

Case Report

Blepharoclonus: Anatomical Localization and Etiological Consideration

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Blepharoclonus refers to myoclonic rhythmic eyelid closure. This is an extremely rare abnormal movement of the eyelids. The symptom has an ill-defined anatomical localization and hypothesized etiologies are diverse. We describe a 42 year-old woman with known poorly controlled hypertension (HTN) who presented with a three-week history of ataxia, dysmetria, and uncontrolled eyelid twitching. The bilateral abnormal eyelid movement occurred during either eyelid closure or opening, and was compatible with blepharoclonus. MRI revealed multiple cerebral infarctions at red nucleus, dentate nucleus, and inferior olives. These foci are within Guillain-Mollaret's triangle. The ataxia and dysmetria gradually improved within three weeks. While the blepharoclonus improved, it persisted after one year of follow-up. Our conclusion was one of HTN leading to a lacunar infarct that manifested partially as blepharoclonus. Due to the neuroimaging findings and clinical course, we propose that blepharoclonus may be a variant of palatal myoclonus and may be considered as another lacunar syndrome.

Keywords: Blepharoclonus, Guillain-Mollaret triangle, Palatal myoclonus

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Blepharoclonus refers to brief, repetitive, clonic, and bilateral contractions of the orbicularis oculi muscles⁽¹⁾. This extremely rare abnormal movement of the eyelids can be elicited by voluntary eye closure^(2,3) and gaze deviation^(4,5) and usually does not coexist with blepharospasm. The rhythm and frequency of blepharoclonus is similar to palatal myoclonus. The reported etiologies are diverse and anatomical localization is ill defined. We report a case of blepharoclonus associated with a lacunar infarction. The relationship of blepharoclonus and palatal myoclonus will be discussed in the present article.

Case Report

A 42-year-old, factory worker, right-handed, and married woman was referred from the local hospital in the eastern Thailand, for evaluation of slurred speech and ataxia. Three weeks prior to admission, she had vertiginous dizziness in the morning. After resting for three hours, the symptoms

seemed to be slightly improved. She noticed a problem of gait unsteadiness in the evening and her symptoms progressed, which led to seeking medical assistance. She was admitted at a local hospital for one day. Intravenous antihistamine and multivitamins were prescribed without any response.

Two days after the initial symptoms, she developed ataxia to the left side and noticed slurred speech. Excessive eye blinking was noted by her husband but the patient was oblivious to it. She denied any problems of diplopia, swallowing, weakness, or numbness of the limbs. Her past medical history was significant only for poorly controlled hypertension (HTN). There was no history of current viral infection or previous neurological diseases.

Physical examinations revealed a normal general appearance. Blood pressure was slightly elevated at 150/100 mmHg with normal cardiovascular examination. Her mental status exam was normal. The visual field and visual acuity as well as the fundoscopic examination were also normal. Excessive eye blinking, at a rate of two to three cycles per second, was present and continued during eyelid closure. This abnormal movement could not be suppressed by distraction but could be evoked by the normal eye closure. It also could be observed when the patient performed

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the gaze deviation or squeezed the eyelids. This symptom persisted during sleep but it did not disturb her. The excessive eye blinking was compatible with blepharoclonus. The extraocular movements were full without abnormal pursuit or saccade movement. No nystagmus or abnormal accommodation was detected. The pupils were 3 mm with normal light reaction. The facial expression, auditory function and other cranial nerve function were normal. She had mildly slurred speech and ataxic gait on the left side. The finger to nose test showed dysmetria on the left more than the right. Dysdiadokokinesia was noted in both hands. Her muscle strength and tone, sensation, superficial and deep tendon reflexes were normal. No abnormal movement of facial, other axial muscles, palate, or the extremities were detected.

Complete blood count, serum chemistry including plasma glucose, blood urea nitrogen (BUN), creatinine, liver function test, and electrolytes were all within normal limits. CT scan of the brain with and without contrast enhancement was unremarkable. MRI of the brain showed previous scattered-high signal intensity lesions at cerebellum, medulla, bilateral periventricular areas, and a recent infarction at midbrain (Fig. 1). Cerebrospinal fluid (CSF) analysis revealed no pleocytosis with normal protein and glucose level. The oligoclonal band was negative. The CSF test for the venereal disease research laboratory

(VDRL), Herpes simplex virus, Epstein Barr virus, Cytomegalovirus, and Varicella zoster virus were negative. Blood test for homocysteine level, protein C level, protein S level, VDRL, and lupus anticoagulant were negative. The diagnosis was brainstem ischemic stroke due to small vessel disease. Aspirin 300 mg, hydration, and rehabilitation were prescribed. The vertiginous dizziness subsided within seven days of treatment. Slurred speech, gait ataxia, and other cerebellar signs resolved within six months. The blepharoclonus was improved within three weeks but persisted after one year of follow-up. Enalapril and Amlodipine have been prescribed for control of HTN. The patient maintained her activities of daily living in spite of her blepharoclonus.

Discussion

Eyelid movements are mediated mainly by the orbicularis oculi and the levator palpebrae superioris muscles. Spontaneous blinking is a symmetric periodic movement of closing and opening of the eyelids that occurs in the absence of an external stimulus or internal effort⁽⁵⁾. The central generator of eyelid blinking is proposed to be located in the brainstem. The nuclei and fibers of posterior commissure may be a generator for eyelid opening, and lesions in this area in monkeys can induce lid retraction⁽⁶⁾. On the other hand, the generator for eye

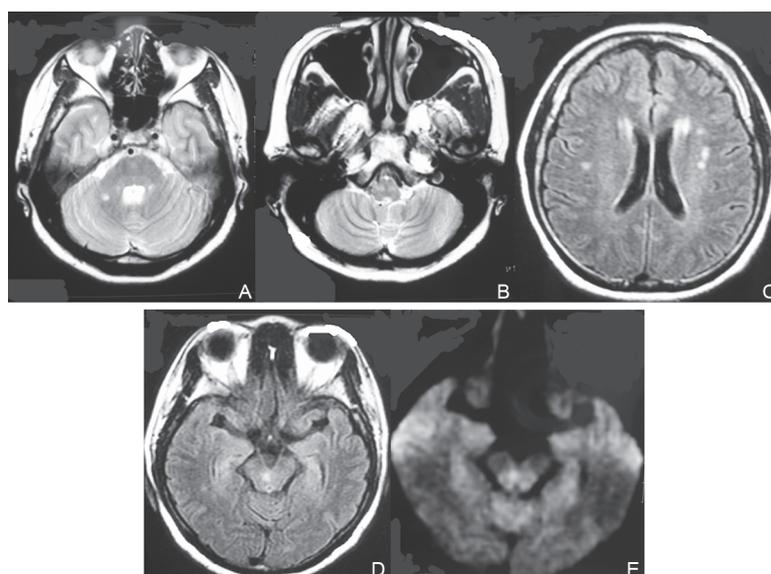


Fig. 1 The axial MRI of the brain illustrated scattered-high signal intensity lesions at cerebellum, medulla, bilateral periventricular areas (A, B, C) and a recent high signal intensity lesion at the midbrain, closed to the eye opening-closing generator on fluid attenuated inversion recovery (FLAIR) and diffusion-weighted imaging (DWI) (D, E).

closing is proposed to be located in the periaqueductal grey matter in humans and stimulation of this area provokes eyelid closure⁽⁷⁾. Blepharoclonus is a rare rhythmical myoclonic contraction of the orbicularis oculi muscles occurring at the rate of two to three cycles per second⁽¹⁾ and it is usually provoked by eye closure^(2,3,8). Occasionally, other events such as speech can provoke it⁽⁹⁾. Blepharoclonus should be differentiated from nystagmus and blepharospasm⁽⁵⁾. Eyelid nystagmus consists of a slow downward drift of the lids with correcting fast upward flicks, and it usually provoked by lateral gaze or convergence⁽¹⁰⁾. In blepharospasm, the movement of the eyelids is characterized by repetitive tonic eye closure caused by sustained contraction of orbicularis oculi muscles⁽¹⁾. In our particular case, the eyelid movement was rhythmically sinusoidal pattern without slow-fast component or sustained contraction and therefore more compatible with blepharoclonus.

The regular sinusoidal pattern and the frequency of blepharoclonus are similar to the abnormal movement seen in palatal myoclonus or tremor. There are two varieties of palatal myoclonus. Essential palatal myoclonus is caused by contractions of the tensor veli palatini, mostly coexisting with ear clicking. Symptomatic palatal myoclonus is caused by the levator veli palatini⁽¹¹⁾, extraocular muscles, and other muscles from the same branchial arch^(12,13). Because of similarities between blepharoclonus and palatal myoclonus, the two entities may be related, at least neuro-anatomically.

The anatomical localization for symptomatic palatal myoclonus is well documented within the Guillain-Mollaret triangle⁽¹⁴⁾ (Fig. 2). This neuro-anatomical functioning triangle is located in the brainstem and is composed of the red nucleus in the midbrain, the dentate nucleus in the cerebellum, and the inferior olives in the medulla. Structures allocated

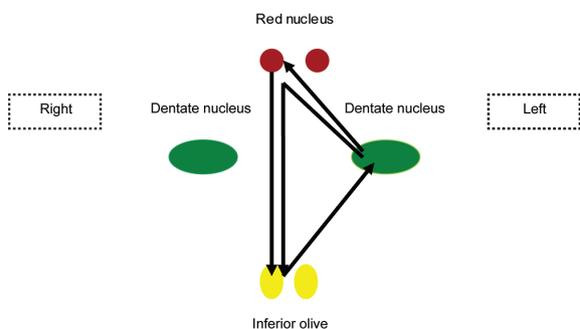


Fig. 2 Guillain-Mollaret triangle.

in this triangle consisted of various connecting pathways: the central tegmental tract, the inferior cerebellar peduncle, and superior cerebellar peduncle^(14,15). One apex of the triangle at the midbrain is close to the eye opening-closing generator.

Previous anatomical localizations of symptomatic blepharoclonus include those of the brainstem, cerebellum, and midbrain^(3,4,16). However, the exact locations had not been well defined due to limitation of imaging technique and no autopsy proven case. The patient had a lacunar infarction at midbrain. Since the anatomical localization of closing and opening of the eyelids, a generator for blepharoclonus is proposed to be located at the midbrain level, the lesion in our patient is compatible with this hypothesis. The midbrain localization for blepharoclonus is also located in Guillain-Mollaret triangle.

The documented pathology in blepharoclonus included demyelination, recovery from severe head trauma, Arnold-Chiari malformation, and Parkinson's disease^(2,3,5,8,16,17). Interestingly, Jacome DE reported four cases of blepharoclonus, pseudoasterixis, restless feet, and migraine⁽¹⁸⁾. The anatomical localization of the syndrome was not proposed and there had been no autopsy proven cases in this series. However, the migraine generator and the anatomical localization of restless leg syndrome may be related to the midbrain⁽¹⁹⁻²¹⁾. The blepharoclonus in this syndrome may be related to the midbrain lesion as well.

From clinical, physiological, and neuro-anatomical points of view, symptomatic blepharoclonus and palatal myoclonus may share a common pathophysiological mechanism and may be related to lesions in Guillain-Mollaret triangle.

Conclusion

The present case was one of an acute onset of blepharoclonus and vascular syndrome in the brainstem. The documented infarction was located at the midbrain level. Lesions located in the Guillain-Mollaret triangle and specifically involved the midbrain were critical for the development of blepharoclonus. The nuclei controlling eye closure and opening in midbrain may be a generator for blepharoclonus. Lacunar infarctions should be considered as one of the etiologies of this unusual eyelid movement disorder. Further investigations implementing functional MRI and PET scan may be important for a better understanding of the pathophysiology in blepharoclonus.

Potential conflicts of interest

None.

References

1. Obeso JA, Artieda J, Marsden CD. Stretch reflex blepharospasm. *Neurology* 1985; 35: 1378-80.
2. Behrman S, Scott DF. Blepharoclonus provoked by voluntary eye closure. *Mov Disord* 1988; 3: 326-8.
3. Safran AB, Moody JF, Gauthier G. Sustained blepharoclonus upon eye closure. *J Clin Neuroophthalmol* 1983; 3: 133-6.
4. Keane JR. Gaze-evoked blepharoclonus. *Ann Neurol* 1978; 3: 243-5.
5. Esteban A, Traba A, Prieto J. Eyelid movements in health and disease. The supranuclear impairment of the palpebral motility. *Neurophysiol Clin* 2004; 34: 3-15.
6. Pasik P, Pasik T, Bender MB. The pretectal syndrome in monkeys. I. Disturbances of gaze and body posture. *Brain* 1969; 92: 521-34.
7. Nashold BS Jr, Gills JP, Wilson WP. Ocular signs of brain stimulation in the human. *Confin Neurol* 1967; 29: 169-74.
8. Jacome DE. Blepharoclonus and Arnold-Chiari malformation. *Acta Neurol Scand* 2001; 104: 113-7.
9. Jacome DE. Synkinetic blepharoclonus. *J Neuroophthalmol* 2000; 20: 276-84.
10. Schmidtke K, Buttner-Ennever JA. Nervous control of eyelid function. A review of clinical, experimental and pathological data. *Brain* 1992; 115 (Pt 1): 227-47.
11. Caviness JN, Brown P. Myoclonus: current concepts and recent advances. *Lancet Neurol* 2004; 3: 598-607.
12. Lapresle J, Hamida MB. The dentato-olivary pathway. Somatotopic relationship between the dentate nucleus and the contralateral inferior olive. *Arch Neurol* 1970; 22: 135-43.
13. Lapresle J. Palatal myoclonus. *Adv Neurol* 1986; 43: 265-73.
14. Salamon-Murayama N, Russell EJ, Rabin BM. Diagnosis please. Case 17: hypertrophic olivary degeneration secondary to pontine hemorrhage. *Radiology* 1999; 213: 814-7.
15. Goyal M, Versnick E, Tuite P, Cyr JS, Kucharczyk W, Montanera W, et al. Hypertrophic olivary degeneration: metaanalysis of the temporal evolution of MR findings. *AJNR Am J Neuroradiol* 2000; 21: 1073-7.
16. Gatto M, Micheli F, Pardal MF. Blepharoclonus and parkinsonism associated with aqueductal stenosis. *Mov Disord* 1990; 5: 310-3.
17. Jacome DE. Blepharoclonus in multiple sclerosis. *Acta Neurol Scand* 2001; 104: 380-4.
18. Jacome DE. Blepharoclonus, pseudoasterixis, and restless feet. *Am J Med Sci* 2001; 322: 137-40.
19. Welch KM, Nagesh V, Aurora SK, Gelman N. Periaqueductal gray matter dysfunction in migraine: cause or the burden of illness? *Headache* 2001; 41: 629-37.
20. Tajti J, Uddman R, Edvinsson L. Neuropeptide localization in the "migraine generator" region of the human brainstem. *Cephalalgia* 2001; 21: 96-101.
21. Bucher SF, Seelos KC, Oertel WH, Reiser M, Trenkwalder C. Cerebral generators involved in the pathogenesis of the restless legs syndrome. *Ann Neurol* 1997; 41: 639-45.

การกระตุกแบบเป็นจังหวะของหนังตา (*blepharoclonus*): ตำแหน่งทางกายวิภาคและสาเหตุของอาการ

กุลธิดา เมธาวาทิน, รุ่งโรจน์ พิทยศิริ, กัมมันต์ พันธุมจินดา, ลารี คอฟแมน

Blepharoclonus คือ การกระตุกแบบเป็นจังหวะของหนังตา เป็นการเคลื่อนไหวที่ผิดปกติของหนังตาซึ่งพบได้ยาก โดยไม่มีตำแหน่งทางประสาทกายวิภาคที่ชัดเจนและเกิดได้จากหลายสาเหตุ รายงานนี้บรรยายถึงผู้ป่วยหญิงอายุ 42 ปี ซึ่งมาพบแพทย์ด้วยประวัติเดินเซ มือจับสิ่งของไม่ตรงทิศทาง และตากระพริบที่ไม่สามารถควบคุมได้ การเคลื่อนไหวที่ผิดปกติของหนังตานั้นเกิดขึ้นทั้งขณะเปิดตาและปิดตา และเข้าได้กับอาการหนังตากระตุกเป็นจังหวะ ภาพถ่ายสมองจากการตรวจด้วยคลื่นแม่เหล็กไฟฟ้า พบรอยโรคจากสมองขาดเลือดบริเวณ *red nucleus*, *dentate nucleus* และ *inferior olives* ซึ่งบริเวณเหล่านี้เป็นส่วนของสามเหลี่ยม *Guillain-Mollaret* ผู้ป่วยยังมีประวัติโรคความดันโลหิตสูงซึ่งรักษาไม่สม่ำเสมอ อาการเดินเซ และมือจับสิ่งของไม่ตรงทิศทางทุเลาลงเป็นลำดับภายในเวลา 3 สัปดาห์ ในขณะที่อาการหนังตากระตุกเป็นจังหวะนั้นทุเลาลง แต่อาการยังคงอยู่ตลอด 1 ปี ที่ติดตามการรักษา สาเหตุที่เป็นไปได้คือสมองขาดเลือดจากหลอดเลือดขนาดเล็กซึ่งสันนิษฐานจากประวัติความดันโลหิตสูงที่รักษาไม่สม่ำเสมอ ภาพถ่ายทางรังสีวิทยาของสมอง และการดำเนินโรค จึงตั้งสมมติฐานว่าอาการหนังตากระตุกเป็นจังหวะน่าจะเป็นความหลากหลายของการกระตุกเป็นจังหวะของเพดานอ่อน (*palatal myoclonus*) และเกิดจากภาวะสมองขาดเลือดจากหลอดเลือดขนาดเล็กชนิดหนึ่ง
