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Synkinetic Blepharoclonus

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Objectives: To analyze the clinical data and test results collected in a group of patients exhibiting eyelid-closure blepharoclonus (BLC) on clinical neurologic examination.

Materials and Methods: Thirty-five patients were referred for neurologic evaluation for reasons other than BLC. Clinical electrophysiologic evaluations, including cranial nerve testing and electromyograms, were done according to standards. All patients had neuroimaging studies, including brain magnetic resonance imaging and head computerized tomography, or both, and many had electroencephalograms. Additional tests were done based on the patient's symptoms or reasons for referral.

Results: Eight patients had reflex BLC. Two cases were precipitated by vertical gaze; one of these patients had hereditary palmoplantar keratoderma and cataplexy, and the other patient had Ehlers-Danlos syndrome and familial BLC. Other precipitants included speech in four cases, postural changes in two cases, and light stimulation in one case. Two patients had generalized myoclonus independent of their BLC, two patients had a history of sleep myoclonus, and several patients had BLC-associated facial myoclonus. One patient had BLC-associated myoclonus of the right shoulder. Synkinetic cranial movements were detected in 11 patients (four oculofacial, three oculopterygoid, one oculolingual, two dual cases, and one case of imitation synkinesis.) Three patients had familial BLC, seven patients had congenital developmental disorders, six patients had synkinetic tremors, and six patients had restless feet. Some indication of peripheral neuropathy was evident in eight patients.

Conclusions: Eyelid-closure BLC is an underrecognized, sporadic or familial, mostly benign, chronic eyelid-movement disorder that may be associated with tremors, myoclonus, cranial synkinesis, and restless feet. Reflex mechanisms may be identified in some patients. Gaze-induced BLC seems to have the greatest clinical relevance. In the current series, there were no examples of posttraumatic BLC, multiple sclerosis, hydrocephalus, or blepharospasm conditions previously reported to be associated with BLC. No electroencephalographic abnormalities were recorded during BLC, ruling out eyelid-closure epilepsy.

Key Words: Blepharoclonus—Blepharospasm—Cranial synkinesis—Eyelids—Movement disorder—Myoclonus—Synkinetic movements.

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Blepharoclonus is the repetitive, easily detectable, myoclonic contractions of the orbicularis oculi muscle (1). It is commonly apparent with light eyelid closure and may be suppressed by forceful eyelid contraction (2). In contradistinction, blepharospasm (BLS) is a focal dystonia manifested by forceful and sustained involuntary closure of the eyelids, often accompanied by great difficulty in opening the eyes on command or free will, which is a clinical phenomenon called "apraxia of lid opening" (3,4). However, attempts to open the eyelids during episodes of BLS may be confused with BLC, or with paretic tremors of the eyelids in a patient with partial denervation of the orbicularis oculi. Blepharoclonus may be provoked by stretching of the obicularis oculi or by gaze deviations (5,6). Synkinetic BLC is defined here as:

1. the involuntary movements, fasciculations, or facial electromyogram (EMG) motor units firing, triggered by, or associated with BLC, normally affecting muscles other than the orbicularis oculi;
2. BLC-enhanced cephalic and extracephalic focal, multifocal, or generalized tremors;
3. BLC in patients exhibiting other cranial synkinesis (synkinetic movements);
4. reflex BLC.

The last subgroup may be identified by the specific mechanism that causes BLC (see below). Those mechanisms are stretching of the orbicularis oculi, stimulation by sudden illumination, speech, changes in body posture, and gaze deviations. Although both patients reported by Obeso et al. (5) had reflex BLS and BLC, either one of these conditions may occur independently. In reflex BLS, the eyes are involuntarily forcefully shut, while in pure-reflex BLC, only rapid myoclonus of the eyelids is observed in the absence of sustained contraction of the orbicularis oculi.

MATERIALS AND METHODS

After a few patients with BLC referred for other neurologic disorders were identified by the author, a systematic search for this condition was performed for all new patients in the author's practice. A total of 35 patients with BLC, ranging in age from 11 to 75 years, was collected over a 5-year period. These patients were identified on routine neurologic examination when asked to

TABLE 1. *Reflex synkinetic blepharoclonus*

Patient/Sex/ Age (y)	Signs	Diagnoses	Symptoms	Tests	Other
1/F/38	Action tremors of hands, frequent rotational feet movements at rest; BLC with light eyelid closure enhanced by sitting or standing, greatly diminished lying down	Demyelinating retrobulbar optic neuropathy and axonal peripheral neuropathy of unknown etiology; synkinetic (reflex) BLC	Objects blurred, lacked color in vision OS; V/A 20/20	VERS showed conduction slowing through optic nerve OS; brain MRI: normal; EMG legs: complex polyphasic MUPs recorded over leg muscles; no spontaneous activity	Progressive improvement of vision in follow-up with no new symptoms
2/F/43	Hypermobile joints, soft skin with very visible veins, tenderness of the spine, left leg weakness, abnormal gait; downward gaze BLC and myokymia of lower eyelid; speech-related BLC; allodynia of teeth	Synkinetic BLC; common migraine; EDS-related LS plexopathy, subcortical nodular gliosis	Back pain, numbness, tingling of left leg; left side pulsatile headaches without warnings, sensitive teeth	LS spine MRI: normal; brain MRI: T2-weighted nodular subcortical white-matter high-intensity signals of greater prominence over the left frontal region; EMG of legs: spontaneous normal MUPs at rest over both TA and left EDB muscles	Family history of EDS, somnambulism, eyelid closure BLC
3/F/44	BLC with upward gaze; palmoplantar hyperkeratosis, greater over feet (Fig. 1)	Palmoplantar keratoderma, focal leukoencephalopathy, cataplexy, sciatica, gaze-evoked BLC	Sudden falls precipitated by emotions, without loss of consciousness; right leg postexertional pain	EEG, ECG, MRI of the LS spine, 2D echocardiogram: normal; no organomegaly by CT of the abdomen; EMG of the right leg: right sciatica; MRI of the brain: focal demyelination (Fig. 2), Hexososaminidase A, aryl sulphatase A, plasma aminoacid levels, cellular cholesterol esterification normal	Family history of hemophilia, common migraine
4/M/44	Chronic ptosis and miosis OD; action tremors of hands on flexion-extension at the wrists; frequent involuntary movements of feet at rest; eyelid-closure BLC; bilateral involuntary myoclonic contractions of the orbicularis oris with lateral gaze; frequent blinking (40–50 blinks/min); BLC triggered by intense light stimulation without LOC	Cluster headaches with residual chronic ipsilateral Horner syndrome; synkinetic BLC	Episodic severe pain behind right eye, numbness of right thigh and right side of face	Brain MRI/MRA, CNT, CT, MRI of LS spine, VERs BAERs: normal	Negative
5/F/47	Eyelid-closure BLC triggered by speech and light stimulation	Migraine with aura, synkinetic BLC	Pounding headaches preceded by compulsive yawning	Brain MRI: normal	Mother had migraines preceded by compulsive yawning
6/F/50	BLC with light eyelid closure, greatly enhanced in supine position	Synkinetic BLC; drug reaction; limited continuous facial muscle-fiber activity	Diplopia and transient confusion after ingestion of lorazepam	Brain MRI: normal; CNT: normal MUPs present at rest over right orbicularis oris and both mentalis muscles on facial EMG; Anti-Yo, anti-Ri antibodies: negative	Breast cancer by history; no previous history of Bell palsy
7/F/66	BLC with eyelid closure and during speech; ipsilateral deviation of jaw with lateral gaze; generalized deep-tendon hyporeflexia	Monoclonal gammopathy-associated peripheral neuropathy, synkinetic BLC, oculopterygoid synkinesis, speech-induced BLC	Intermittent numbness of limbs and left side of face	IgG lambda monoclonal gammopathy; C-spine MRI: spinal stenosis; left leg EMG: complex prolonged polyphasic MUPs over RF and EDB muscles with no F-wave responses	Hypertension
8/F/73	Eyelid closure and speech-induced BLC; leans toward left when sitting; rigidity, akinesia of right arm	Synkinetic BLC, corticobasal ganglionic degeneration, truncal dystonia	Writing tremors, poor mobility, abnormal posture	Head CT: cortical atrophy; EEG, CNT, SPECT: normal	Negative

BAER, brain stem auditory-evoked responses; BLC, blepharoclonus; CNT, cranial nerve testing; CT, computed tomography; EDB, extensor digitorum brevis; ECG, electrocardiogram; EDS, Ehlers-Danlos; EEG, electroencephalogram; Ig, immunoglobulin; LOC, loss of consciousness; LS, lumbosacral; MRA, magnetic resonance angiogram; MRI, magnetic resonance imaging; MUP, motor unit potentials; RF, rectus femoris; SPECT, single proton emission CT; TA, tibilias anterior; V/A, visual acuity; VER, visual-evoked response.

TABLE 2. *Blepharoclonus and tremors*

Patient/Sex/ Age (y)	Signs	Diagnoses	Symptoms	Tests	Other
9/F/12	BLC, action tremors of hands on flexion-extension movements at the wrists; repetitive movements of feet at rest while sitting; BLC-induced generalized multifocal tumors	Synkinetic BLC, essential benign tremors (?), episodic tension headaches	Generalized morning tremors; headaches	Normal EEG, EMG/NCV of the legs, MRI of the brain	Mother and sister had somnambulism
10/F/17	Eyelid-closure BLC; action tremors of the hands on flexion-extension at the wrists; restless feet; hypermobile joints, scoliosis, fusion of second and third toes of each foot; unilateral twitching of mentalis and orbicularis oris muscles with ipsilateral gaze	Catamenial migraine with postdromal fatigue; synkinetic familial BLC; EDS, continuous muscle fiber activity; action tremors of the hands and restless feet	Monthly pulsatile headaches around menses followed by fatigue for 5 days, "internal shaking"; easy bruising	Normal EEG, MRI of the brain, NCV, CNT: delayed left; R2 component of blink reflex; EMG: spontaneous normal MUPs at rest over right TA and EDB muscles	Mother and maternal grandmother with BLC; family history of ruptured intracranial aneurysms, somnambulism, EDS
11/M/32	Cephalic tremors associated with eyelid-closure BLC	Synkinetic BLC; posttraumatic right brachial plexopathy, right arm paroxysmal dystonia essential nonepileptic subcortical myoclonus	Generalized intermittent shaking, right shoulder pain, right hand numbness and painless spasms of right arm induced by exercise, beginning after serious chest injury	Normal EEG during generalized tremors; normal head CT and EMG/NCV of right arm	Negative
12/F/37	Eyelid-closure BLC associated with head tremors; action tremors of hands	Synkinetic BLC; antiphospholipid antibody syndrome; migraine with aura and persistent visual phenomena; transformed migraine	Recurrent pulsatile headaches preceded by phosphenes; daily background headaches	Elevated IgG/IgA cardiolipin antibodies; brain MRI, EEG, CNT, CSF studies: normal	Family history of migraine
13/F/46	Head/postural hand tremors simultaneous with eyelid-closure BLC; pain on palpation of muscles; rare fasciculations of legs	Right sciatica (?), C6 and L4 disc herniations; postexertional fatigue and myalgias; autoimmune disorder (celiac disease without gastrointestinal manifestations?); synkinetic BLC	Right leg pain, weakness; left facial numbness, "internal shaking," postexertional muscle pain, fatigue	Brain MRI, EEG, EMG/NCV of legs, CNT, CSF studies: normal; MRI of C-spine: mild central herniation C6 disc; MRI of LS-spine: right side L4 disc herniation; gliadin antibodies: positive; TPO titer: 59 u/mL; euthyroid	Hashimoto thyroiditis, anemia, leukopenia
14/M/49	Eyelid-closure BLC; action tremors of hands on flexion-extension of wrists; restless feet; hypermobile joints, scoliosis, fusion of second and third toes on each foot; unilateral twitching of mentalis and orbicularis oris muscles with ipsilateral gaze	Synkinetic BLC, axonal peripheral neuropathy (lithium?), action tremors of hands, chronic unilateral deafness	Numbness and tingling of hands and feet	EMG/NCV testing left arm: complex prolonged MUPs of FDI, APB, biceps, deltoid, pronator teres muscles; low amplitude left ulnar sensory potential	Bipolar affective illness treated with lithium for 18 y
15/F/63	Midline linear sebaceous nevus; eyelid-closure BLC and orbicularis oculi myokymia	Vasodepressor syncope, familiar midline linear sebaceous nevus, silent lacunar strokes, synkinetic BLC	Fainting	Normal carotid ultrasound and EEG; head CT: multiple small subcortical white-matter lacunar strokes	Hypertension; son and grandson with midline nevus
16/F/11	Eyelid closure BLC associated with facial myoclonus	Synkinetic BLC	Headaches	Head CT: normal	Somnambulism; attention deficit disorder; mother has migraine and history of somnambulism as a child

See Table 1 for definitions of additional abbreviations.
CSF, cerebrospinal fluid; NCV, nerve conduction velocities; TPO, thyroid peroxidase antibody.

lightly close their eyelids for a minimum of 10 seconds. The patients were also examined for clinical or electrophysiologic cranial nerve testing evidence of facial synkinesis and for evidence for any reflex precipitants, including stretching of the orbicularis oculi, sudden illumination of the eyes, speech, changes in body posture, and gaze deviations. The patients were classified at a later time into five subgroups, based upon the kind of

reflex mechanism (Table 1), associated tremors (Table 2), myoclonus (Table 3), synkinetic movements (Table 4), or presence of synkinesis evident by facial EMG only (Table 5). The patients were examined by the author on more than one occasion and followed for a minimum of 2 years. There was no consanguinity among the patients examined. The patients were referred for neurologic consultation for reasons other than BLC. The majority of patients were women, in part due to local patterns of referral that include gynecologists in the role of primary care physicians.

Patients either did not experience or were not incapacitated by their eye twitching, but most were aware of their involuntary eyelid movements, especially at night when they closed their eyes before falling asleep. None were aware of having cranial synkinesis. Myoclonus was distinguished from tremors based on the larger amplitude and slower frequencies of the movements in myoclonus. Restless feet consisted mostly of rotational movements of the feet while sitting or lying down and was differentiated from restless legs by the lack of sensory symptoms in the legs, the absence of premonitory urge to move the feet, and when attempts to control the movements did not generate anxiety in the patient. Cranial nerve testing consisted of blink reflexes, facial EMG, and mental and facial nerve latencies. Nerve conduction velocity testing included motor and sensory nerves. Cranial nerve testing and EMG/nerve conduction velocity studies were performed at the author's office using a Nicolet Compass portable EMG unit (Nicolet Biomedical Inc., Madison, WI), following standard procedure. Other laboratory and imaging studies were done at the local hospital. Additional tests were completed according to the symptoms of each patient and according to the reasons for referral.

RESULTS

Of the eight patients with reflex BLC, none exhibited BLS or had BLC provoked by stretching of the orbicularis oculi muscle. Blepharospasm was not observed in the three patients with frequent blinking rates (>30/min). Gaze-evoked BLC was present in two patients; one patient had Ehlers-Danlos syndrome and familial BLC, and the other patient had hereditary palmoplantar keratoderma, focal hemispheric subcortical demyelination (leukoencephalopathy), and cataplexy without narcolepsy.

TABLE 3. *Blepharoclonus and myoclonus*

Patient/Sex/ Age (y)	Signs	Diagnosis	Symptoms	Tests	Other
17/F/25	Eyelid-closure BLC; ipsilateral facial myoclonus with monocular eyelid closure and BLC	Notalgia paresthesica; chronic daily headaches; synkinetic BLC	Daily global headaches, burning sensation between scapulas	EMG/NCV of left leg, CNT, brain MRI: normal; EEG: normal background with occasional brief, generalized, nonspecific theta discharges without clinical manifestations	Negative
18/F/39	BLC with eyelid closure associated with right-shoulder myoclonus; action tremors of hands on flexion-extension at wrists with fingers hyperextended; restless feet	Synkinetic BLC, action tremors of hands; restless feet; axonal peripheral neuropathy	Muscle pain, postexertional exhaustion, global daily headaches	EEG, brain MRI: normal; EMG of legs: complex prolonged MUPs, no genetic duplication or deletion of PMP-22 gene; TPO titer: 3.8 u/mL; euthyroid	Hashimoto thyroiditis by history, IBS, chronic daily headaches, anxiety disorder, fibromyalgia
19/F/70	BLC with light eyelid closure associated with rhythmic contraction of left frontalis muscle; old right Bell palsy and facial contracture; action tremors of left hand	Synkinetic BLC; temporal arteritis (?)	Severe, constant right temple pain	Brain MRI, CSF studies: normal; temporal artery biopsy negative; sedimentation rate: 42 mL/hr; TPO titer: 160 u/mL; euthyroid	Hashimoto thyroiditis, IBS
20/F/73	Generalized startle myoclonus without LOC; asymmetric eyelid-closure BLC (>OD) associated with bilateral facial myoclonus; pectus excavatum	Startle (nonepileptic) myoclonus, synkinetic BLC, trigeminal neuralgia; remote history of left hemifacial spasms	Left facial paroxysmal "stabbing" pain; generalized severe body twitching triggered by startle	Brain MRI, head CT, EEG: normal; delayed right R2 component of blink reflex	Remote history of twitching/spasms of left side of face relieved by posterior fossa vascular decompression; hypertension
21/F/74	Eyelid-closure BLC associated with facial myoclonus	Synkinetic BLC, paroxysmal hyperhidrosis	Dizziness, poor balance, headaches with visual aura aborted by repetitive volitional eye movements; episodes of abrupt-onset generalized sweating	Normal head CT	Ulcerative colitis, osteoarthritis, migraine with aura, family history of migraine

See tables 1 and 2 for definitions of additional abbreviations.
IBS, irritable bowel syndrome.

TABLE 4. *Blepharoclonus and synkinetic movements*

Patient/Sex/ Age (y)	Signs	Diagnosis	Symptoms	Tests	Other
22/M;12	Eyelid-closure BLC; ipsilateral deviation of jaw with lateral gaze (Figs. 3A, B, and C)	Mesial temporal sclerosis, secondary generalized seizures, eyelid-closure BLC, oculopterygoid synkinesis	Recent onset of tonic-clonic seizures	Normal EEG; brain MRI, CT: right temporal ventricular enlargement and right mesial temporal atrophy with no enhancing lesions	Congenital (surgically corrected) encephalocele and imperforated anus; family history of polydactyly
23/F/14	Light eyelid-closure BLC with alternating periods of rapid/slow myoclonic eyelid contractions; ipsilateral elevation of eyebrow and jaw deviation with lateral gaze	BLC with oculopterygoid and oculofrontalis synkinesis; familial BLC; episodic tension headaches	Pressure-like bilateral headaches	CNT, head CT: normal	Asthma
24/M/20	Rhythmic elevation of eyebrows with eyelid-closure BLC; postural and action tremors of hands; tenderness of neck on palpation; hypoactive deep tendon reflexes	Synkinetic BLC, posttraumatic headaches, cervical sprain; congenital Arnold Chiari malformation and cervical syrinx	Headaches and neck pain after lateral whiplash injury	Normal EEG; Arnold Chiari malformation detected on brain MRI; small central syrinx on cervical MRI	Negative
25/F/22	Elevated optic discs with no exudation or peripapillary hemorrhages; normal venous pulsations; eyelid-closure BLC; ipsilateral jaw deviation with lateral gaze; obesity	Idiopathy intracranial hypertension? (declined lumbar puncture); "icepick-like pain"; synkinetic BLC, oculopterygoid synkinesis	Headaches, sharp head pain; blurred vision 30 times/d ("like looking through glass"); dizziness, occasional tinnitus	Normal EEG, brain MRI, head CT; CNT: MUPs at rest recorded from frontalis, orbicularis oris, and mentalis mucles bilaterally, greater on left side	Family history of epilepsy; congenital strabismus corrected with surgery during childhood
26/F/25	BLC, action tremors of hands, ipsilateral deviation of jaw with lateral gaze, occasional multifocal muscle fasciculations of limbs	Posttraumatic basilar artery migraine, facial motor axonopathy and (restricted) continuous muscle fiber activity; synkinetic BLC; oculopterygoid synkinesis	Recurrent occipital headaches, neck pain, blurred vision after minor head trauma	EEG, brain MRI, NCV right arm: normal; CNT: abnormal polyphasic MUPs recruited over right mentalis and orbicularis oris muscles; MUPs at rest of left mentalis and both frontalis muscles	Negative
27/M/31	BLC with light eyelid closure; bilateral contraction of chin muscles on lateral gaze	Synkinetic BLC, postinfectious eustachian tube dysfunction, anxiety disorder, episodic tension headaches	Global pressure headaches; occasional crackling sound of right ear after acute sinusitis	Brain MRI, CNT, EMG-NCV of left arm: normal	Negative
28/F/34	Alternating "see-saw" elevation of eyebrows during speech; light eyelid-closure BLC; forceful opening of mouth induced yawning (Fig. 4); no echopraxia otherwise	Focal epilepsy; complex partial seizures with secondary generalization; imitation synkinesis (reflex yawning), BLC	Episodes of confusion and automatic behavior preceded by bad taste in mouth, exceptionally terminating in convulsions	Brain MRI, CT; normal; EEG: generalized slow wave discharges; CNT: absent right R1 blink reflex component; abnormal polyphasic MUPs of bilateral frontalis muscles	Negative
29/F/35	Monocular BLC, action tremors of hands, restless feet, tonic pupils, focal nodular atrophy of subcutaneous tissue; extreme startle response to unexpected stimuli; ipsilateral deviation of jaw and tongue with lateral gaze	Synkinetic and monocular BLC; oculopterygoid and oculolingual synkinesis; hyperekplexia, continuous muscle fiber activity syndrome, restless feet; lipodystrophy, tension headaches, terminal axonal neuropathy	Headaches, back pain, nocturnal leg muscle twitching, postexertional exhaustion	CNT, MRI of LS-spine, EEG, left quadriceps muscle/sural nerve biopsy and NCV of legs: normal; negative PMP-22 genetic deletion or duplication; EMG of legs: spontaneous MUPs at rest of gastrocnemius, TA, and EDB muscles	Posttraumatic stress disorder; bipolar affective illness; asthma
30/F/40	Right facial weakness and contracture; pulling of right corner of mouth with blinks; eyelid-closure BLC	Synkinetic BLC; catamenial left retroauricular pain, postparalytic facial synkinesis, facial contracture	Pain behind left ear with menses; chronic pulling sensation of right side of face; muscle twitching after ipsilateral Bell palsy years earlier; facial twitching worse with menses	Brain MRI, EEG, CSF studies; normal; CNT: tonic motor unit discharges recorded over right zygomaticus major muscle with eye closure; BLC; complex prolonged MUPs over right facial muscles (chronic reinnervation); no denervation	Negative

TABLE 4 (*Continued*)

Patient/Sex/ Age (y)	Signs	Diagnosis	Symptoms	Tests	Other
31/F/36	Eye-closure BLC; mild contraction at corners of mouth with eye blinks; sustained, eyelid-closure induced upward pulling of right corner of mouth; unable to wink OD	Recurrent vestibular neuronitis; synkinetic BLC	Paroxysmal nonpositional vertigo	CNT: normal MUPs present at rest over both mentalis muscles; brain MRI, EEG, CSF studies, and EMG/NCV of left arm: normal	No history of Bell palsy, no evidence of subclinical peripheral neuropathy
32/F/56	Eyelid-closure BLC; ipsilateral deviation of the tongue with lateral gaze	Vestibular neuronitis, congenital venous angioma, eyelid-closure BLC, oculolingual synkinesis	Dizziness	EEG: nonspecific brief generalized theta episodes while awake; brain MRI; right cerebellar venous angioma (Fig. 5); normal CNT	Nocturnal myoclonus and hypertension

See Tables 1 and 2 for definitions of additional abbreviations.
PMP, peripheral myelin protein.

Blepharoclonus was induced by speech in only two patients. In addition, one patient with light-induced BLC and one patient with gaze-induced BLC also exhibited speech-induced BLC. Speech-induced BLC was distinguished from BLC-like tics during normal speech on the basis of a longer duration and a larger amplitude of eyelid myoclonus in the former. In addition, these patients had eyelid-closure BLC. Unconscious sustained closure of the eyelids during speech may have precipitated the appearance of BLC in these four patients. Specific posture was the precipitating mechanism of BLC in two of the patients. Several patients had BLC-associated facial myoclonus, but there were two patients with generalized myoclonus independent of BLC and two patients with nocturnal (sleep) myoclonus. One patient had BLC-induced focal myoclonus of the right shoulder. Seven patients had BLC-associated tremors, three patients had abnormalities detected by facial EMG only, and 11 patients had BLC-synkinetic movements (three oculofacial and three oculopterygoid cases, and one oculolingual case; Figs. 3A–C). There were two cases of dual synkinetic movements; one with oculolingual and oculopterygoid synkinesis, and the other with oculofacial and oculopterygoid synkinesis. One patient had imitation synkinesis (reflex yawning with imitation of yawning by widely opening her mouth; Fig. 4), and another patient was unable to close her right eye voluntarily. One patient exhibited monocular BLC in isolation, and another patient had asymmetric BLC. One patient had alternating rapid and slow BLC. Three patients with familial BLC and seven patients with congenital developmental disorders are described. Restless feet syndrome was present in six patients, three of whom had features of peripheral neuropathy. Eight patients had signs or symptoms of mild axonal peripheral neuropathy, including examples of continuous muscle fiber activity syndrome. Three patients had Hashimoto thyroiditis, but they were euthyroid and had low thyroid peroxidase antibody titers. There were no examples of multiple sclerosis or brain tumors. One patient had a cerebellar venous angioma (Fig. 5).

TABLE 5. *Blepharoclonus and EMG synkinesis*

Patient/Sex/ Age (y)	Signs	Diagnosis	Symptoms	Tests	Other
33/F/15	Rapid blinking (>30/min); eyelid-closure BLC	Familial synkinetic BLC	Pounding, recurrent bilateral headaches	Brain MRI and EEG: normal; CNT: MUP discharges both mental and right orbicularis oris muscles with right lateral gaze	Asthma, seasonal depression, migraine without aura; mother and maternal grandmother had similar BLC
34/M/42	Pain on pressure applied behind right ear, radiating to ipsilateral frontal region and eye; mild right facial hemiatrophy (no history of facial palsy)	Congenital facial hemiatrophy, synkinetic BLC, osteoarthritis of C-spine, great auricular neuralgia, sleep myoclonus	Intermittent right retroauricular pain, generalized nocturnal body twitching	Brain MRI with contrast and EEG: normal; sleep myoclonus recorded during overnight sleep studies; C-spine x-rays: DJD. CNT: MUPs at rest recorded at right mentalis muscle during light eyelid closure	Negative
35/F/75	Frequent blinking (>30 blinks/min); eyelid-closure BLC, hypoacusis in left ear	Midbrain lacunar stroke? synkinetic BLC	Transient diplopia with downward gaze	Head CT: normal; CNT: spontaneous normal MUPs of orbicularis oris bilaterally at rest and during eyelid closure	Osteoarthritis

See tables 1 and 2 for definitions of additional abbreviations.
DJD, degenerative joint disease.

Two patients had epilepsy but exhibited no focal epileptic activity related to eye movements or eyelid closure during their electroencephalograms (EEGs). Details of the clinical data and results of testing for each patient are listed in the accompanying tables, which divide the different subgroups.

DISCUSSION

I believe BLC is underdetected because it is not spontaneously reported by patients; its presence is frequently missed by the examiner during routine neurologic examination because the patient is asked to close his or her eyes only briefly, not waiting long enough for BLC to appear after a variable latency period, or because he or she is asked to close the eyes forcefully (to determine the presence of facial weakness), while at the same time suppressing BLC.

Previously recognized causes of BLC are head trauma, hydrocephalus, and multiple sclerosis (1,2,6,7). Multiple sclerosis was the underlying condition in the two patients of Keane (6) with gaze-evoked BLC. Obeso et al. (5) reported the case of a patient with essential BLS. None of the patients herein reported experienced major head trauma, had evidence of hydrocephalus, had signs of multiple sclerosis, or had BLS. Three patients had Hashimoto thyroiditis (patients 13, 18, and 19), but they were euthyroid and had no cognitive disturbance or alteration of consciousness level. Their blood thyroid peroxidase titers were not significantly elevated to explain their BLC on the basis of Hashimoto encephalopathy that potentially may have caused myoclonus of the orbicularis oculi muscles (8). History of Bell palsy was elicitable only in two patients (patients 19 and 30), and only two patients (patients 32 and 34) had nocturnal (sleep) myoclonus. No patients showed evidence of epilepsy on EEG during BLC, including the two individuals with epilepsy, and no patients exhibited EEG epileptic activity associated with their tremors, synkinesis, or myoclonus. Although six patients (patients 1, 4, 9, 10, 18, and 29) had restless feet, and three patients (patients 4, 33, and 35) had frequent blinking, none developed additional involuntary movements, including dystonia, BLS, and oculogyric crisis.

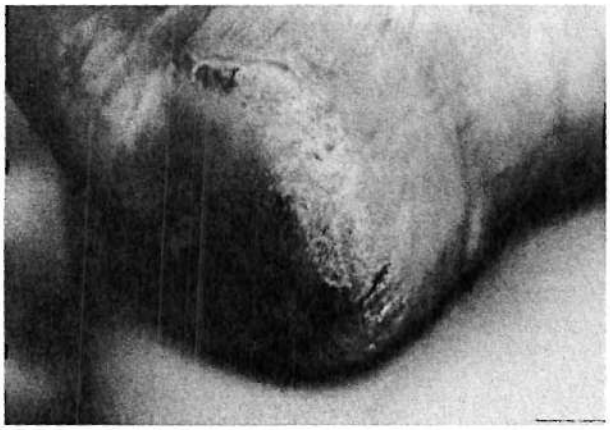

FIG. 1. Plantar hyperkeratosis (keratoderma) of the left foot (patient 3).

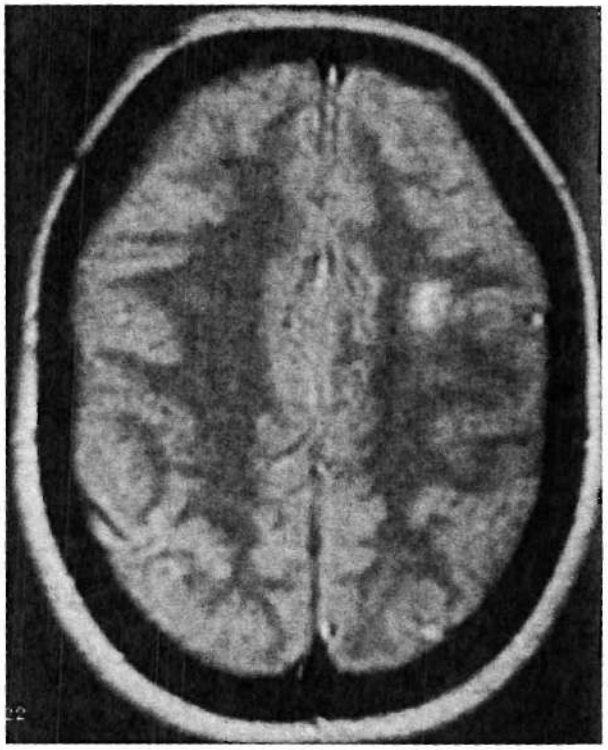

FIG. 2. Brain MRI T2-weighted images show an area of white-matter increased signal over the left hemisphere corona radiata compatible with focal demyelination (patient 3).

Patient 3 had palmoplantar keratoderma, which is an inherited condition recently reported in association with leukoencephalopathy (9) (Fig. 1). She presented with painful gaze-evoked BLC and cataplexy similar to the cases of Niemann Pick disease type C (10). Her brain MRI showed a small globular area of hyperintensity on the T2-weighted images localized to the left centrum semiovale, which was consistent with focal demyelination (restricted leukoencephalopathy) (Fig. 2). However, her cultured skin fibroblasts did not demonstrate the cytochemical abnormalities typical of Niemann Pick disease type C (10). To my knowledge, neither of these clinical signs have been reported in patients with palmoplantar keratoderma.

Cranial synkinesis is often overlooked by the examiner because it is rarely symptomatic. Some signs are very subtle and require close examination because synkinetic facial movements may be isolated, unsustained, or of small amplitude; they may be congenital or acquired, as in the example of synkinesis after Bell palsy, in which case they are more apparent. Many types have been described before and after the landmark paper on the subject by Schwarz (11) in 1962. The pathogenesis of synkinetic BLC cannot be ascertained. In cases with no apparent immediate cause, aberrant crossed innervation established during fetal development of the cranial nerves may be postulated. Patient 34, who had congenital facial hemiatrophy, is an example that supports the de-

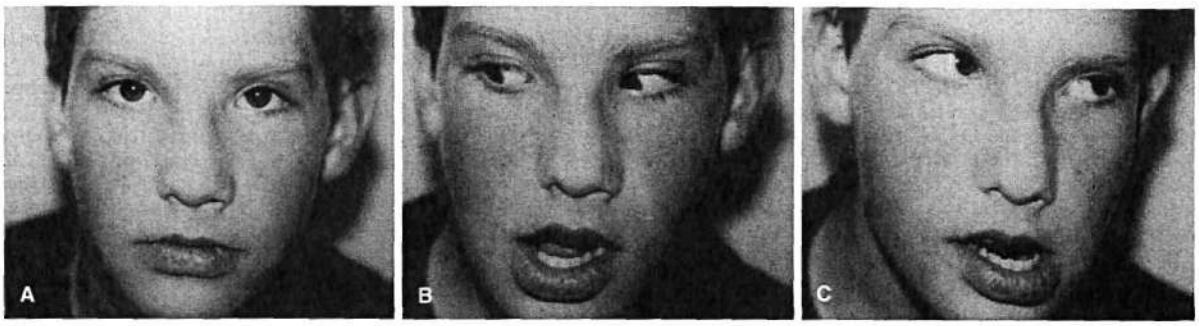

FIG. 3. A–C: Lateral jaw deviation with lateral gaze (oculopterygoid synkinesis) (patient 22).

velopmental theory. In acquired cases (i.e., after Bell palsy), misdirected regeneration of cranial nerve axons is the usual explanation without excluding the potential participation of the mechanisms of peripheral ephapsis and central synaptic reorganization (11–13). Because synkinetic movements do not always involve the facial muscles, it cannot be proposed in every case that the associated movements were precipitated by peripheral facial nerve fibers, or that BLC represents an abnormality of the innervation of the obicularis oculi muscle. In examples of BLC-induced or enhanced tremors, a state of central hyperexcitability could be adduced, although future additional electrophysiologic testing with somatosensory-evoked potentials and transcranial magnetic stimulation are needed on similar patients in order to support this hypothesis.

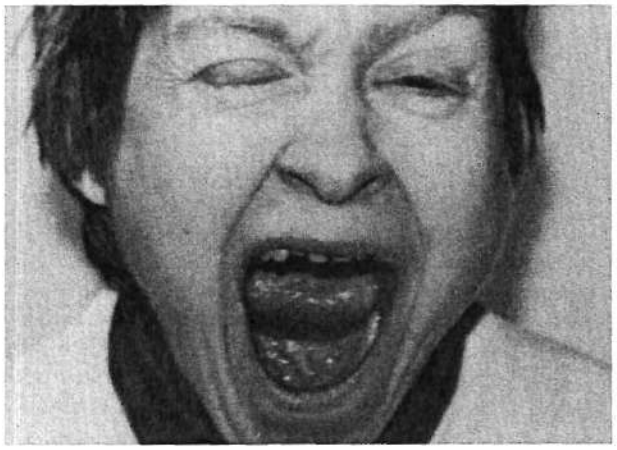

FIG. 4. Forceful mouth opening triggers reflex yawning (patient 28).

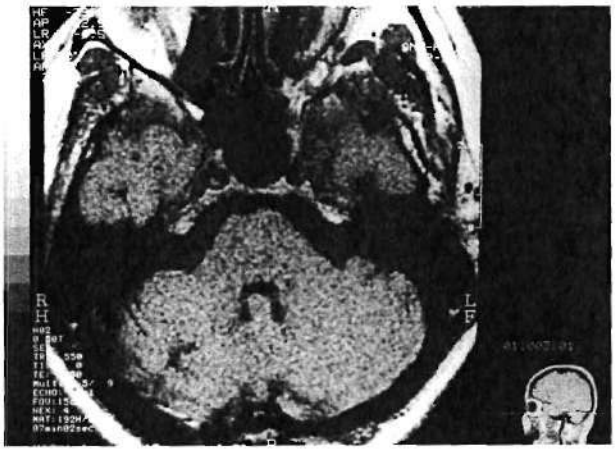

FIG. 5. Venous angioma of the right cerebellar hemisphere (brain MRI T1-weighted images) (patient 32).

The original reports on BLC suggest that its presence constitutes a sign of major neurologic illness (1,2). None of these patients suffered from a serious progressive neurologic illness, at least on a short-term basis. Instead, the clinical data presented here indicate the following:

1. BLC is a focal tremor of the obicularis oculi, at times forming part of more widespread benign tremors or myoclonus;
2. BLC can be the expression of a familial trait (as in patients 10, 23, and 33);
3. BLC often constitutes an isolated fortuitously discovered clinical sign;
4. BLC at times is associated with (underdiagnosed) cranial synkinesis and has a benign course in most individuals;
5. BLC may have different precipitants, but gaze-evoked BLC probably has the greater clinical relevance or is more likely to be found in individuals with active or progressive neurologic disease (i.e., multiple sclerosis, Niemann Pick disease, palmoplantar keratoderma).

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