

CASE REPORT

Stroke-induced resolution of primary blepharospasm: evidence for the lenticular nucleus as a control candidate

John Christopher Bladen,¹ Jasdeep Singh Gill,² Katherine Miskiel,³ Daniel George Ezra¹

¹Department of Oculoplastics, Moorfields Eye Hospital, London, UK

²Development, Ageing and Disease, UCL Institute of Ophthalmology, London, UK

³Victor Horsley Department of Neurosurgery, National Hospital for Neurology and Neurosurgery, London, UK

Correspondence to

John Christopher Bladen, john.bladen1@nhs.net

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SUMMARY

Primary blepharospasm is an adult-onset focal dystonia characterised by involuntary contractions of the orbicularis oculi, leading to bilateral spasmodic closure of the eyelids. While spasms of this muscle constitute the hallmark of disease, other motor manifestations include increased spontaneous blinking and apraxia of eyelid opening. Originally misdiagnosed as a psychiatric condition, blepharospasm is now well established as being of neurological origin although questions remain as to its pathophysiological mechanisms.

We report a 66-year-old woman who had a 14-year history of primary blepharospasm which completely resolved following a left medial cerebral artery thromboembolic infarct of the lenticular nucleus. This report provides supporting evidence of the lenticular nucleus as a key structure mediating the disease which can lead to functional blindness.

BACKGROUND

Primary (essential) blepharospasm is a focal dystonia characterised by involuntary contractions of the orbicularis oculi (OO), triggering bilateral spasmodic closure of the eyelids.¹ Although classically associated with OO spasms, it also constitutes other motor manifestations including increased spontaneous blink rate and apraxia of eyelid opening; the latter is a relatively rarer manifestation more commonly associated with extrapyramidal disease.^{2,3} Clinical characteristics include a female preponderance, age of onset between the fifth and seventh decade and a propensity for spread to adjacent muscle groups.^{4,5} Most cases of primary blepharospasm occur sporadically, however, up to 25% of patients have at least one family member affected by dystonia, implicating a genetic component in its aetiology.^{6,7}

With a greater frequency of psychiatric disturbances occurring in patients, such as depression and anxiety, blepharospasm was long misdiagnosed as a psychiatric condition.^{8,9} Its neurological origin is now well established with neurotoxic agents rendering it a curable condition, although questions remain regarding its pathophysiology.^{10,11}

Both neurophysiological and structural/functional neuroimaging studies have implicated dysfunction of basal ganglia circuitry in disease aetiology. Electromyogram (EMG) activity in the OO

of blepharospasm patients is significantly greater than healthy subjects,¹² with a case reporting associated increased single-cell firing in the internal globus pallidus.¹³ Anatomically, MRI has shown volumetric increase in putamen grey matter in patients,^{14,15} with functional MRI (fMRI) demonstrating its corresponding activation.¹⁶ Execution of motor function is ascribed to the putamen through multiple connections with other components of the basal ganglia. Modulation of motor response is expected to have a contributory role, thus making the lenticular nucleus a likely candidate area for the initiation of primary blepharospasm. In view of the significant effect of blepharospasm on patient quality of life, it is of great importance to further elucidate its aetiology to guide prevention.^{17,18}

CASE PRESENTATION

A 66-year-old woman had suffered from a 14-year history of primary blepharospasm. The frequency of blinking episodes increased with time, becoming almost constant in nature and impacting on her ability to drive. Subsequently, she was referred to the Botulinum Toxin Clinic for periorbital injections at 4 monthly intervals, which temporarily resolved the symptoms to good effect. Her medical history included hypercholesterolaemia treated with simvastatin, while her social history included being an ex-smoker and stopping 3 years prior.

She awoke with sudden onset of right-sided hemiparesis involving the hand, leg and face, associated with slurred speech. She was taken to the local hyper-acute stroke unit for an urgent CT brain, which demonstrated a cerebral infarct secondary to a left medial cerebral artery thrombus (see [figure 1](#)), so was thrombolysed within 3 hours of onset. She made excellent progress with recovery of most of her neurological deficit over the following few days. Notably, her symptoms of blepharospasm had completely resolved from the time of the stroke.

OUTCOME AND FOLLOW-UP

On examination 3 months after the event, she had normal visual acuity, normal visual fields and full ocular movements. There was mild residual weakness of her right facial and accessory nerves (cranial nerves VII and XI, respectively). The ocular surface was normal, as was the rest of the ophthalmic examination. Importantly, no blepharospasm



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Figure 1 CT brain within 3 hours of stroke symptoms. A thrombus is lodged in the left medial cerebral artery (MCA); reduced attenuation is seen in the left lenticular nucleus with subtle loss of grey/white matter differentiation in the left precentral gyrus, consistent with acute left MCA ischaemia.

was observed over a continuous period of 1 hour, which was confirmed by video recording. Review at 12 months demonstrated continued resolution of the primary blepharospasm despite full recovery of the hemiparesis.

DISCUSSION

The aetiology of primary blepharospasm is unknown but likely to be multifactorial, involving central control mechanisms with the added possibility of individual variation. Triggers such as pain (including ocular surface irritation), light, stress or emotion can also induce the spasm. Treatment is thus partly directed to reducing these triggers, including lubricants, tinted glasses and behaviour modification.^{19–20} Paralysis of the spasmodic muscles using botulinum toxin remains the mainstay of treatment, however, can exacerbate ocular surface dryness and cause diplopia or blepharoptosis.²¹

The role of the lentiform nucleus in primary blepharospasm is supported by microstructural abnormalities found by Yang *et al* in structural neuroimaging,^{22,23} while functional studies demonstrate its overactivity alongside the cerebellum and supplementary motor regions.²⁴ More recently, resting-state fMRI revealed dysfunctional neural fluctuations at the bilateral striatum, which correlated with clinical symptoms of blepharospasm.²⁵ Moreover, subthalamic nucleus induction of blepharospasm during deep brain stimulation can be ablated by stimulation of the internal globus pallidus, thus highlighting an area of control within the basal ganglia.²⁶

We report the first case of definitive resolution of blepharospasm following infarction to an area encompassing the left lenticular nucleus. Moreover, the unilateral infarct gave bilateral resolution and, importantly, there was no return of the blepharospasm despite recovery of the hemiparesis. This bears similarity to parkinsonian tremor, the resolution of which following

internal globus pallidus infarction led to the development of functional neurosurgery.²⁷ The proposed mechanism of resolution is either the loss of a dominant excitatory signal that was inducing blepharospasm, or stimulation of a dominant control centre that suppresses the blepharospasm by the infarct. In the case of the latter, this may be within the internal globus pallidus as identified by the aforementioned deep brain stimulation study.

In contrast to our stroke-induced resolution of blepharospasm, other stroke cases report its secondary induction including after unilateral hemispheric cerebral infarction,²⁸ bilateral thalamic infarction,^{29,30} unilateral striatal infarction³¹ and unilateral parietotemporal infarction.³² This supports accumulating evidence for several brain regions, not just the basal ganglia, in causation of blepharospasm, thus implicating it as a network disorder resulting from dysfunction of one particular component.³³ This hypothesis also rationalises the heterogeneity seen in its clinical presentation, including frequent non-motor manifestations such as ocular sensory symptoms and cognitive disturbance.^{34,35}

A limitation of this case is that no MRI was performed as this could have localised the infarct to the putamen or medial/lateral basal ganglia. We can postulate, however, that the loss of control leading to the primary blepharospasm in this individual originated in the left lenticular nucleus.

Learning points

- ▶ Primary blepharospasm is a focal dystonia characterised by involuntary contractions of the orbicularis oculi.
- ▶ Blepharospasm is a neurological condition, although often misdiagnosed as psychiatric, and is eminently treatable with neurotoxic agents.
- ▶ Aetiology of primary blepharospasm is likely multifactorial, involving central control mechanisms and individual variation.
- ▶ Neurophysiological and neuroimaging studies both support a role of the basal ganglia in blepharospasm.
- ▶ Resolution of primary blepharospasm in this patient who had a stroke with an infarct encompassing the left lenticular nucleus implicates this as a key structure in pathogenesis.

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