Acquired Periodic Alternating Nystagmus

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Periodic alternating nystagmus is a rare form of horizontal jerk nystagmus characterized by a periodical reversal in the direction of nystagmus. It implies a cerebellar disorder or lesions involving the vestibulocerebellar connections. We report a patient with an acquired form of periodic alternating nystagmus associated with meningoencephalitis. Its waveform characteristics were demonstrated by a video-nystagmogram. The brainstem lesions in our patient were thought to be responsible for her nystagmus.

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Periodic alternating nystagmus (PAN) is a rare type of spontaneous horizontal nystagmus, characterized by periodical reverse of direction with a transition period in between.1-10

PAN can occur in both congenital and acquired forms.1-4 We report a patient with acquired PAN associated with meningoencephalitis. To our knowledge, only a case of congenital PAN has been previously reported in Korea10 and our patient is the first case of acquired form. We were interested in describing and demonstrating the clinical features and videonystagmographic findings of this peculiar nystagmus.

Case

A 26-year-old woman was admitted to the neurologic clinic because of blurred vision and disequilibrium. She had been well until two months earlier, when she had fever, headache, and vomiting. She progressively became drowsy and examination revealed stuporous mental status, anisocoria (3 mm/4 mm) with sluggish response to light, a right beating nystagmus and neck stiffness. Brain MRI showed increased signals in bilateral ventral midbrain, posterior limb of the internal capsules, and dorsal aspect of the right thalamus (Fig. 1). A provisional diagnosis of meningoencephalitis was made and antiviral agent was started. One week after admission, her symptoms markedly improved, but were followed by blurring of vision, with severe dizziness and gait instability. On examination, right beating nystagmus, severe hand tremor and gait imbalance were noted. She was referred to our hospital.

There was no family history of neurologic disease. Right and left pupil diameters were 3 and 5 mm, respectively, and right pupil reacted promptly but the left pupil sluggishly to light. Visual acuity was 0.8/0.6 in each eye. The slit lamp and both fundus findings were normal. She had a spontaneous horizontal jerk nystagmus, continuously changing its
direction alternatively to the right and then to the left, with a short quiet phase in between. Smooth pursuit was impaired while the spontaneous nystagmus beats. Limb strength and sensation were normal. There was a moderate symmetric intention tremor. Deep tendon reflexes were brisk bilaterally and Babinski sign were negative. Severe body tremulousness occurred when she stood or sat up from a supine position and diminished when she lied in bed. She could not remain standing or walk without support. Her gait was broad and unsteady.

Results were negative for all laboratory data, including a serologic test for syphilis, HIV, Borrelia and Japanese B virus; antinuclear antibodies; viral, bacterial and fungal CSF cultures. MR scan showed only some residual high signal in the right thalamus (Fig. 2).

Videonystagmographic (VNG) recording revealed: (1) a spontaneous alternating nystagmus changing its direction regularly approximately every 140 seconds (Fig. 3B) with a pause of low amplitude jerks lasting approximately 8-10 seconds (range 5-10 sec) (Fig. 3A, 3B). The highest amplitude of the right–beating (12° to 15°) phase was slightly larger than the left–beating (7° to 11°) phase, (2) PAN was not influenced by eye position. Head position change did not stop or after the

**Figure 1.** FLAIR MR scans. These show increased signals in the midbrain, posterior limb of the internal capsules, and dorsal aspect of the right thalamus (red arrows).

**Figure 2.** Follow-up FLAIR MR scans. These show only some residual high signal in the right thalamus (red arrow).

**Figure 3.** (A) Videonystagmogram (VNG). A spontaneous right-beating horizontal jerk nystagmus changes its direction to left after a quiet (transition) phase of low amplitude nystagmus of about 8-10 seconds (red arrows). The amplitude of right-beating nystagmus (between the blue lines) is 13.2° and of left-beating nystagmus (between the blue dot lines), 15.8°. (B) Videonystagmogram (VNG). The right-beating phase lasts about 140 seconds (first row to third row) (amplitude between blue dot lines is 15°). Two transition phases are shown (red arrows in first and third row).
direction of the nystagmus, (3) PAN increased in darkness (52%), (4) saccadic eye movements, smooth pursuit recordings were impaired, and optokinetic nystagmus (OKN) was decreased bilaterally, all superimposed by the spontaneous nystagmus, (5) caloric test showed normal responses, but visual suppression in the presence of visual fixation was bilaterally decreased (with cold water: right 26%, left 19%; with warm water: right 42%, left 32%; normal>50%).

The patient was treated initially with valproic acid 1200 mg/day, clonazepam 1.5 mg/day and baclofen 15 mg/day. Four days after, body tremulousness and unsteadiness on walking improved considerably, but findings of PAN were unchanged. Baclofen was gradually increased up to 20 mg/day and one week later, she was able to walk with aid of one person without any improvement in her eye movements.

A month after discharge with baclofen 20 mg/day, she still had mild dizziness and imbalance, but the extent of oscillopsia was lessened. PAN remained but the amplitude of right–beating nystagmus decreased. Baclofen 25 mg/day was prescribed and another month later, only left gaze–evoked nystagmus was noted intermittently. PAN was not evident and baclofen was stopped at that point. After one year follow–up, PAN was again not evident.

Discussion

PAN or nystagmus alternans, is an uncommon form of spontaneous horizontal nystagmus. Typically, it changes its direction periodically with a cycle length of about 90 seconds in each direction with a short, low-intensity transition period, lasting about 20 seconds.1-10

PAN in our patient is acquired in origin. It was associated with viral meningoencephalitis, a diagnosis made on the basis of her initial clinical presentation with CSF pleocytosis. Various acquired factors have been previously reported with PAN.1-3,5,8

PAN also occurs congenitally.3,4,6-8 Patients with congenital PAN tend not to complain of visual disturbances and show normal neurological examination. As we could see in our patient, however, those with acquired PAN usually suffer from oscillopsia, blurred vision and symptoms related to cerebellar disturbance such as gait ataxia and dysarthria.

PAN suggests a lesion in the cerebellum,1-5 but may result from any process involving the cerebellum or its brainstem connections. Our patient did not have any cerebellar lesion and bilateral midbrain lesions might not be thought to be responsible for PAN. But clinically, cerebellar signs, such as disequilibrium, tremulousness, horizontal jerk nystagmus and ataxia, were evident, which implies a cerebellar dysfunction, and we suspected that the potential lesions, not shown on MRI, may have affected the vestibulocerebellar connections, resulting in the cyclic phenomenon of PAN.

The pathophysiology of its cyclic nature is poorly understood. Interestingly, some animal experiments reported that PAN appeared only in darkness after removal of the nodulus and ventral uvula and it was abolished by administrating baclofen.1,4,9 The nodulus and uvula in the cerebellum are known to control the ‘velocity storage system’ of nystagmus and dysfunction of their activity causes instability of the velocity storage and vestibule–ocular reflex (VOR), provoking PAN.

The acquired PAN is associated with diminished OKN response and preservation of caloric responses with lack of ocular fixation suppression of caloric nystagmus.1-5 Our VNG illustrated similar findings to other reports of acquired PAN. Congenital PAN is typically characterized by inverted OKN and augmentation of nystagmus by fixation.4,7-8

It was of interest in that the amplitude of each–side nystagmus in our patient was slightly larger in the right–beating phase than in the left–beating phase. This may be explained by the asymmetric involvement of the lesions, not demonstrated on MRI.

Beneficial effect of baclofen on PAN was not clear in our patient; improvement seemed more likely to be related to the self–limited course of the disease, rather than to baclofen.

Since most cases of PAN are associated with acquired disease, it is important to identify this peculiar nystagmus, because it implies cerebellar and brainstem disorders which may be treatable. Careful observation of the patient’s nystagmus long enough, with sufficient time, is essential.

REFERENCES

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