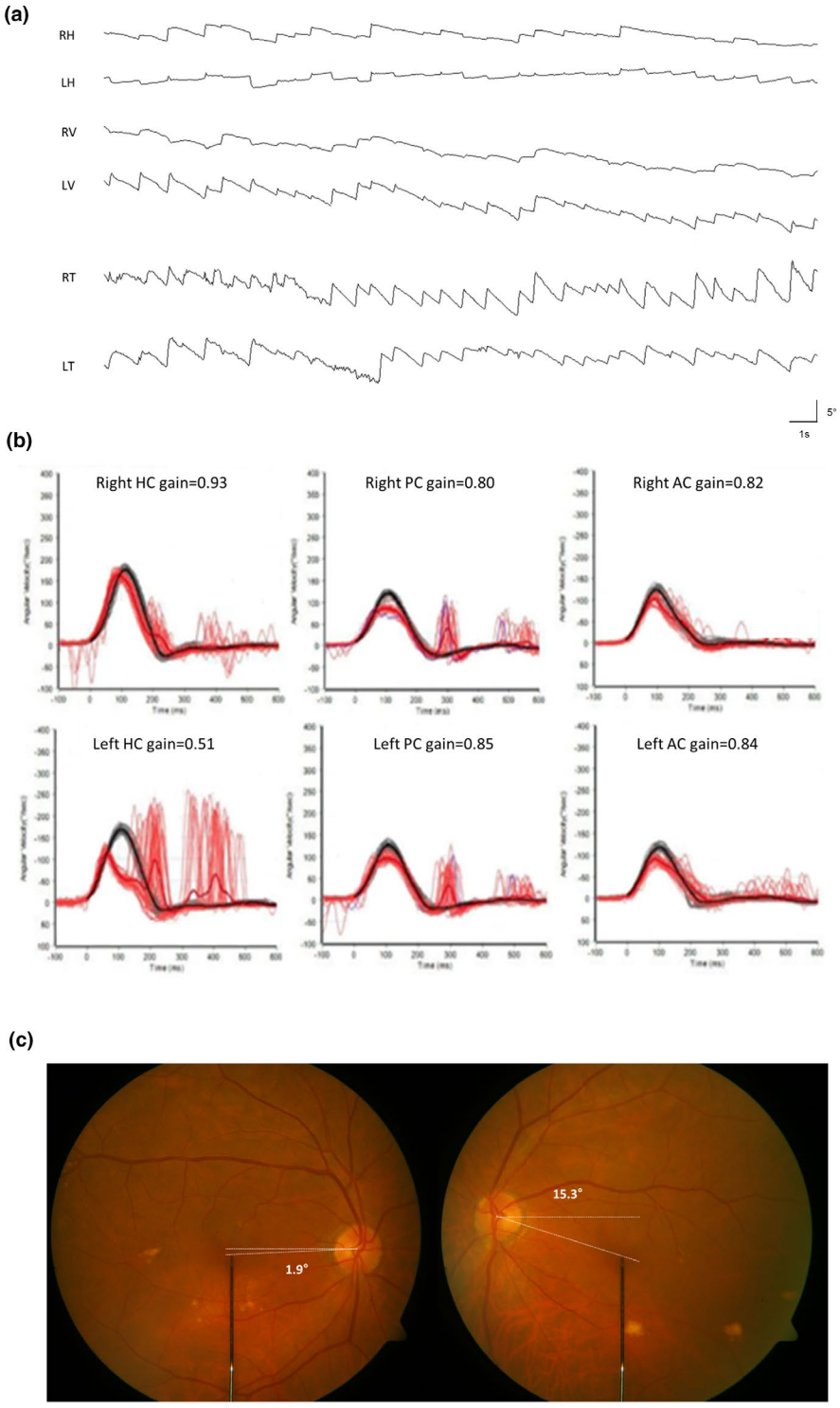

FIGURE 6 Ocular motor findings in patient 17 with left VN infarction. (a) Video-oculography shows asymmetric contraversive torsional nystagmus (clockwise from the patient's perspective, right eye>left eye) with markedly asymmetric upbeat components (left eye>right eye). (b) Video head impulse tests reveal decreased vestibulo-ocular reflex gains for the left HC and both PCs. (c) Fundus photography discloses extorsion of the left eye (15.3°; normal range, 0°–12.6°). AC, anterior semicircular canal; HC, horizontal semicircular canal; LH, horizontal position of left eye; LT, torsional position of left eye; LV, vertical position of left eye; PC, posterior semicircular canal; RH, horizontal position of right eye; RT, torsional position of right eye; RV, vertical position of right eye; VN, vestibular nucleus.

involving larger numbers of patients in multiple centers are needed to verify our results. We defined the involved structures based on MRI findings rather than on clinical features. Although the involved structures were independently assessed by two experts blinded to clinical information, it might be impossible to exactly delineate the involved structures based only on imaging findings. Thus, it remains possible that multiple structures including the vestibular subnuclei and ICP had been compromised in various combinations.

CONCLUSION

This study has demonstrated that patients with unilateral DLP lesions frequently present isolated AVS with a broader range of eye-movement abnormalities than previously documented. These characteristics may be due to the complex involvement of afferent or efferent fibers to and from the VN within the DLP. Since false-negative initial MRI results are also common in DLP infarctions, it

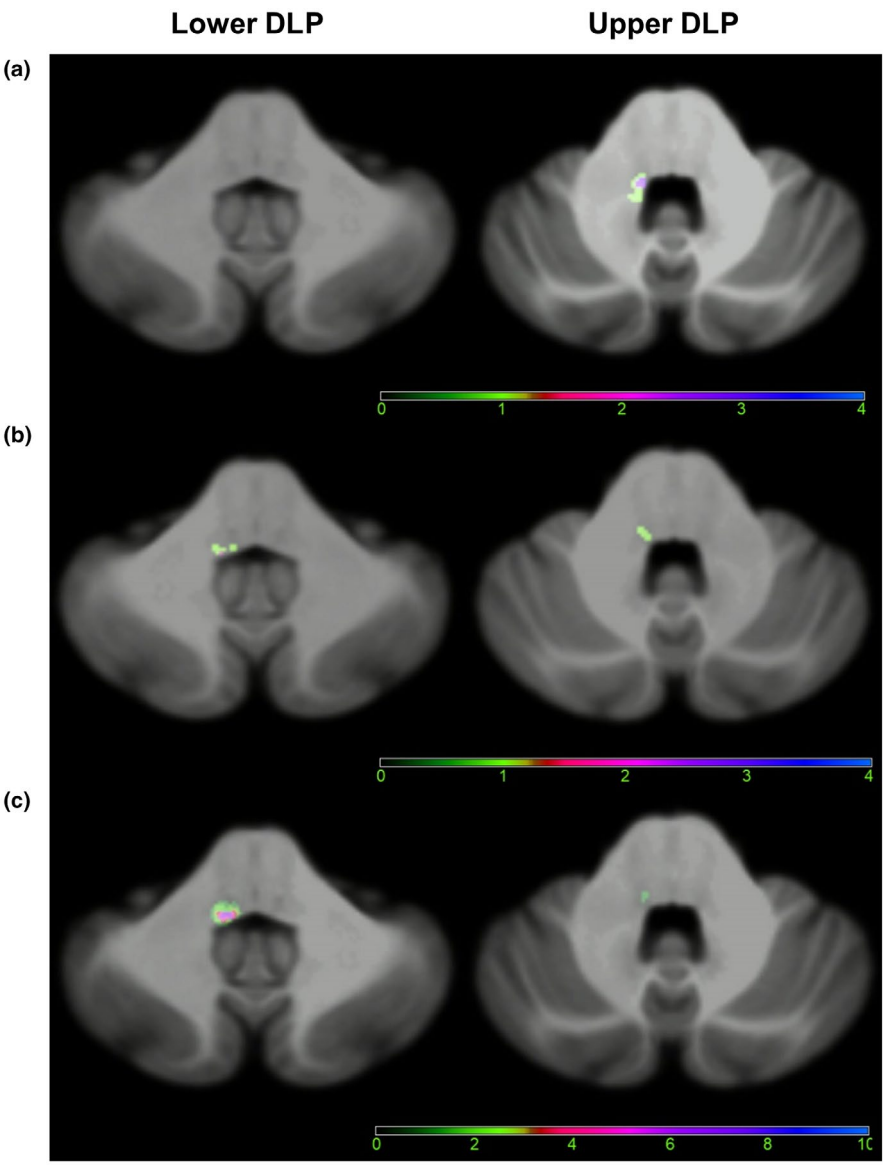

FIGURE 7 Results from lesion mapping analysis in patients with unilateral DLP lesions. In overlay plots, ICP lesions are located on the lateral wall of the fourth ventricle in the upper DLP (a), whereas VN lesions are mainly on the floor of the fourth ventricle at the level of the lower DLP (b and c). The distribution of VN lesions does not differ between patients with typical (b) and atypical (c) ocular motor abnormalities. The color scale represents the number of patients who had a lesion in the area shown on the map. DLP, dorsolateral pons; ICP, inferior cerebellar peduncle; VN, vestibular nucleus.

is essential to thoroughly examine abnormal eye movements when diagnosing this type of stroke in patients with AVS.

AUTHOR CONTRIBUTIONS

Hyun Sung Kim: Conceptualization; data curation; investigation; writing – original draft. **Jae-Hwan Choi:** Conceptualization; data curation; investigation; methodology; supervision; writing – review and editing. **Eun Hye Oh:** Conceptualization; data curation; investigation; methodology. **Seo Young Choi:** Conceptualization; data curation; investigation; methodology. **Kwang-Dong Choi:** Conceptualization; data curation; funding acquisition; investigation; supervision; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

All authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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