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Episodic Dizziness with Bradykinesia of Unilateral Upper Limb related to Hypertensive Ischemic Leukoaraiosis of Unilateral Frontal Lobe

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Episodic dizziness/vertigo can be attributed to many etiologies, but it is impressed with a central lesion if complicated with a movement disorder. A 55-year-old man had daily episodic dizziness with left-hand bradykinesia for eight years. Hypertension was noted in the afternoons. A vestibular function test showed that he could not gaze ahead steadily during a head thrust test. The left-hand movement was tremulous, rigid and slower than that of the right hand. An electronystagmogram revealed abnormal pursuit, saccade and optokinetic nystagmus. Magnetic resonance imaging showed white matter change in the right frontal lobe. Extracranial neck color-coded duplex scanning showed lower cerebral blood flow and higher resistance index when the patient was symptomatic than at other times. Thus, an oral β-antagonist, atenolol, 100 mg was given daily. The patient had no symptoms over the following year. The clinical history, radiological findings, and neurological study attributed his episodic dizziness with left-hand bradykinesia to hypertensive ischemic leukoaraiosis of the right frontal lobe.

Key words: frontal lobe, hypertension, electronystagmogram, extrapyramidal dysfunction

INTRODUCTION

Episodic dizziness/vertigo might be attributed to cervical origins, peripheral vertigo, migrainous vertigo, vertebrobasilar insufficiency, dysautonomia causing orthostatic hypotension, intracranial hypotension, intracranial hypertension and other causes. In most cases, a central lesion is highly suspected if the episodic dizziness/vertigo is complicated with a movement disorder. Leukoaraiosis is defined as a periventricular white matter lesion with a hyper-intense signal on T2 magnetic resonance imaging (MRI) or fluid-attenuated inversion recovery (FLAIR) MRI, and no prominent hypo-intense signal on T1 MRI. It has been thought of as cerebral ischemia from hypoperfusion in the distal deep arterial or arteriolar territories, associated with aging, hypertension and various cerebrovascular risk factors, rather than hyperlipidemia or diabetes mellitus.[1-3] Ischemic leukoaraiosis is defined as radiological leukoaraiosis with a clinical history of lacunar stroke.[4] Herein, we describe a patient with hypertensive ischemic leukoaraiosis of a unilateral frontal lobe, which causes daily episodic dizziness and bradykinesia of unilateral upper limb.

CASE REPORT

Our patient was a 55-year-old man who worked in a tea factory. His height was 160 cm; body weight, 76 kg; and body mass index, 29.7kg/m^2. He had smoked a pack of cigarettes daily for over 20 years. He was not addicted to alcohol, areca or any drugs. He did not have diabetes mellitus, heart disease or other systemic diseases, but had experienced a holocephalic throbbing headache once or twice per year since he was a teenager. The duration was between 4 and 6 hours, accompanied by phonophobia, photophobia, nausea and vomiting. It was induced by insomnia the previous night. A visual aura, vertigo and bilateral tinnitus were noted before each episode. Insomnia-related basilar-type migraine had been diagnosed (the International Classification of Headache Disorders, 2nd edition).

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Since 1999, he had daily episodes of dizziness. Symptoms always occurred in the late afternoon, accompanied by nausea, vomiting, and left-side bradykinesia. The duration was between 30 minutes and 1 hour. Bed rest or closing his eyes relieved the dizziness. There was no headache, tinnitus, paresthesia, phonophobia, photophobia or other neurologic signs.

The patient experienced one of these afternoon episodes just when visiting the author's clinic. His blood pressure was 161/101 mmHg with a heart rate of 79/min. He was alert and oriented to time, place and person. His mini-mental state score was 30. His muscle power in the four limbs was grade 4 (Medical Research Council Scale). Deep tendon reflexes in all four limbs were symmetrically normal. Both sides of his body, including the limbs and trunk, were sensitive to pain on a pinprick test (10/10). Taste sensations to bitter, salty and sweet stimulants were all intact. There was no gaze nystagmus, positional nystagmus or positioning nystagmus. The Romberg test, tandem gait and tests for head-shaking, and orthostatic hypotension showed no abnormalities, but he could not gaze ahead steadily during a head thrust test. Tests for diadochokinesia and finger-to-nose tracing showed accurate targeting of both hands, but the left-hand movement was tremulous, rigid and slower than that of the right hand. Over the following two weeks, a battery of exams was performed and he was asked to record daily his blood pressure and heart rate in the morning and afternoon.

During an episode of dizziness, extracranial neck color-coded duplex scanning revealed mild atherosclerosis of the bilateral common carotid arteries, internal carotid arteries and carotid bodies. The total average cerebral flow was 632.2 mL/min (Table 1A). An electronystagmogram revealed that horizontal gaze, vertical gaze, and optokinetic after-nystagmus were normal, but pursuit, saccade and optokinetic nystagmus were abnormal (Figure 1). A caloric test (20°C, 20 secs) was normal with positive visual suppression. An air-conducted vibration cervical vestibular evoked myogenic potential test (ACV-cVEMP) revealed that the latency (amplitude) of p13 and n23 were 14.09 msec (-13.49 μV) and 22.73 msec (11.69 μV) in the right side, and 13.46 msec (-11.79 μV) and 21.27 msec (17.81 μV) in the left side, respectively. Other blood serum biochemistry, thyroid function, immunology, and virology tests were all within normal limits. His blood pressure recordings for two weeks were 116.6±5.0/70.9±3.9 (average±standard deviation) mmHg with a heart rate of 63.9±3.8/min in the morning, and 157.7±3.9/101.1±3.9 mmHg with 86.4±2.5/min in the afternoon.

Table 1 Extracranial neck color-coded duplex scanning (EnVisor, Philips, USA)

	A: symptomatic				B: follow-up			
	Vertebral artery		Internal carotid artery		Vertebral artery		Internal carotid artery	
	Right	Left	Right	Left	Right	Left	Right	Left
Diameter (mm)	4.18	3.74	4.11	4.86	4.19	3.81	4.18	4.88
Average velocity (cm/sec)	11.4	11.7	24.8	23.7	13.5	14.1	26.9	26.5
Average flow (mL/min)	93.9	77.1	197.4	263.8	111.7	96.4	221.5	297.4
Resistance index	0.69	0.70	0.54	0.51	0.53	0.56	0.52	0.50
Total average cerebral flow	632.2 mL/min				727.0 mL/min			

T1 MRI showed no abnormalities, but white matter change with a mild hypo-intense signal was noted in the right frontal lobe (Figure 2A). Both T2 and FLAIR MRI showed that the lesion had a hyper-intense signal (Figure 2B), which was more of upward extension by diffusion-weighted imaging (Figure 2C) than by T1, T2 or FLAIR MRI.

The patient was prescribed an oral β-antagonist, atenolol, 100 mg daily. One week later, the dizziness had subsided, and his blood pressure was 137/83 mmHg with a heart rate of 83/min in the afternoon. Thereafter, he was prescribed the same anti-hypertensive medication. He had no recurrence of dizziness over the following year. A series of follow-up studies showed that tests for diadochokinesia and finger-to-nose tracing did not show any abnormality. Extracranial neck color-coded duplex scanning showed a total average cerebral flow of 727.0 mL/min (Table 1B). Blood pressure recordings for two weeks was 122.6±2.2/69.9±2.9 mmHg with a heart rate of 64.0±1.7/min in the morning, and 128.1±3.2/72.5.1 ±2.3 mmHg with 64.2±2.7/min in the afternoon. Although T1, T2 and FLAIR MRI disclosed the same lesion as before in the left frontal lobe, the hyper-intense signal was decreased in diffusion-weight imaging (Figure 2D).

DISCUSSION

The orthostatic hypotension test in our patient was negative, so dysautonomia was unlikely to be the cause of his dizziness. In one study, subjects with hypertension suffered dizziness/vertigo more frequently than those in a

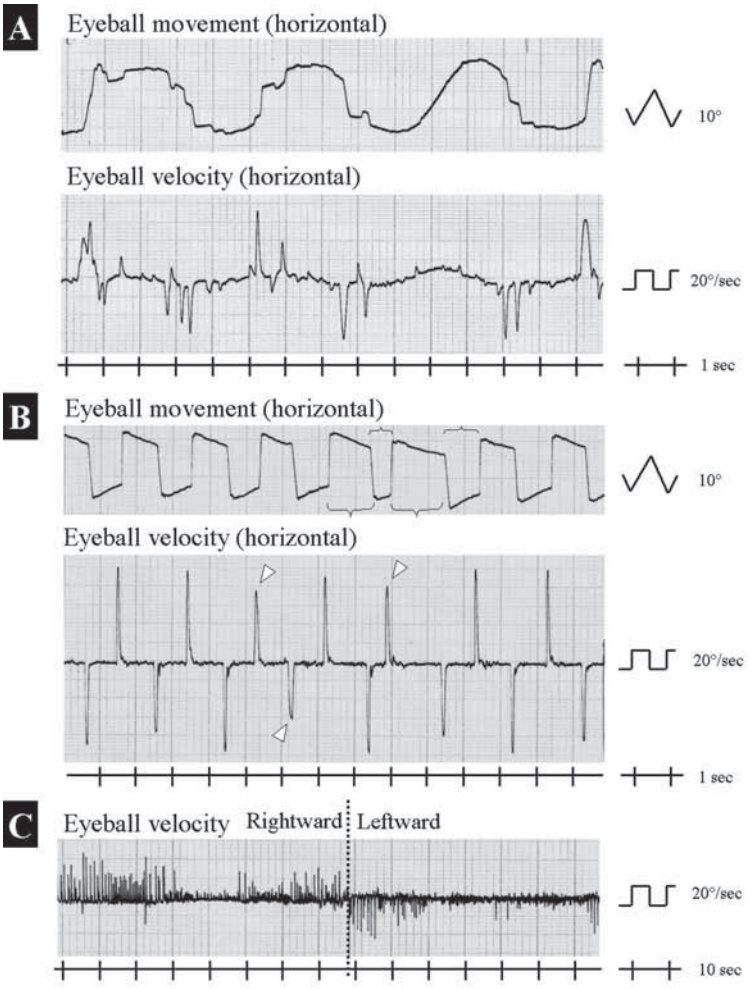

Fig. 1 **A:** The electronystagmogram shows unsmooth trace of pursuit, with spiking waves in its velocity phase. **B:** Saccade shows the several square waves (brackets) are irregular in its movement phase, and the amplitudes of several waves (hollow arrow-head) are either not regular in its velocity phase. **C:** Optokinetic nystagmus shows poor manifestations bilaterally. Neither slow velocity phase nor fast velocity phase presents as an arc form.

control group, possibly because of cochlear dysfunction associated with hypertensive vascular disease,[5] or brainstem hypertensive encephalopathy associated with hypertensive crisis.[6,7] Because our patient's dizziness was accompanied by high blood pressure as well as tremor and bradykinesia of left upper limb, extrapyramidal system impairment from hypertension-related encephalopathy was highly suspected. The pinprick test and deep tendon reflex test were normal, and the targeting movements of diadochokinesia and finger-to-nose tracing were accurate, indicating that the sensory system, pyramidal system and cerebellum were not involved. Although his head-shaking test was normal, he could not gaze ahead steadily during a head thrust test, indicating that the problem was beyond the central or peripheral vestibule.

Pursuit tests investigate the occipito-mesencephalic system, which passes through the occipital lobe, brainstem (midbrain and pons), and is modulated by the caudate nucleus and flocculus.[8,9] In addition, assessment of visual motion direction and programming appropriate eye movements of pursuit are also modulated by the frontal cortex.[10] Saccade tests investigate the fronto-mesencephalic system, which passes through the frontal lobe, superior colliculus and brainstem (pons), and is modulated by the caudate nucleus and vermis.[8,9] Optokinetic nystagmus tests, composed of 1) a slow eyeball-movement phase during the pursuit test and 2) a fast eyeball-movement phase during the saccade test, investigate the frontal lobe, occipital lobe and their projection, with a pathway through the brainstem, modulated by the vermis and flocculus.[11] In the patient, abnormal pursuit (Figure 1A), abnormal saccade (Figure 1B) and abnormal optokinetic nystagmus (Figure 1C) imply two conditions: (1) impairment of the frontal cortex, or (2) impairment of both the occipital-mesencephalic and the fronto-mesencephalic system.

Optokinetic after-nystagmus follows optokinetic nystagmus and implicates control of the vestibular nucleus on optokinetic nystagmus.[12] The caloric test investigates the vestibular ocular reflex pathway, which passes through the upper brainstem. In addition, its visual suppression implicates the function of the flocculus.[13] In healthy Taiwan adults, the latencies of ACV-cVEMP p13 and n23 are 16.3±3.2 and 24.4±5.0 (average±two standard deviations) msec, respectively.[14] In our patient, normal optokinetic after-nystagmus and normal caloric tests indicated that the caudate nuclei, upper brainstem, and cerebellum were well. In addition, the latencies of ACV-cVEMP p13 and n23 were all within the reference range, so his inferior vestibular nerve, vestibular nuclei and lower brainstem were free of illness.

The resistance index of both internal carotid arteries was in the acceptable range (< 0.75), but was higher when the patient was symptomatic than at other times. In addition, the total average cerebral flow was lower when he was symptomatic (Table 1). Furthermore, when

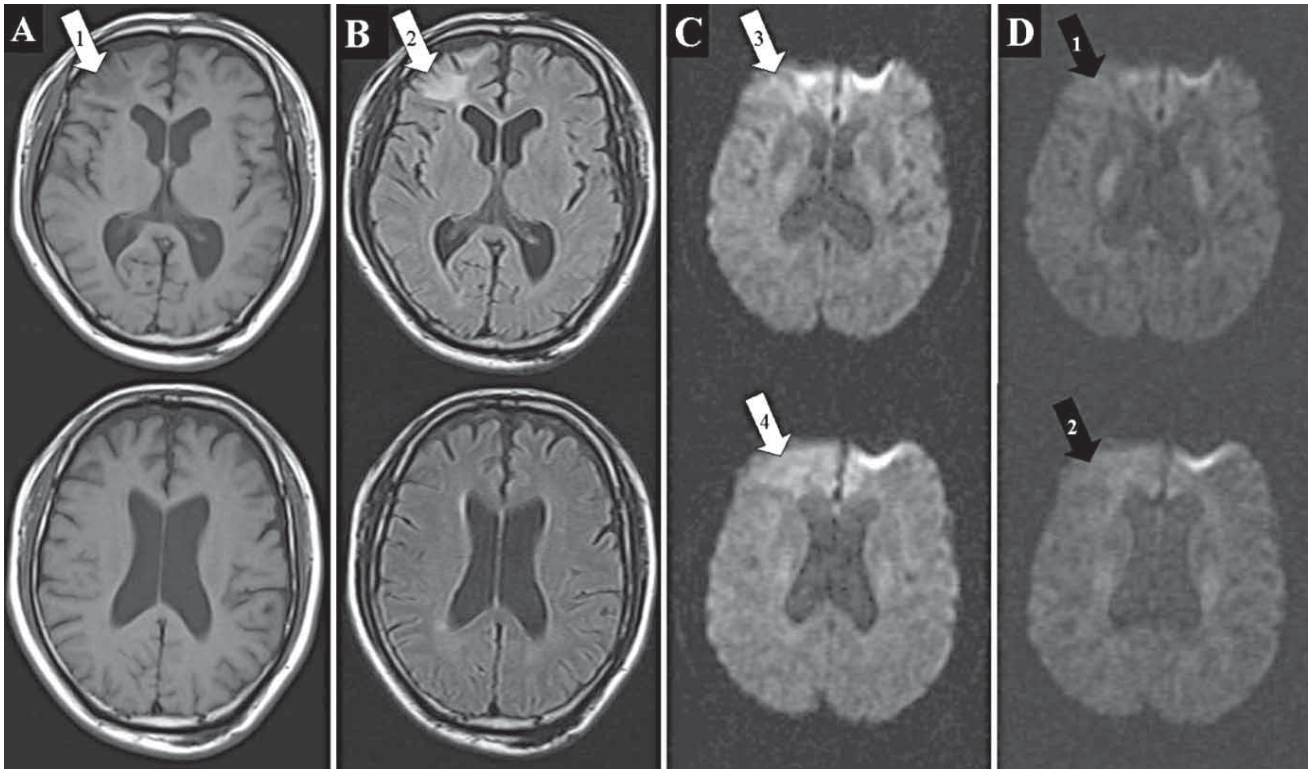

Fig. 2 **A:** T1 MRI (TR/TE/excitation: 500/12/1) shows a patchy of mild hypo-intense signal in the right frontal lobe (hollow arrow 1), and dilatation of lateral ventricles. **B:** FLAIR MRI (TR/TE/excitation: 6,000/84/1) shows a white matter change of hyper-intense signal in the right frontal lobe (hollow arrow 2). **C:** Diffusion-weighted imaging (TR/TE/excitation: 8,374/148/1) shows the ischemic change of white matter (hollow arrow 3) is more of upward extension (hollow arrow 4) than T1 and FLAIR MRI. **D:** Although the follow-up T1, T2 and FLAIR MRI still disclose the same as before, diffusion weighted imaging (8,374/148/1) shows the ischemic change of white matter is reduced (filled arrow 1&2).

he was symptomatic, the total average blood flow of the vertebral arteries was 171.0 mL/min, which is in the acceptable range (> 100 mL/min), so vertebrobasilar insufficiency was excluded. There is a relationship between migraine and white matter change, regardless of comorbidities.[15] However, Kruit et al.[16] considered migraine an independent risk factor for white matter change, especially that over the posterior circulation territory. Therefore, the relationship between migraine and white matter change should be addressed in the future. In our patient, basilar-type migraine did not recur in the past eight years, so white matter change is hardly related to migraine.

The patient had hypertension in the afternoon for eight years. The long-term hypertension contributed to atherosclerosis of not only the bilateral carotid arteries but also the intracranial arteries, resulting in leukoaraiosis in the right frontal lobe.[1] We suggest that at the onset of each episode of hypertension, intracranial hypertension facilitated vasogenic cerebral edema, not only influencing the extrapyramidal system but also restricting the compliance of the intracranial arteries and increasing their vascular resistance. As a result, the total cerebral blood flow decreased contrarily (Table 1A), inducing ischemic changes in the right frontal lobe, and aggravating the white matter change (Figure 2C).[4]

The white matter change in the right frontal lobe influenced our patient's visual target selection, and it is thus evident that pursuit, saccade and optokinetic nystagmus showed impairment (Figure 1). Surprisingly, his recognition and personality were spared, indicating that the prefrontal-subcortical circuit remained well. During body motion, his vision did not coordinate with vestibular input, so dizziness occurred. Bed rest or closing his eyes relieved the dizziness by excluding vestibular or visual factors. Furthermore, the white matter change impeded to some extent the right motor cortex from mastering the right caudate nucleus, so extrapyramidal dysfunction was noted over the left upper limb.

To sum up, hypertensive ischemic leukoaraiosis of the right frontal lobe was confirmed. There is no effective strategy for treatment other than control of hypertension. Therefore, blood pressure control was recommended to prevent further cerebrovascular complications. To prevent basilar-type migraine, a β-antagonist was first recommended.[17] Over the following year, his hypertension was well controlled. Dizziness, bradykinesia and basilar-type migraine did not recur. The difference between the morning and afternoon blood pressure readings also decreased. Although T1, T2 and FLAIR MRI disclosed the same irreversible leukoaraiosis of the right frontal lobe, the ischemic hyper-intense signal was reduced in diffusion-weight imaging (Figure 2D), further proving that his daily episodic dizziness with bradykinesia of unilateral upper limb was related to hypertensive ischemic changes in the lesion.

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