Periodic alternating gaze deviation and nystagmus in posterior reversible encephalopathy syndrome

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Practical Implications

Periodic alternating gaze deviation and nystagmus may result from reversible causes of neurologic dysfunction, such as posterior reversible encephalopathy syndrome.

Video

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A 73-year-old man with benign prostatic hypertrophy, but no history of hypertension, presented with acute urinary retention and severe headache followed by sudden loss of vision.

On examination, he was obtunded but arousable. There was no blink to threat. Pupillary responses to light were normal. Alternating lateral gaze deviation was observed with a period of approximately 240 seconds. In addition, subtle intermittent nystagmus was observed, with fast phases opposite the direction of gaze deviation (figure 1, A–C; video at Neurology.org/cp). Transient downbeating nystagmus was observed during null periods between changes in direction of gaze. Vestibulo-ocular reflex testing with fast head rotations did not overcome the gaze deviation. No spontaneous saccades were observed. The optic disc margins were sharp and no retinal cotton-wool spots or hemorrhages were observed. Spontaneous limb movements were normal and symmetric. Reflexes were brisk throughout with bilateral ankle clonus. The plantar reflex responses were extensor bilaterally. Blood pressure was 208/100 mm Hg.

Brain MRI demonstrated fluid-attenuated inversion recovery signal abnormality with vasogenic edema in the cerebellum and temporo-occipital lobes bilaterally, consistent with the clinical diagnosis of posterior reversible encephalopathy syndrome (PRES) (figure 2, A and B). The cerebellar uvula and nodulus showed no obvious abnormalities. Serum creatinine was 2.5 mg/dL (increased from 1.1 mg/dL 6 weeks prior). Renal ultrasound demonstrated bilateral hydronephrosis.

A Foley catheter was placed, yielding 1 liter of urine. Blood pressure was slowly normalized with IV nicardipine. Prolonged EEG recording demonstrated mild background disorganization and frequent bursts of frontal intermittent rhythmic delta activity, without epileptiform discharges or seizure activity, consistent with moderate encephalopathy.

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Figure 1 Periodic alternating gaze deviation

The eyes are initially deviated to the right (A) and after 120 seconds are deviated to the left (B). At 240 seconds, gaze deviation has returned to the right (C).

Periodic gaze deviation and nystagmus resolved within 48 hours. The patient demonstrated agitation and visual hallucinations that recovered over several days. Level of arousal returned to normal, with intact attention, memory, and language. Vision was greatly improved at the time of discharge on hospital day 7. At 1 month follow-up, vision was at baseline; the acuity was 20/20 in the right eye and 20/40 in the left eye, with deficits attributed to cataract and epiretinal membrane. Repeat brain MRI 2 months later demonstrated resolution of the previous abnormalities (figure 2, C and D).

DISCUSSION

Periodic alternating gaze deviation (PAGD) refers to involuntary horizontal conjugate deviation of the eyes, with the direction alternating approximately every 1–2 minutes.^{1,2} The time constant for this phenomenon is the same as that of periodic alternating nystagmus (PAN), in which spontaneous horizontal nystagmus occurs with fast phases alternating between left and right. These 2 entities likely share a common pathophysiologic mechanism relating to instability of the brain-stem velocity storage mechanism.^{1,2} The velocity storage function refers to intrinsic properties of the central vestibular system that regulate the temporal course of normal rotationally induced nystagmus. Dysfunction of vestibulocerebellar pathways or loss of visual inputs may destabilize the velocity storage mechanism and give rise to PAGD or PAN.^{3,4} While human cases of PAN studied at autopsy do not suggest a single anatomic localization, in monkeys PAN is produced by removal of the nodulus and ventral uvula of the vestibulocerebellum.^{5,6}

Figure 2 MRI brain fluid-attenuated inversion recovery sequence shows posterior reversible encephalopathy syndrome

Temporo-occipital and cerebellar hyperintensity on initial presentation, secondary to posterior reversible encephalopathy syndrome (A, B). Two months later, the hyperintensity had resolved (C, D).

PAGD may be considered a variant of PAN, in which fast-phase eye movements are impaired or absent due to concomitant dysfunction of brainstem saccade generators.¹ According to this hypothesis, lateral gaze deviation and the slow phases of superimposed alternating nystagmus would be in the same direction, as observed in our patient. Both the examination and brain MRI demonstrated occipital and cerebellar abnormalities. Although abnormal signal was not detected in the brainstem, clinically significant brainstem edema below the threshold of radiographic detection could not be excluded. The findings were attributed to PRES—a cause of PAGD and PAN that, to our knowledge, has not been previously described in the medical literature. A possible mechanism for PRES includes fluid extravasation from hyperperfusion-induced blood–brain barrier breakdown. Edema leads to reversible dysfunction of the involved brain regions. The cerebellum and brainstem are affected in a substantial minority of patients with PRES (34% and 18% in 1 series),⁷ which suggests that transient PAGD and PAN may be underrecognized features of PRES.

Following treatment for urinary obstruction and hypertension, the clinical and radiographic abnormalities in our patient fully reversed. It is important to recognize PAGD and PAN clinically, as these findings may result from reversible causes of neurologic dysfunction, such as PRES, that carry a favorable prognosis if diagnosed early and treated appropriately.

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