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Spontaneous inversion of nystagmus without a positional change in the horizontal canal variant of benign paroxysmal positional vertigo

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Abstract.
OBJECTIVE: We investigated the neuro-otological findings, including nystagmus, and the clinical course of patients with the horizontal canal variant of benign paroxysmal positional vertigo (HC-BPPV), who showed spontaneous inversion of nystagmus without a positional change. Furthermore, we speculated on the possible mechanism of spontaneous inversion of nystagmus without a positional change.
PATIENTS AND METHODS: The characteristics of spontaneous inversion of positional nystagmus without a positional change were analyzed in 7 patients with HC-BPPV.
RESULTS: All patients were diagnosed as having HC-BPPV. During the positional test, the spontaneous inversion of nystagmus was observed in the same head position in all patients. Spontaneous inversion was observed on both sides in 5 patients, and only on 1 side in 2 patients. All patients presented with geotropic nystagmus in the first phase, and ageotropic nystagmus in the second phase.
CONCLUSIONS: The coexistence of cupulolithiasis and canalolithiasis appears to be a possible mechanism of the spontaneous inversion of positional nystagmus.

Keywords: Horizontal canal BPPV, lateral canal BPPV, positional nystagmus, benign paroxysmal vertigo

1. Introduction

The horizontal canal variant of benign paroxysmal positional vertigo (HC-BPPV) is characterized by a bi-directional-changing positional nystagmus with a positional change, and involves 2 types of nystagmus, namely, geotropic (beating to the ground) and ageotropic (beating away from the ground). Canalolithiasis and cupulolithiasis may both play a role in HC-BPPV, and can occur with the head turned to either side. Geotropic nystagmus presumably results from the accumulation of otoconial clots in the long arm of the horizontal semicircular canal (HSC). When the head is rapidly turned to the abnormal side, the mass accelerates downward in the canal. Movement of the clot within the canal results in an ampullopetal deviation of the cupula and a burst of geotropic nystagmus. When the clot stops moving, the cupula returns to its primary position. Rotation of the head to the opposite

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side causes the clot to move in the opposite direction and produces ampullofugal displacement of the cupula and geotropic nystagmus. This pathological condition is referred to as canalolithiasis. Persistent direction-changing ageotropic nystagmus that is detected in the supine roll test is often associated with a pathological condition involving otoconial debris attached to the cupula of the HSC ampulla [2,3,10,11]. This pathological condition is generally referred to as cupulolithiasis. Ageotropic nystagmus also results from the accumulation of otoconial clots within the short arm of the HSC or within the ampullary segment of the long arm of the HSC [6].

Some patients with HC-BPPV present with spontaneous inversion of nystagmus without a positional change; in other words, biphasic nystagmus sometimes occurs in the same head position during the positional test. Namely, when the patient's head is turned to 1 side in the supine position, a horizontal paroxysmal nystagmus occurs and regresses; and when the head is subsequently kept on the same side, static opposite-direction nystagmus occurs. The spontaneous inversion of nystagmus without a positional change has already been reported by Stahle and Terins in 1965 [13]; they called the second nystagmus attack as the secondary period, which has also been described briefly in earlier reports [1,5,8,9]. Meilleure et al. [8] reported that nystagmus inversion without a change in head position is often observed, and that the secondary nystagmus is ageotropic and less paroxysmal with a smaller amplitude and frequency. They also reported that nystagmus inversion was observed on the pathological side and never on the contralateral side [8]. Lee et al. [5] reported that nystagmus inversion was observed on both sides in 5 out of 21 patients, and on 1 side in 16 patients.

To date, three theories have been proposed to explain why spontaneous inversion occurs. The first theory stated that nystagmus inversion can be explained by sensory adaptation or reversal of direction of otoconial clot movement due to gravitational forces [8]. Baloh et al. [1] reported that nystagmus inversion without a change of head position is common when the initial nystagmus is brisk. The second theory by Pagnini et al. [12] stated that ageotropic second-phase nystagmus is caused by a spontaneous reflux of endolymph between the debris in the canal and the membranous walls. The third theory by Lee et al. [5] stated that the co-existence of canalolithiasis and cupulolithiasis may generate initial geotropic nystagmus, followed by a transition into ageotropic-predominant nystagmus.

We encountered 7 patients with spontaneous inversion of positional nystagmus without a positional change in the positional test, and 5 of the 7 patients showed nystagmus inversion not only on the pathological side, but also on the contralateral side. In these patients, although the initial nystagmus was not brisk, nystagmus inversion still occurred. Previous reports did not sufficiently describe the mechanism of the second-phase nystagmus that occurs on both sides, which occurs even when the initial nystagmus is not brisk. In this study, we describe the neuro-otological findings, including nystagmus, and the clinical course of patients with HC-BPPV who showed a spontaneous inversion of nystagmus without a positional change. We also speculate on the possible mechanism of the nystagmus inversion.

2. Patients and methods

From October 2011 to March 2013, there were 66 patients with HC-BPPV in our clinic. In these patients, we encountered 7 patients (1 man and 6 women; 41 to 69 years of age) with HC-BPPV, who showed spontaneous inversion of horizontal nystagmus without a positional change in the positional test. The patients were referred for a neuro-otological work-up owing to their vertigo. Examinations included pure tone audiometry and basic neuro-otologic examinations, such as the cranial nerve examination, the Romberg test, the eye-tracking test, and the optokinetic nystagmus test; the results of these tests were normal. Nystagmus tests, including the gaze test, positional test, and positioning test were performed. The positional test and positioning test were performed while the patients' eyes were open and covered with an infrared CCD camera [4].

The positional test was performed by placing patients in the following positions: the supine position, head to the right while in the supine position, and head to the left while in the supine position. The patients were kept in the same position (head to the left or head to the right) to search for static positional nystagmus after turning of the head [4].

The paroxysmal positioning test was performed in the supine position and the sitting position in the pitch plane. Patients were moved rapidly from the sitting position to the supine position and from the supine position to the sitting position [4]. The positional test and the paroxysmal positional test were performed without visual fixation.

Positional nystagmus was analyzed using a macro program in Image J (National Institutes of Health,

USA), which was provided from the Department of Otolaryngology, Yamaguchi University, Japan. We measured the direction and maximal slow-phase velocity (SPV, °/s) of positional nystagmus, and studied the characteristics of the spontaneous reversal of positional nystagmus.

3. Results

Results of the general, neurologic, and otologic examinations of all 7 patients were normal (Table 1). In the neuro-otologic examination, no nystagmus was detected using a CCD camera when the patients were sitting. In the positioning test, horizontal nystagmus was observed in 2 patients when they were moved from the supine position to the sitting position. None of the patients showed vertical nystagmus in the positioning test. In the positional test, all patients developed horizontal direction-changing nystagmus (either geotropic or ageotropic), and they were all diagnosed as having HC-BPPV. Also during the positional test, spontaneous inversion of nystagmus was observed in the same head position in all patients. Spontaneous inversion was observed on both sides in 5 patients, and on only 1 side in 2 patients. All patients presented with geotropic nystagmus in the first phase, and once it attenuated, there was a short interval, and then the second-phase ageotropic nystagmus appeared. The first-phase geotropic nystagmus was paroxysmal in character, involving a rapid increment and a slow decrement. The second-phase ageotropic nystagmus was nonparoxysmal and long lasting. The SPV of the first-phase geotropic nystagmus was 11°/s to 127°/s, and the SPV of the second-phase ageotropic nystagmus was 1°/s to 10°/s. The duration of the nystagmus-free interval between the first phase and the second phase was 3 to 8 seconds.

The period to recovery (defined as the disappearance of nystagmus) from the first hospital visit was 5 to 14 days, with an average of 7.6 days. The number of visits from the initial visit to the time of recovery was 2 to 4 times. In all patients, dizziness disappeared concurrently with the disappearance of nystagmus.

A positional maneuver for treating HC-BPPV, which consisted of a single 270° rotation around the yaw axis (barbecue rotation) in rapid steps of 90° with 30-second intervals, was performed in 6 of the 7 patients [7]. After performing the positional maneuver for treating HC-BPPV, nystagmus disappeared in 2 patients and geotropic nystagmus disappeared and apogeotropic nystagmus remained in 4 patients.

4. Case report

We here present the case of 1 of the 7 patients with HC-BPPV that we encountered.

4.1. Case 3: 69-year-old man

Previous history: Obstructive sleep apnea syndrome and hypertension.

Present illness: The patient developed dizziness and positional vertigo after he fell and bruised his hip. He underwent MRI of the head at a nearby hospital, but no abnormalities were detected. The patient then visited our hospital for detailed investigation of positional vertigo. He showed no hearing loss in either ear. No nystagmus was detected using a CCD camera when the patient was in the sitting position. The positional test revealed direction-changing geotropic nystagmus, and the nystagmus on both sides was paroxysmal and attenuated. The left-beating horizontal nystagmus in the left-lateral position was stronger than the right-beating horizontal nystagmus in the right-lateral position. The patient was diagnosed as having HC-BPPV affecting the left ear. The positional maneuver for treating HC-BPPV [7] was performed. At the second visit, the patient still had direction-changing positional nystagmus, showing spontaneous inversion of direction on both sides during the positional test. In the right-ear-down position, right-beating horizontal nystagmus developed and then attenuated, and when the same position was maintained, the second-phase left-beating horizontal nystagmus appeared (Fig. 1A). In the left-lateral position, left-beating paroxysmal nystagmus appeared and then attenuated, and when the left-ear-down position was maintained, secondary right-beating nystagmus developed (Fig. 1B). The positional maneuver for treating HC-BPPV [7] was performed. The patient showed ageotropic direction-changing nystagmus without directional inversion 2 days later, and this nystagmus disappeared spontaneously 3 days later.

5. Discussion

The spontaneous inversion of positional nystagmus without a positional change has already been reported by Stahle and Terins in 1965 [12], but the mechanism involved is still unclear.

Pagnini et al. [12] reported that the secondary nystagmus has a lower velocity and lasts longer than the primary nystagmus. All our patients had geotropic nys-

Table 1
Clinical summary of the patients with HC-BPPV who show spontaneous inversion of positional nystagmus without a positional change

Case	Age	Sex	Changing of nystagmus	Time to healing	SPV (°/s)			
					Rt ear down		Lt ear down	
					1st phase	2nd phase	1st phase	2nd phase
1	49	F	AGo→BI→DI	9 days	14	3	78	8
2	54	F	GE→BIo→AG→DI	7 days	11	4	41	/
3	69	M	GEo→BIo→AG→DI	5 days	18	4	5	4
4	42	F	GE→BI→DI	5 days	41	4	10	2
5	49	F	GE→BIo→AG→DI	7 days	32	/	127	10
6	63	F	BIo→AG→H/S→GE→DI	14 days	32	2	21	1
7	68	F	BIo→DI	6 days	74	5	8	1

The "o" indicates that the positional maneuver for treating HC-BPPV was performed at that point. The "/" indicates that the second-phase nystagmus was not observed and the SPV was not measured. AG: ageotropic; GE: geotropic; BI: biphasic; DI: disappearance; HS: head shaking; SPV: slow-phase velocity.

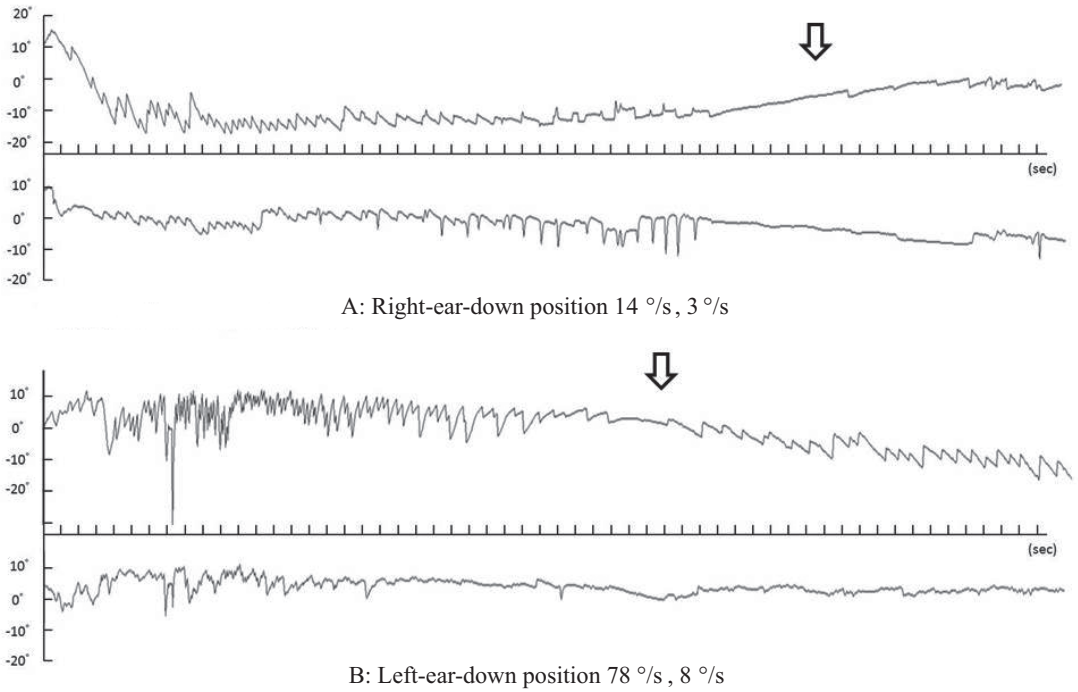

Fig. 1. Recordings of positional nystagmus of case 3, showing bilateral spontaneous inversion. A: The right-ear-down position elicits right-beating nystagmus (maximal velocity = 14°/s), with a spontaneous inversion to left-beating nystagmus (maximal velocity = 3°/s). B: The left-ear-down position elicits left-beating nystagmus (maximal velocity = 78°/s) with a spontaneous inversion to right-beating nystagmus (maximal velocity = 8°/s). The upper recording shows the horizontal component, and the lower recording shows the vertical component. Arrows indicate an inversion in nystagmus direction.

tagmus in the first phase and ageotropic nystagmus in the second phase; the first-phase geotropic nystagmus was paroxysmal with a rapid increment and a slow decrement, and the second-phase ageotropic nystagmus was nonparoxysmal and long-lasting, similar to the previous reports [8,12].

Meilleure et al. [8] also reported that nystagmus inversion was seen on the pathological side in 36 out of 63 patients with HC-BPPV, and it never occurred on the contralateral side. Lee et al. [5] reported that nystagmus inversion was observed on both sides in 5 out of 21 patients, and on 1 side in 16 patients. In our study, 5 out of 7 cases showed nystagmus inversion not only on the pathological side, but also on the contralateral side.

Baloh et al. [1] reported that nystagmus inversion without a change of position is common when the initial nystagmus is brisk. A reversal in the direction of SPV occurred when the SPV of the initial response exceeded 50°/s, and this phenomenon also occurred in

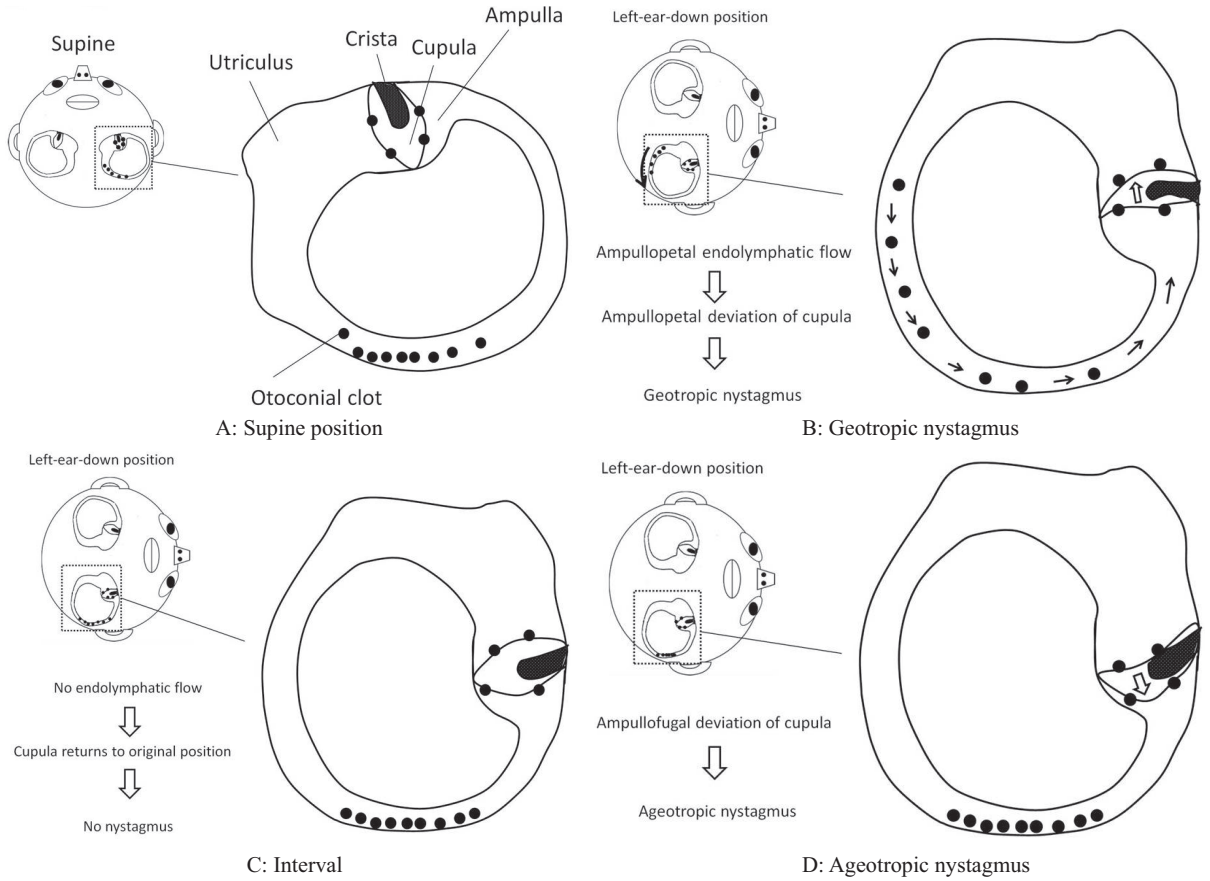

Fig. 2. Pathophysiological mechanism of spontaneous nystagmus inversion in left-side HC-BPPV. In the neutral supine position, debris clots are located in the lowest part of the horizontal canal, and some debris clots are also attached to the cupula (A). When the head is turned to the left side, the clots in the lowest part move toward the ampulla as the ampullopetal endolymphatic flow occurs. The endolymphatic flow induces an ampullopetal deviation of the cupula, giving rise to geotropic nystagmus (B). After the endolymphatic flow slows down, the cupula returns to its original position (C). Subsequently, the cupula is displaced to the ampullofugal side owing to the weight of the cupula and otoconial clots, giving rise to ageotropic nystagmus (D).

rotational-induced nystagmus after step changes in angular velocity, if the SPV of the primary response exceeded 50 or 60°/s. In the semicircular canal of the frog, mechanical stimulation of the ampullary nerve induces potassium shifting from the endolymph [13]. Upon excitation, the perilymphatic potassium concentration initially increases, and then gradually decreases owing to modulation of the Na^+/K^+-ATPase in the dark cells. Subsequently, a less intense but more prolonged undershoot period develops. The enhancement in nerve firing rate is responsible for the primary-phase nystagmus, and the undershoot period is responsible for the second-phase nystagmus [5,9,14]. However, this adaptation mechanism may not explain the reversal during head turning to the healthy side, because an increase in the perilymphatic potassium concentration and activation of the Na^+/K^+-ATPase should not occur by head turning to the healthy side, which inhibits the ampullary nerve [5].

Pagnini et al. [12] hypothesized that primary geotropic nystagmus is caused by the ampullopetal endolymphatic flow, resulting in the movement of clots in the semicircular canal upon a positional change. After cessation of the movement of the otoconial mass in the lower part of the canal, the deviated cupula returns to the ampullofugal side, generating the ampullofugal endolymphatic flow. The ageotropic second-phase nystagmus is subsequently caused by this ampullofugal endolymphatic flow.

Lee et al. [5] reported that the co-existence of canalolithiasis and cupulolithiasis may generate initial geotropic nystagmus, followed by a transition into ageotropic-predominant nystagmus. In our cases, we also speculate that the spontaneous inversion of po-

sitional nystagmus was caused by the co-existence of cupulolithiasis and canalolithiasis in the unilateral HSC. Degenerative debris clots may enter the non-ampullary side of the pathological horizontal side. Upon rolling of the head toward the pathological side, the debris sinks ampullopetally into the horizontal canal and causes geotropic nystagmus. After attenuation of the geotropic nystagmus and a short interval, the cupula is displaced ampullofugally and causes ageotropic nystagmus (Figs 2A-D). This hypothesis is consistent for our cases in which nystagmus occurred on both sides. In our cases, although the initial nystagmus was not brisk, nystagmus inversion still occurred.

Meilleure et al. [8] reported that the duration of the nystagmus-free intervals between the first-phase nystagmus and the second-phase nystagmus varied between 3 and 22 seconds. In our cases, the duration of the nystagmus-free intervals was 3 to 8 seconds. The nystagmus-free intervals appeared to correspond to the time during which deflection of the cupula from the ampullopetal to ampullofugal side occurred.

In this study, a single 270° rotation around the yaw axis (barbecue rotation) was performed in 6 of the 7 patients [7]. In 4 patients, the barbecue rotation was performed at the session in which spontaneous inversion of positional nystagmus without a positional change occurred, and at the next session, the geotropic nystagmus had disappeared and ageotropic nystagmus remained. From these results, we speculate that the spontaneous inversion of positional nystagmus in our patients was caused by the co-existence of cupulolithiasis and canalolithiasis in the unilateral HSC.

Studies of cupulolithiasis performed on animal models have demonstrated that the otoconia of cupulolithiasis may not easily detach from the cupula surface, because of the strong adhesion between the cupula and the otoconia [10,11]. All our patients developed direction-changing ageotropic nystagmus during the follow-up, but they all recovered relatively rapidly. One of our patients (case 6) showed direction-changing ageotropic nystagmus during the follow-up, as a result of performing head shaking to remove the clots from the cupula, and the direction-changing ageotropic nystagmus changed to direction-changing geotropic nystagmus. In the other patients, the direction of nystagmus changed several times during the follow-up. We speculate that the presence of otoconial clots in the semicircular canals and the cupula, both of which are likely to stick and detach, results in the coexistence of canalolithiasis and cupulolithiasis.

In all our patients, the slow-phase velocity of the second-phase nystagmus was slower than that of the first phase. We speculate that the amount of debris attached to the cupula is much smaller than that floating in the canal; therefore, we concluded that the geotropic nystagmus (inhibitory nystagmus) is stronger and faster than the apogeotropic nystagmus (excitational nystagmus).

We encountered 7 patients who showed spontaneous inversion of nystagmus without a positional change in HC-BPPV. All patients had geotropic nystagmus in the first phase and ageotropic nystagmus in the second phase; the first-phase geotropic nystagmus was paroxysmal with a rapid increment and a slow decrement, and the second-phase ageotropic nystagmus was nonparoxysmal and long-lasting. In our study, 5 out of 7 patients showed nystagmus inversion, not only on the pathological side but also on the contralateral side. From these features, we speculate that the spontaneous inversion of positional nystagmus in our patients was caused by the co-existence of cupulolithiasis and canalolithiasis in the unilateral HSC. As the number of cases in this study was small, the accumulation of cases and further studies are required in the future.

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Conflict of interest

The authors declare no conflicts of interest associated with this study.

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