

Pursuit-Paretic and Epileptic Nystagmus in MELAS

Seo Young Choi, MD, Yeonjung Kim, MD, Sea Won Oh, BSc,
Seong-Hae Jeong, MD, Ji Soo Kim, MD, PhD

Abstract: A 27-year-old man with MELAS 3243 mutation developed a right homonymous hemianopia, left beating nystagmus, and impaired smooth pursuit (SP) to the left. Intermittently, the left beating nystagmus changed to right beating with rightward eye and head deviation and associated altered mental status. Each episode lasted several minutes. MRI revealed restricted diffusion in left parieto-temporo-occipital cortices. During the ictus, electroencephalogram showed epileptic discharges in the left temporo-occipital region, and single photon emission computed tomography demonstrated hyperperfusion in the same area. The interictal left beating nystagmus may be ascribed to contralesional bias of SP imbalance since the parieto-temporo-occipital region is involved in the generation of SP. The ictal right beating nystagmus and rightward head and eye deviation indicate coactivation of the SP areas and parietal eye field. This report documents the novel co-occurrence of pursuit-paretic and epileptic nystagmus.

Journal of Neuro-Ophthalmology 2012;32:135–138

doi: 10.1097/WNO.0b013e31824d2a15

© 2012 by North American Neuro-Ophthalmology Society

The presence of nystagmus usually indicates a lesion involving the brainstem or cerebellum (1). Rarely, cerebral hemispheric lesions give rise to nystagmus. In pursuit-paretic

Department of Neurology (SYC, SWO, JSK), Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seoul, Korea; Department of Neurology (YK), Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; and Department of Neurology (S-HJ), Chungnam National University Hospital, Chungnam National University College of Medicine, Daejeon, Korea.

The authors report no conflict of interest.

Supplemental digital content is available for this article. Direct URL citations appear in the full text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.jneuro-ophthalmology.com).

Address correspondence to Ji Soo Kim, MD, PhD, Department of Neurology, College of Medicine, Seoul National University, Seoul National University Bundang Hospital, 300 Gumi-dong, Bundang-gu, Seongnam-si, Gyeonggi-do, 463-707, Korea; E-mail: jisookim@snu.ac.kr

nystagmus, lesions involving the human homologues of medial temporal (MT) and middle superior temporal (MST) areas in monkeys induce an imbalance favoring contraversive smooth pursuit (SP), and resultant nystagmus beating toward the side of the lesion (2,3). In contrast, epileptic nystagmus has been ascribed to irritation of the cortical areas involved in the generation of saccades or SP (4,5). We report pursuit-paretic and epileptic nystagmus in a MELAS patient whose MRI demonstrated an area of restricted diffusion involving left parieto-temporo-occipital cortices.

CASE REPORT

A 27-year-old man with known MELAS 3243 mutation complained of dizziness and difficulty with vision after drinking alcohol heavily. The diagnosis of MELAS was made 4 years previously when, again after heavy drinking, he developed visual blurring, left homonymous hemianopia, and headache. MRI showed high T2 signal intensities in the right occipital cortex, and genetic testing confirmed the diagnosis of MELAS. His visual field deficit resolved. Two years ago, the patient suffered status epilepticus after drinking alcohol. He had a younger brother with the same MELAS mutation.

General physical examination showed normal vital signs but a short and thin body habitus. On visual field testing, the patient had a right homonymous hemianopia. Eye movements showed spontaneous left beating nystagmus in primary gaze (Fig. 1A), which increased on leftward gaze. (See **Video 1, Supplemental Digital Content 1**, <http://links.lww.com/WNO/A33>. Video recording shows interictal spontaneous left beating nystagmus with fixation, which increases during leftward gaze. During the ictus, the nystagmus changes into right beating with rightward eye deviation.) The patient also had a receptive (Wernicke) aphasia, as well as optic ataxia, simultagnosia, acalculia, agraphia, finger agnosia, and right-left disorientation, findings consistent with Balint and Gerstmann syndromes. Horizontal saccades appeared to be normal, but horizontal SP was impaired in both directions, left

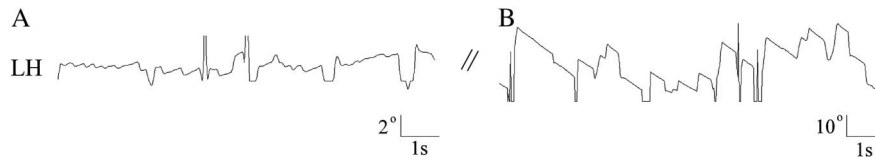


FIG. 1. Video-oculography showing left beating nystagmus between the ictus (**A**), which intermittently changes into right beating nystagmus (**B**). Upward deflection indicates rightward and upward eye motion in each tracing. Note the different scales for eye movements. LH, horizontal position of left eye.

greater than right. (See **Video 2, Supplemental Digital Content 2**, <http://links.lww.com/WNO/A34>. Video recording shows interictal spontaneous left beating nystagmus with fixation, which increases during leftward gaze. During the ictus, the nystagmus changes into right beating with rightward eye deviation.) Intermittently, the patient suddenly exhibited altered mental status and rightward head turning. At this time, the left beating nystagmus changed to right beating with rightward eye deviation (Fig. 1B; see **Video 1, Supplemental Digital Content 1**, <http://links.lww.com/WNO/A33>). Each episode lasted several minutes and recurred several times.

MRI of the brain disclosed restricted diffusion in left parieto-temporo-occipital lobes (Fig. 2A, B). Single photon emission computed tomography demonstrated hyperperfusion in the corresponding area (Fig. 2C). Electroencephalogram (EEG) showed epileptiform discharges in the left temporo-occipital cortices (Fig. 3).

The patient was treated with 1,000 mg of phenytoin a day and then switched to 1,000 mg of levetiracetam a day for more than 15 days. The seizure attacks disappeared 5 days later with the resolution of epileptiform discharges on follow-up EEG. Twenty days later, the patient was discharged with mild aphasia and right

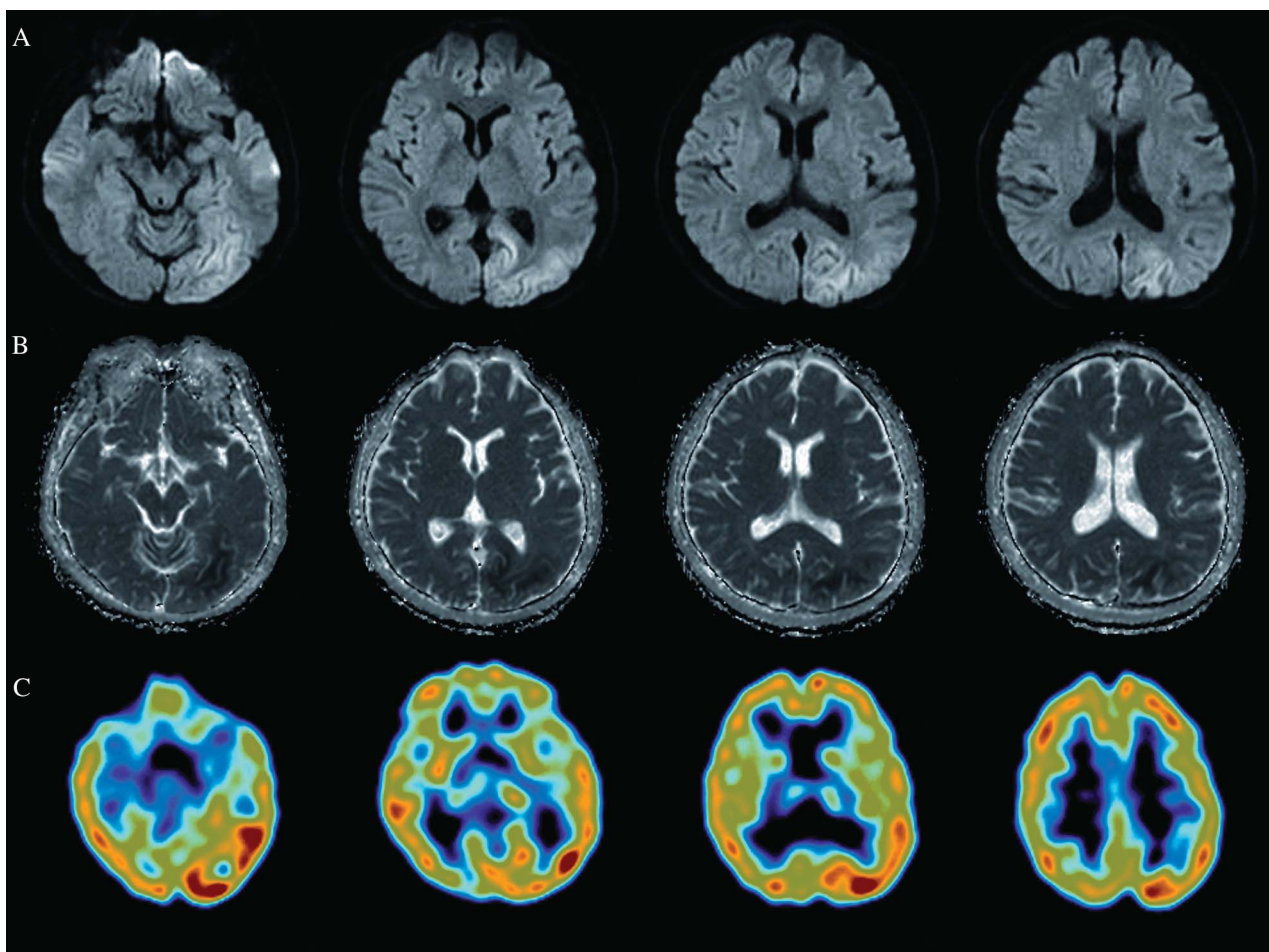


FIG. 2. **A.** Diffusion-weighted imaging demonstrates area of restricted diffusion in the left temporo-parieto-occipital region. **B.** Apparent diffusion coefficient maps confirms restricted diffusion. **C.** Ictal single photon emission computed tomography shows hyperperfusion in the left temporo-parieto-occipital region.



FIG. 3. Ictal EEG discloses sharp waves and spikes of 8–10 Hz in the left temporo-occipital region (T5, O1). EEG, electroencephalogram.

homonymous hemianopia but without spontaneous nystagmus or impaired SP.

DISCUSSION

The cerebral cortex contributes to voluntary control of eye movement in human, including SP (1). The frontal eye fields, supplementary eye fields, and posterior parietal cortex are all involved in the control of horizontal SP in monkeys and humans (1,6). Anatomic regions, MT and MST areas, are important parts of the neural pathways controlling horizontal SP (1,7).

Patients with hemispheric lesions may show horizontal nystagmus along with horizontal SP asymmetry (1,2). The nystagmus is usually of low amplitude with the slow phase away from the side of the lesion (3). Because these patients also show impaired SP more to the lesion side, this nystagmus is ascribed to an imbalance in horizontal SP tone and has been termed as “pursuit-paretic nystagmus” (3,7).

The lesion in our patient involved the human homologue of MT and MST areas (Brodmann areas 19, 37, 39) (8). Accordingly, impaired SP, more to the left, and the left beating nystagmus between the ictus may be explained by the temporo-parieto-occipital abnormality detected on MRI.

The left beating nystagmus in our patient intermittently changed to right beating nystagmus with rightward eye and head deviation and altered mental status. EEG revealed ictal discharges in the left temporo-occipital area (T5–O1), confirming seizure activity. Epileptic nystagmus has been attributed to irritation of the cortical areas involved in generating eye movements. Activation of centers involved with either saccadic or SP could generate contralesional nystagmus (4,5). When the saccadic areas are stimulated, the epileptic nystagmus has a decreasing slow-phase velocity (SPV) and occurs only in the contraversive hemifield, without

crossing the midline (4). In contrast, the epileptic nystagmus generated from the SP region has a linear SPV with the eyes crossing the midline. Irritation of the SP region would induce ipsiversive deviation of the eyes and corrective quick phases returning the eyes near to the midline (4,9,10).

Our patient had features of both contraversive eye deviation and nystagmus with linear SPV. Yet, the nystagmus occurred only in the contraversive hemifield without crossing the midline. The parietal eye fields and human homologue of MT/MST are located near each other, and both could be affected by seizure activity. Our patient showed sharp waves and spikes of 8–10 Hz on EEG. It is known that 10 Hz of epileptic discharge is the minimum frequency required to generate nystagmus (4).

Reports of eye movement disorders in MELAS patients are rare. Shinmei et al (11) described persistent ocular motor dysfunction (including downbeat nystagmus, square wave jerks, impaired SP, and hypermetric and hypometric saccades) in patients with MELAS and normal MRI. In contrast, with anticonvulsant therapy, our patient showed resolution of nystagmus and SP asymmetry and had an abnormal MRI. While the exact mechanism remains unknown, the stroke-like episodes in MELAS have been ascribed to neuronal hyperexcitability from abnormal mitochondrial RNA and diffuse endothelial necrosis of the small vessels in the brain (12).

REFERENCES

1. Leigh RJ, Zee DS. *The Neurology of Eye Movement*. 4th ed. Oxford, England: Oxford University Press, 2006.
2. Sharpe JA, Lo AW, Rabinovitch HE. Control of the saccadic and smooth pursuit systems after cerebral hemidecortication. *Brain*. 1979;102:387–403.
3. Sharpe JA. Pursuit paretic nystagmus. *Ann Neurol*. 1979;6:458.
4. Kaplan PW, Tusa RJ. Neurophysiologic and clinical correlations of epileptic nystagmus. *Neurology*. 1993;43:2508–2514.

5. **Tusa RJ**, Kaplan PW, Hain TC, Naidu S. Ipsiversive eye deviation and epileptic nystagmus. *Neurology*. 1990;40:662–665.
6. **Dursteler MR**, Wurtz RH, Newsome WT. Directional pursuit deficits following lesions of the foveal representation within the superior temporal sulcus of the macaque monkey. *J Neurophysiol*. 1987;57:1262–1287.
7. **Sharpe JA**. Neurophysiology and neuroanatomy of smooth pursuit: lesion studies. *Brain Cogn*. 2008;68:241–254.
8. **Morrow MJ**, Sharpe JA. Retinotopic and directional deficits of smooth pursuit initiation after posterior cerebral hemispheric lesions. *Neurology*. 1993;43:595–603.
9. **Weber YG**, Roesche J, Lerche H. Epileptic nystagmus: two case reports, clinical and pathophysiological review of the literature. *J Neurol*. 2006;253:767–771.
10. **Thurston SE**, Leigh RJ, Osorio I. Epileptic gaze deviation and nystagmus. *Neurology*. 1985;35:1518–1521.
11. **Shinmei Y**, Kase M, Suzuki Y, Nitta T, Chin S, Yoshida K, Goto Y, Nagashima T, Ohno S. Ocular motor disorders in mitochondrial encephalopathy with lactic acid and stroke-like episodes with the 3271 (T-C) point mutation in mitochondrial DNA. *J Neuroophthalmol*. 2007;27:22–28.
12. **Koga Y**, Povalko N, Nishioka J, Katayama K, Kakimoto N, Matsuishi T. MELAS and L-arginine therapy: pathophysiology of stroke-like episodes. *Ann N Y Acad Sci*. 2010;1201:104–110.