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Transition Rates from Benign Paroxysmal Positional Vertigo to Persistent Postural-Perceptual Dizziness

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Abstract

Persistent postural-perceptual dizziness (PPPD) is a chronic dizziness disorder that is newly listed in the World Health Organization (WHO)'s International Classification of Diseases (ICD-11) revised in 2018. In this study, I selected definite cases of the first occurrence of benign paroxysmal positional vertigo (BPPV) among vertigo patients who visited our clinic in the past 1 year, and retrospectively reviewed the age at the first visit, gender, affected side, previous medical conditions, type of BPPV, and their tendency toward transition to PPPD. Eligible patients were new first-ever cases of BPPV who visited our clinic during the 1-year period from June 1, 2020, to May 31, 2021, and who met the diagnostic criteria for BPPV established by the Japan Society for Equilibrium Research. There were 311 cases, including 120 men and 191 women, with a male:female ratio of 1:1.6; hence, the majority of patients were women. The mean age ± standard deviation was 60.7 ± 17.8 years. Men ranged in age from 14 to 88 years, with a mean age of 64.2 ± 16.3 years. Women ranged in age from 11 to 90 years, with a mean age of 58.5 ± 18.5 years. Thus, the average age of the men was higher. As for the type of BPPV, there were 172 cases of posterior semicircular canal-type BPPV (canalolithiasis), 79 cases of lateral semicircular canal-type BPPV (canalolithiasis), and 60 cases of lateral semicircular canal-type BPPV (cupulolithiasis), with the posterior semicircular canal-type BPPV (canalolithiasis) being the most common. In regard to the affected side, the right side was affected in 164 cases and the left side in 147 cases; thus, involvement of the right side was more common. The time to remission was less than 0.5 months in 86 cases, less than 1 month in 69 cases, less than 2 months in 50 cases, less than 3 months in 22 cases, and more than 3 months in 57 cases. Remission was achieved in less than 3 months in 72.9% of cases. The course remained unknown in 27 cases, as the patients discontinued their clinic visits. There was only one case of a 75-year-old man and one case of a 70-year-old woman who transitioned to PPPD. Both cases had left-sided posterior semicircular canal-type BPPV (canalolithiasis). The man had underlying hypertension, while the woman had underlying hypertension and diabetes mellitus. The rate of transition from BPPV to PPPD was 0.6% when cases with an unknown course were included, and the rate was as low as 0.7% when cases with an unknown course were excluded. Thus, the frequency of transition from BPPV to PPPD is low.

Keywords

- persistent postural-perceptual dizziness
- benign paroxysmal positional vertigo
- dizziness

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Introduction

Persistent postural-perceptual dizziness (PPPD) is characterized by chronic dizziness as the chief complaint and has been newly listed in the 2018 revision of the 11th version of the International Classification of Diseases (ICD-11) provided by the World Health organization (WHO).[1] The diagnostic criteria listed by the Barany Society include lightheadedness as the chief complaint and unsteadiness or nonspinning vertigo persisting for at least 3 months. Furthermore, the patient must view moving objects and complex visual patterns, and symptoms must be aggravated by standing or walking as well as during active or passive body movements. Typically, PPPD is secondary to balance disorders, such as vestibular diseases. Although organic vestibular disorders or psychiatric diseases may be present as comorbidities or complications, they do not account for the symptoms[2–5] (►**Table 1**). To date, although cases of transition from peripheral vertigo disorders, such as Meniere's disease (MD) or benign paroxysmal positional vertigo (BPPV), to PPPD have been reported in Japan,[6,7] there is a paucity of data on the rate of and tendency to such transitions.

In this study, I describe the identification of first-onset cases of definite BPPV among patients with vertigo and then retrieve and retrospectively review the data for such cases, including age at the initial visit, sex, affected side, complications, type of BPPV, time to transition to PPPD, and the rate of transition to PPPD.

Materials and Methods

Among the patients who visited my clinic between June 1, 2020, and May 31, 2021, only those who had been newly diagnosed with BPPV as per criteria for definite diagnosis established by the Japan Society for Equilibrium Research were included in the study and their medical records were reviewed. The following data were retrieved for analysis: age at initial visit, sex, affected side, interval between the first vertigo episode and the initial visit, time to remission, hypertension, hyperlipidemia, diabetes mellitus, heart diseases such as arrhythmia, insomnia, migraine, complications such as psychiatric diseases, type of BPPV, rate of transition to PPPD, and time to transition to PPPD.

Definite BPPV was diagnosed according to the diagnostic criteria for dizziness and vertigo established by the Japan Society for Equilibrium Research. These diagnostic criteria are based on reference diagnostic criteria that were last revised in 2017.[8] Atypical cases and probable cases were excluded. All cases of PPPD met the diagnostic criteria established by the Barany Society in 2017.[2–4] Migraine was diagnosed based on International Headache Society (IHS) criteria.[9,10] Patients meeting both the Barany Society criteria and the IHS criteria were considered to have vestibular migraine (VM).[9–11] Patients whose medical interview results indicated a history of peripheral vertigo, such as vestibular neuritis or MD, and those suffering from recurrent peripheral vertigo were excluded. An infrared charge-coupled device (CCD) camera was used to check for nystagmus. Medical evaluation was conducted for hypertension, insomnia, hyperlipidemia, migraine, heart diseases such as arrhythmia, diabetes mellitus, and psychiatric diseases (e.g., any previous mental health clinic visits).

Time to remission (duration of clinic visits) was determined based on patient complaints during a follow-up period of up to 12 months after the initial visit. Remission was defined as improvement in both nystagmus and subjective symptoms, such as the entire spectrum of subjective dizziness, namely, lightheadedness and unsteadiness, as well as vertigo at the time of nystagmus provocation. Cases wherein follow-up visits were not completed because the

Table 1 Criteria for the diagnosis of persistent postural-perceptual dizziness (PPPD)

PPPD is a chronic vestibular disorder defined by criteria A–E below. All five criteria must be fulfilled to make the diagnosis:
A. One or more symptoms of dizziness, unsteadiness, or non-spinning vertigo are present on most days for 3 months or more
1. Symptoms last for prolonged (hours-long) periods of time, but may wax and wane in severity
2. Symptoms need not be present continuously throughout the entire day
B. Persistent symptoms occur without specific provocation; but are exacerbated by three factors:
1. Upright posture
2. Active or passive motion without regard to direction or position, and
3. Exposure to moving visual stimuli or complex visual patterns
C. The disorder is precipitated by conditions that cause vertigo, unsteadiness, dizziness, or problems with balance including acute, episodic, or chronic vestibular syndromes, other neurologic or medical illnesses, or psychological distress
1. When the precipitant is an acute or episodic condition, symptoms settle into the pattern of criterion A as the precipitant resolves, but they may occur intermittently at first, and then consolidate into a persistent course
2. When the precipitant is a chronic syndrome, symptoms may develop slowly at first and worsen gradually
D. Symptoms cause significant distress or functional impairment
E. Symptoms are not better accounted for by another disease or disorder

Source: Staab JP, Eckhardt-Henn A, Horii A, et al. Diagnostic criteria for persistent postural-perceptual dizziness (PPPD): consensus document of the committee for the Classification of Vestibular Disorders of the Bárány Society. J Vestib Res 2017;27(04):191–208.[2]

patient relocated or the visits were cancelled at the patient's discretion were recorded as having unknown outcome.

Results

Data from 311 cases (120 men and 191 women) were included, with a mean age (±standard deviation) of 60.7 ± 17.8 years. Men were aged 14 to 88 (mean age, 64.2 ± 16.3) years, whereas women were aged 11 to 90 (mean age, 58.5 ± 18.5) years; the mean age of men was higher (►**Fig. 1**).

►**Fig. 2** indicates the time elapsed between the first episode and the initial visit: within 3 days in 137 cases, within 7 days in 63 cases, within 14 days in 46 cases, within 21 days in 7 cases, within 28 days in 15 cases, and ≥29 days in 43 cases. These data indicate that 64.3% of the patients had their initial visit within 7 days of the first episode. BPPV type was posterior semicircular canal in 172 cases, lateral semicircular canal in 79 cases, and lateral semicircular canal in 60 cases. Thus, posterior semicircular canal BPPV was the most common form observed in this cohort. Furthermore, 164 and 147 cases were affected on the right and left sides, respectively, making the right side the most frequently affected side in this cohort.

►**Fig. 3** indicates that the time to remission from the initial visit was <0.5 months in 86 cases, <1 month in 69 cases, <2 months in 50 cases, <3 months in 22 cases, and ≥3 months in 57 cases. Treatment outcome was unknown in 27 cases as follow-up could not be completed. Moreover, 57 patients required ≥3 months to achieve remission; they represent patients who may be diagnosed with PPPD. Next, 11 (19.3%) patients were diagnosed with refractory disease due to nystagmus or persistent symptoms, 27 (47.4%) required long-term follow-up because of repeated symptom relapse despite improvement, 12 (21.1%) met the diagnostic criteria for VM and were diagnosed with VM/BPPV overlapping syndrome (VBOS, characterized by coexistence of episodic vertigo and VM),[12] and 5 (8.8%) were suspected of having VM or were refractory to BPPV treatment but showed improvement with concomitant migraine treatment; that is, it is unclear if they had VBOS or if symptoms were unrelated to episodic vertigo. Thus, there were only two cases (3.5%) of transition from BPPV to PPPD, yielding in a transition rate of 0.6% overall or 0.7% when the 27 cases with unknown outcomes are excluded. The two cases of transition were that of a 75-year-old man and a 70-year-old woman, and both patients had left-sided posterior semicircular canal-type BPPV.

Comorbidities included hypertension in 48 cases, hyperlipidemia in 33, heart disease in 28, diabetes mellitus in 22, and insomnia in 16 cases. Furthermore, 29 patients had migraine (multiple answers allowed) and 13 patients had

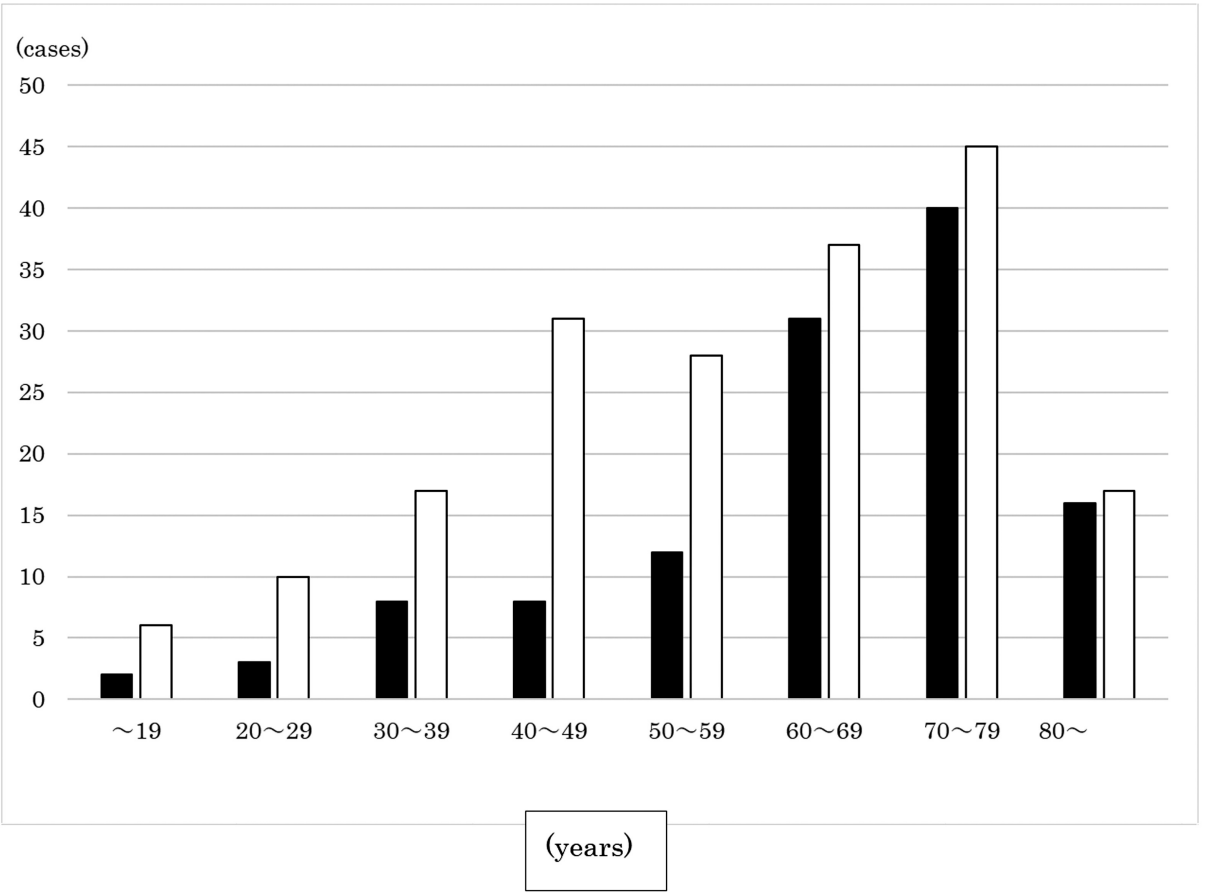

Fig. 1 Age and sex distribution patterns in patients with benign paroxysmal positional vertigo. ■ Men; □ Women. Patients aged 60 to 70 years accounted for the greatest proportion of both men and women and for ~50% of all patients included in this study.

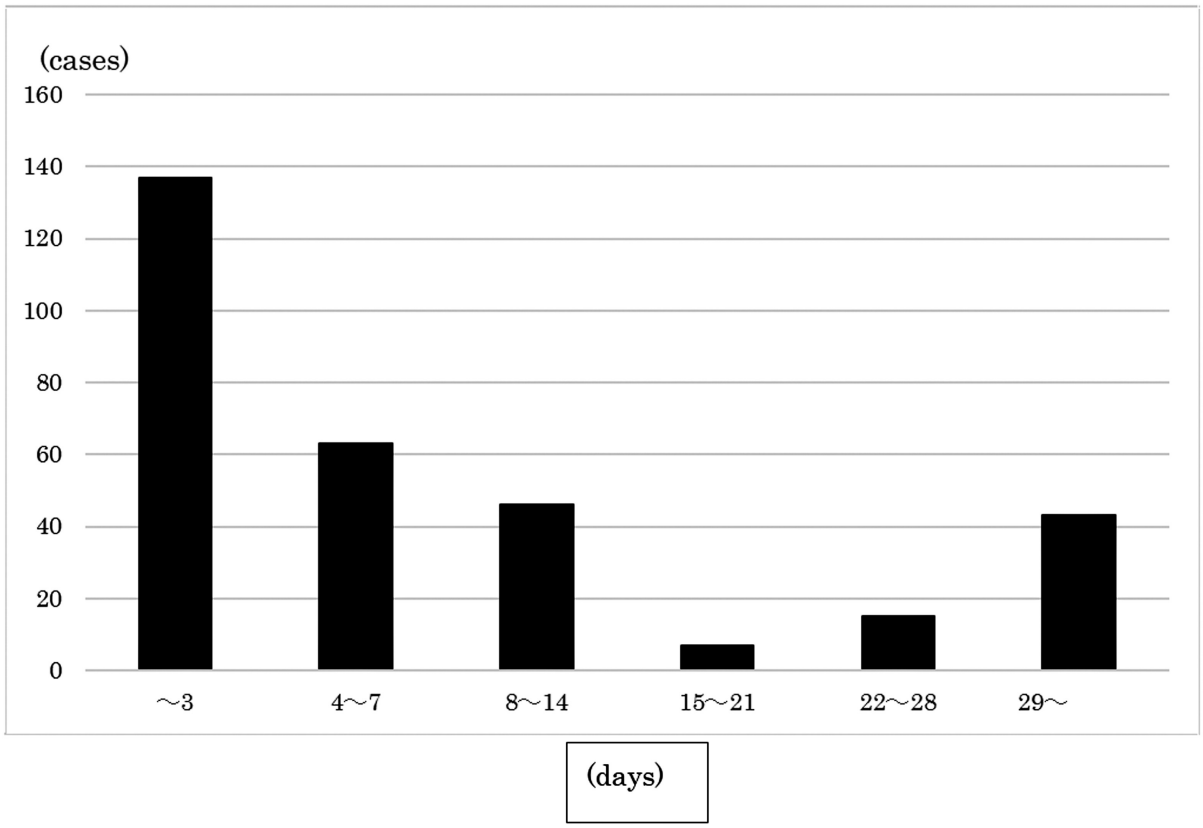

Fig. 2 Time interval (days) between the first episode and the initial visit. Of all the included patients, 64.3% had their initial visit within 7 days after onset.

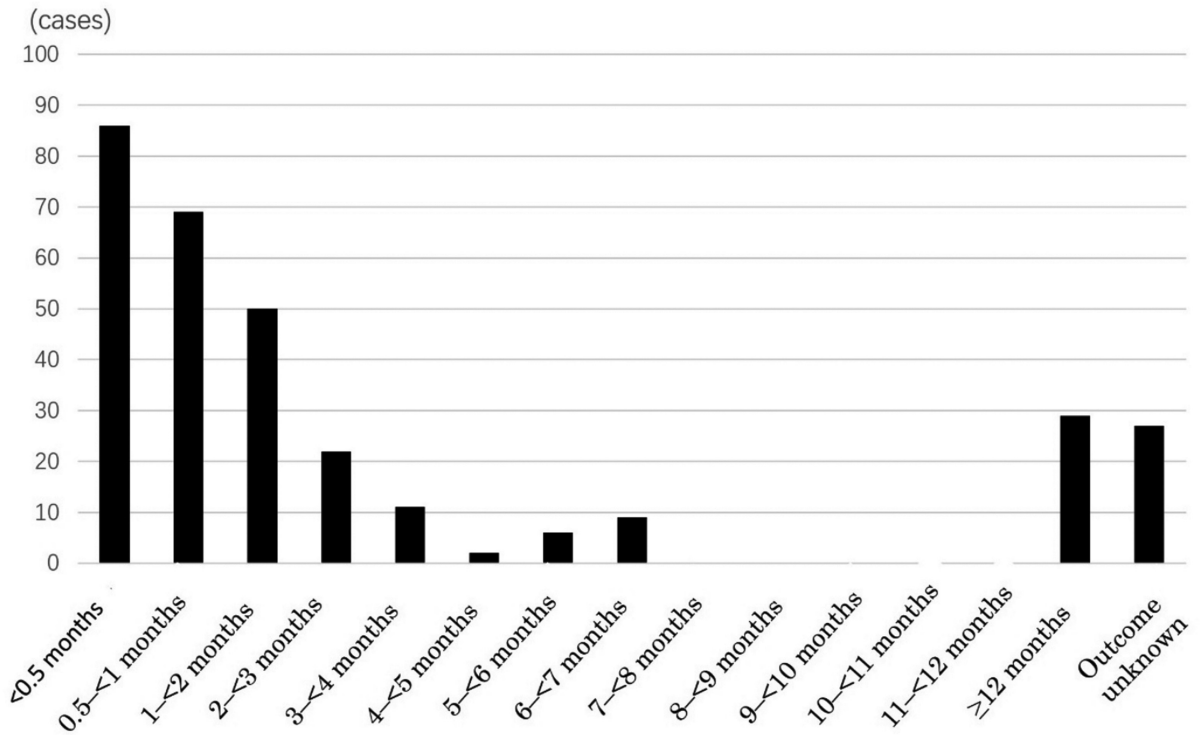

Fig. 3 Time to remission from the initial visit (duration of clinic visits; in months). Of all the included patients, 72.9% achieved remission within 3 months after the first visit.

undergone or were undergoing outpatient treatment for psychiatric disorders. As described earlier, there were 12 cases of probable VBOS, 5 cases of suspected VBOS or refractory BPPV that improved with concomitant treatment for migraine (remained inconclusive whether they had VBOS or were unrelated to episodic vertigo), and 12 cases where migraine was merely a complication with no effects on dizziness. Of the two patients who underwent a transition to PPPD, the man had hypertension and the woman had both diabetes mellitus and hypertension.

Case 1

Patient: A 75-year-old man.

Chief complaint: Vertigo.

History of present illness: The patient became aware of vertigo associated with head movements when he rolled over in his sleep. Additionally, he had experienced vertigo on other occasions during the past 5 days before he first presented to the clinic. Therefore, he visited a local neurosurgery clinic where he underwent head magnetic resonance imaging (MRI) and other evaluations, but as the neurosurgeon found no abnormalities, he was referred to our clinic.

Past medical history: Hypertension was being managed by an internist.

Family history: Unremarkable.

Pure-tone audiometry: High-frequency sensorineural hearing loss attributable to aging was noted, with no difference between the left and the right ears.

Infrared CCD camera and Frenzel goggles: Gaze nystagmus was not seen. As shown in ►**Fig. 4**, torsional nystagmus with latent time and damping was noted during positional and positioning tests.

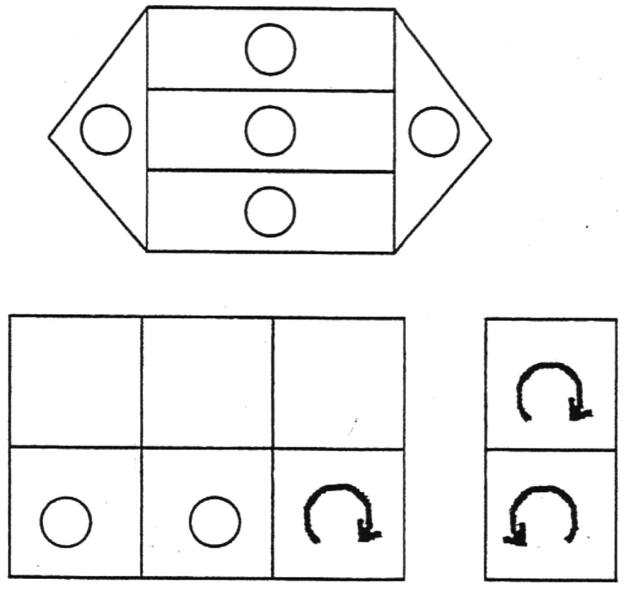

Fig. 4 Nystagmus findings at the initial visit in Case 1. Nystagmus was not noted during the gaze test; however, torsional nystagmus with latent time and damping was noted during the positional and the positioning tests.

Caloric nystagmus test: No difference between left and right ears was noted.

Otorhinolaryngologic findings: Unremarkable.

Neurological assessment: No abnormal findings were noted.

Blood tests: Unremarkable.

Disease course: Based on the results of the positional and the positioning tests conducted at the initial visit, the patient was diagnosed with definite left-sided posterior semicircular canal-type BPPV. He was prescribed ryokeijutsukanto and betahistine mesylate and the Semont maneuver was performed. The patient was further instructed to perform Brandt-Daroff exercises at home. The Semont maneuver had to be repeated as his subjective symptoms did not improve and nystagmus persisted even after 2 weeks. However, even though lightheadedness persisted, nystagmus was no longer detected by the positional or the positioning test conducted 1 month later. Similarly, 2 months later, nystagmus remained undetectable but lightheadedness continued. Furthermore, as nystagmus had resolved with no improvement in lightheadedness even at 3 months, an interview with the patient revealed that persistent lightheadedness occurred when he moved his body, walked, or looked at supermarket or convenience store shelves. His Niigata PPPD Questionnaire (NPQ)[3] score was as high as 54 out of 72 points. Based on the aforementioned, a provisional diagnosis of PPPD was provided, and he was prescribed a selective serotonin reuptake inhibitor (paroxetine hydrochloride hydrate) and Yokukansan, which resulted in an improvement of his NPQ score to 25 points.

Case 2

Patient: A 70-year-old woman.

Chief complaint: Vertigo.

History of present illness: The patient presented to the clinic 7 days after she became aware of vertigo associated with head movements that occurred when she rolled over in her sleep and on some other occasions.

Past medical history: Hypertension and diabetes mellitus managed by an internist.

Family history: Unremarkable.

Pure-tone audiometry: High-frequency sensorineural hearing loss attributable to aging was noted with no difference between the left and the right ears.

Infrared CCD camera and Frenzel glasses: Gaze nystagmus was not seen. As shown in ►**Fig. 5**, torsional nystagmus with latent time and damping was noted upon positional and positioning testing.

Caloric nystagmus test: No differences were noted between the left and the right ears.

Otorhinolaryngologic findings: Unremarkable.

Neurological examinations: No abnormal findings were noted.

Blood tests: Unremarkable.

Imaging examinations: Head MRI and MRA were unremarkable.

Disease course: The patient was diagnosed with definite left-sided posterior semicircular canal-type BPPV based on

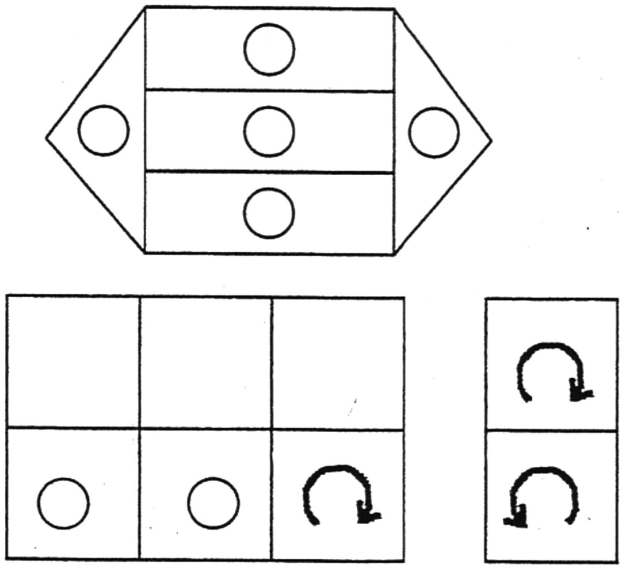

Fig. 5 Nystagmus findings at the initial visit in Case 2. Nystagmus was not noted during the gaze test; however, torsional nystagmus with latent time and damping was noted during the positional and the positioning tests.

the results of the positional and positioning tests at the initial visit. Nystagmus was seen (►**Fig. 5**). Pure-tone audiometry indicated high-frequency sensorineural hearing loss with no differences between left and right ears; this was presumed to be age-related. Therefore, Ryokeijutsukanto and betahistine mesylate were prescribed and the Semont maneuver was performed. The patient was also instructed to perform Brandt-Daroff exercises at home. The Semont maneuver was repeated 2 weeks later because nystagmus persisted and subjective symptoms had not improved. Precautionary head MRI and MRA were performed, but no abnormalities were found. Two months later, although nystagmus had resolved, lightheadedness persisted, and there was no change at 2.5 months after the initial visit. As nystagmus had resolved but no improvements in lightheadedness were seen at 3 months, an interview with the patient about her condition revealed that persistent lightheadedness occurred when she moved her body, walked, or looked at supermarket or drug store shelves. Furthermore, as her NPQ score was as high at 56 out of 72 points, she was diagnosed with PPPD and prescribed a selective serotonin reuptake inhibitor (paroxetine hydrochloride hydrate) and Yokukansan, which led to an improvement in her NPQ score to 20 points.

Discussion

Since the publication of diagnostic criteria for PPPD by the Barany Society,[2] there has been a renewed focus on conditions that can transition to PPPD.[2–4] Here, cases of definite BPPV that were diagnosed after the first episode were identified and case data were retrospectively reviewed to understand the factors associated with transition to PPPD. BPPV was selected because patients can subjectively perceive disease onset, which enables the accurate determination of time taken to transition from BPPV onset to PPPD. Even though this is also applicable to vestibular neuritis, this study focused on BPPV because of the relative rarity of vestibular neuritis.

There were 311 cases of first-onset BPPV in this study cohort, and women accounted for a greater proportion of the population. Previous studies have also reported that BPPV is more common in women.[13,14] Peak age of BPPV onset in this study was in 60s and 70s and patients in these age groups accounted for approximately 50% of all patients. Uno et al also reported that BPPV was most common in individuals aged 60 to 79 years.[15]

Most of the patients in this study presented to the clinic relatively early after the first episode, probably because only first-onset cases were included. Additionally, general otorhinolaryngology clinics are easier to visit than hospitals or dizziness clinics through appointment only. The short time interval between the first episode and the first visit may also have contributed to the relatively large sample size of this study (311 cases). Importantly, the higher detection frequency of nystagmus and greater accuracy of information from patient interviews helped increase the rate of definitive diagnosis. Posterior semicircular canal type was the most common type of BPPV, followed by the lateral semicircular canal type, and the lateral semicircular canal type. Likewise, Uno et al reported that $\geq$60% of cases were of the posterior semicircular canal type.[15]

The right side was more commonly affected than the left side and most patients (72.9%) showed an improvement in $<$3 months. As shown in ►**Table 1**, diagnostic criteria for PPPD include symptom persistence for at least 3 months; thus, $<$20% of first-onset cases were candidates for diagnosis, and the duration of time to remission alone could confirm that the rate of transition from BPPV to PPPD was not high. Specifically, cases where improvement was seen after more than 3 months included 11 (19.3%) patients with refractory disease, 27 cases (47.4%) that required long-term follow-up because of repeated symptom relapse despite improvement, 12 cases (21.1%) of probable VBOS,[12] and 5 cases (8.8%) of suspected VM or conditions that are refractory to BPPV treatment. In many of these cases, patients were diagnosed with BPPV at the initial visit and later confirmed to have VM through a second medical interview because subjective vestibular symptoms persisted after 1 month even though nystagmus had resolved. Furthermore, approximately 30% of patients who required clinic visits for $\geq$3 months had migraine-related conditions. Thus, it appears that BPPV cases requiring long-term visits are often related to VM. For this reason, some patients with VBOS might also suffer from concomitant PPPD; however, VBOS improved in most cases when physical therapy for BPPV and pharmacotherapy for migraine were provided concurrently. Notably, no VBOS patients met the diagnostic criteria for PPPD.

Only two individuals in their 70s with left-sided posterior semicircular canal-type BPPV were considered to have undergone transition to PPPD. An analysis of variables such as sex, time taken to transition to PPPD, characteristics in previous illness, and age were not possible.

Diseases similar to PPPD have been reported since the establishment of the diagnostic criteria for PPPD by the Barany Society in 2017,[2] and examples include phobic postural vertigo, space motion discomfort, visual vertigo, and chronic subjective dizziness. Thus, the Barany Society considers these diseases to represent different aspects of the same pathological condition, that is, the newly defined PPPD. In Japan, no large-scale epidemiological studies on PPPD have been conducted to date but overseas studies, such as those by Bittar and Lins[16] and Yan et al,[17] have reported that PPPD is common in women aged 40 to 69 years and that the prevalence of anxiety disorder or neuroticism was higher in PPPD patients than in healthy individuals. Horii reported that PPPD accounted for approximately two-thirds of all cases of dizziness and that it was the most common cause of chronic dizziness.[4] While the pathophysiology of PPPD has not been fully understood, it is considered to be a functional disorder, similar to irritable bowel syndrome.[17]

Diagnosis of PPPD requires detailed medical interviews about symptoms and past medical history, and questionnaires such as NPQ are effective tools.[5] Here, NPQ was used to rule out the possibility of PPPD in refractory cases or in those requiring long-term follow-up visits. Notably, NPQ scores were less than 27 in such patients, and an NPQ cutoff score of 27 has a reported sensitivity of 70% and a specificity of 68%.[3] Given that NPQ scores were too low and that these cases did not meet diagnostic criterion A (lightheadedness, unsteadiness, or non-spinning vertigo), PPPD was considered an unlikely diagnosis. The NPQ scores in two of the VBOS cases were higher than 27; however, they did not satisfy diagnostic criterion A ("symptoms are present on most days" because of fluctuation due to weather and stress).

The first necessary step in the treatment of PPPD is to provide the patient with information to help understand the condition. Other effective therapeutic options include selective serotonin reuptake inhibitors, vestibular rehabilitation, and cognitive behavioral therapy.[5,17–19] Nevertheless, it is most important to fully explain vertigo/dizziness-causing conditions that precede PPPD to affected patients because such information will facilitate a reduction in risk for transition to PPPD. Moreover, some PPPD patients have also stated that just being provided an explanation about the presumed precipitants of PPPD relieved their concerns and alleviated their symptoms. Although precipitants are unknown in some cases, it is essential to explain likely precipitants of PPPD whenever possible.

The results of this study suggest that the rate of transition from definite BPPV to PPPD is around 1%; thus, the likelihood of transition to PPPD in first-onset cases is expected to be low. Further studies in patients experiencing repeated BPPV episodes are needed to understand transition to PPPD.

Conclusions

1. This study identified first-onset cases of definite BPPV among patients with vertigo and retrospectively reviewed data on age at the initial visit, sex, affected side, past illnesses, type of BPPV, time to remission, and tendency of transition to PPPD.
2. BPPV was found to be more prevalent among women than in men.
3. BPPV patients were predominantly aged 60 to 79 years and accounted for ~50% of all patients included in this study.
4. The interval between the first episode and the initial visit was within 3 days in 137 cases and within 7 days in 63 cases; thus, ≥60% of the patients had the initial visit within 7 days after the first episode.
5. Posterior semicircular canal-type BPPV was most common, followed by the lateral semicircular canal type and the lateral semicircular canal type.
6. The right side was affected more commonly.
7. The most common comorbid conditions, in decreasing order of prevalence, were hypertension, hyperlipidemia, heart diseases such as arrhythmia, diabetes mellitus, and insomnia. Migraine was seen in 29 cases and 13 patients had undergone or were undergoing outpatient treatment for psychiatric disorders.
8. A majority of the patients showed improvement in <3 months, and only 18% of the patients needed longer than 3 months; thus, the latter group of patients are candidates for PPPD.
9. Only two patients in this cohort underwent transition to PPPD. Both patients had left-sided posterior semicircular canal-type BPPV and preexisting conditions included hypertension and diabetes mellitus.
10. The rate of transition from first-onset BPPV to PPPD was 0.6% in all cases and is not considered to be high.

Conflict of Interest
None declared.

Acknowledgment
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