CASE REPORT

Ocular Neuromyotonia Associated with Chronic Inflammatory Demyelinating Polyneuropathy

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ABSTRACT

Ocular neuromyotonia (ONM) is a neuro-ophthalmic disorder characterized by episodic diplopia caused by contraction of one or more ocular muscles due to spontaneous excitation of the respective ocular motor nerve. We report a patient whose ocular neuromyotonia arose in the setting of a subacute demyelinating polyneuropathy consistent with chronic inflammatory demyelinating polyneuropathy (CIDP) and subsequently resolved following the initiation of intravenous immunoglobulin (IVIg) for her neuropathy. Our patient provides additional evidence towards the role of demyelination and ephaptic neurotransmission in ocular neuromyotonia and also represents the first reported case of ocular neuromyotonia associated with a systemic neurological condition.

Keywords: Chronic inflammatory demyelinating polyneuropathy, diplopia, ocular motility, ocular neuromyotonia

INTRODUCTION

Ocular neuromyotonia (ONM) is a neuro-ophthalmic disorder characterised by episodic diplopia caused by contraction of one or more ocular muscles due to spontaneous excitation of the respective ocular motor nerve.¹ Most patients with ONM have a history of cranial irradiation or local intracranial pathology.^{1–5} We report a patient whose ocular neuromyotonia arose in the setting of a subacute demyelinating polyneuropathy consistent with chronic inflammatory demyelinating polyneuropathy (CIDP) with cranial nerve involvement.

CASE REPORT

A 78-year-old woman with a 2-year history of polyneuropathy was referred to us for 3–4 months of intermittent binocular diplopia. On presentation, she

reported 6–10 daily stereotyped episodes of vertical diplopia lasting approximately 1 minute, each with spontaneous resolution. She denied any oscillopsia or unilateral oscillation. There was no diurnal variability, and the episodes were not accompanied by ptosis, dysarthria, dysphagia, or proximal muscle weakness.

Her initial neuro-ophthalmic examination was normal. Visual acuity was 20/20 OU with normal colour perception, fields, pupils, and fundi. Neither ptosis nor diplopia was provoked by sustained upgaze. There was no Cogan lid twitch. The orbicularis oculi and orbicularis oris muscles were strong. There was normal facial symmetry. Smooth pursuit and saccades were normal, and alternate cover testing showed orthophoria at near and far in all cardinal directions of gaze (see Supplementary Video).

Following the initial examination, she experienced an episode of diplopia in the office. Repeat measurements using cross-cover testing showed 8 prism dioptres of right hypertropia and 6 prism dioptres of

exodeviation in primary gaze, which spontaneously resolved after 1 minute. There were no torsional saccades noted during this time (see Supplementary Video).

Brain magnetic resonance imaging (MRI) and head magnetic resonance angiography (MRA) revealed no abnormalities. She had no history of cranial irradiation. Antibody testing and single-fibre electromyography (EMG) of the right frontalis muscle did not suggest myasthenia gravis. Given her normal baseline neuro-ophthalmologic examination and the witnessed nature of her diplopia, a diagnosis of ocular neuromyotonia was made. Subsequent titrations of gabapentin and carbamazepine modestly improved the frequency of her symptoms, but the latter was not well tolerated and later discontinued.

We then inquired further into neuropathy and referred her to our neuromuscular clinic for a second opinion. At the time, she revealed a 2-year history of progressive lower-extremity dysesthesias that had recently worsened with an ataxic gait and multiple falls that improved following a one-time dose of intravenous immunoglobulin (IVIg).

Her examination showed weakness in the distal upper and lower extremities bilaterally (4/5 by Medical Research Council [MRC] criteria), severe sensory loss with ataxia, and diffuse areflexia. Electromyography and nerve conduction studies (EMG-NCS) revealed markedly prolonged median and ulnar motor conduction velocities and also markedly prolonged R1 and R2 latencies on blink reflex testing, consistent with a severe demyelinating polyneuropathy with cranial nerve involvement. An extensive evaluation for causative monoclonal proteins and serum autoantibodies including serum paraneoplastic antibodies was negative (see online Supplementary Materials).

She was therefore diagnosed with chronic inflammatory demyelinating polyneuropathy (CIDP) with cranial nerve involvement.⁶ Within 3 months of initiating monthly infusions, she reported a marked improvement in gait and was liberated from her wheeled walker. Quantitative muscle strength testing by dynamometry demonstrated a 40–80% improvement in distal upper and lower extremity strength.

Interestingly, her persistent and daily episodes of ONM nearly resolved following the initiation of monthly IVIg for her CIDP. She reported only three brief episodes of diplopia in the subsequent 6 months after starting IVIg therapy, a significant improvement from her prior 6–10 daily episodes prior to IVIg.

DISCUSSION

Our patient's episodes of stereotyped episodic diplopia best fit ocular neuromyotonia (ONM). The clinical features favouring ONM include the

repetitive and episodic nature, the stereotypy, her persistently normal inter-ictal ocular motor examination, and her initial modest response to gabapentin and carbamazepine. The characteristics of her history and clinical examination were not consistent with decompensated phoria, superior oblique myokymia, oculomotor palsy with cyclic spasms, or myasthenia gravis, other conditions that can also cause episodic diplopia. The specific extraocular muscle involved in our case is uncertain, but we suspect involuntary contraction of the right inferior oblique (CN3) or left superior oblique (CN4) given the right hypertropia and exodeviation witnessed during the induced episode.

Most prototypical patients with ONM are able to induce their diplopia with prolonged eccentric gaze in the direction of action of the affected ocular motor nerve. However, our survey of the literature identified seven patients reported by Shults et al.,¹ Ezra et al.,³ Lessel et al.,⁷ and Inoue et al.,⁸ who did not have this characteristic feature. Furthermore, six of these seven patients had completely normal inter-ictal examinations with no history of focal ocular motor nerve paresis prior to the onset of the ONM. None had any involvement of the eyelid or pupil, and several demonstrated only small angles of vertical misalignment during the witnessed symptomatic episodes. On the basis of her clinical characteristics and these reports, we therefore believe that our patient's recurrent stereotyped episodes of diplopia represent ocular neuromyotonia.

Ocular neuromyotonia in the setting of CIDP with electrodiagnostic evidence of cranial nerve involvement supports a unique pathophysiological basis for ONM. It has been postulated that the pathophysiology of CIDP involves active demyelination of nerves with myelin phagocytosis by macrophages due to breakdown of the blood-nerve barrier. This breakdown of nerve fibre integrity likely predisposes to the ephaptic (i.e., fascicle to fascicle) neurotransmission postulated to underlie ocular neuromyotonia. If our patient's ONM were due to neurovascular compression or other local structural aetiology, it would not have resolved so definitively following the initiation of IVIg.

Nearly all prior cases of ONM were due to local intracranial disease that would have been visible on today's high-quality MRI and MRA scans of the brain.^{4,5} Because of our newly associated findings, both ocular neuromyotonia and CIDP should prompt a complete neurological history and examination of the patient, even in the presence of a normal brain MRI and MRA.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

REFERENCES

- [1] Shults WT, Hoyt WF, Behrens M, et al. Ocular neuromyotonia: a clinical description of six patients. *Arch Ophthalmol* 1986;104:1028–1034.
- [2] Frohman EM, Zee DS. Ocular neuromyotonia: clinical features, physiological mechanisms, and response to therapy. *Ann Neurol* 1995;37:620–626.
- [3] Ezra E, Spalton D, Sanders MD, et al. Ocular neuromyotonia. *Br J Ophthalmol* 1996;80:350–355.
- [4] Giardina AS, Slagle WS, Greene AM, et al. Novel case of ocular neuromyotonia associated with thyroid-related orbitopathy and literature review. *Optom Vis* 2012;89: e124–e134.
- [5] Roper-Hall G, Chung SM, Cruz O. Ocular neuromyotonia: differential diagnosis and treatment. *Strabismus* 2013;21: 131–136.
- [6] Latov N. Diagnosis and treatment of chronic acquired demyelinating polyneuropathies. *Nat Rev Neurol* 2014;10: 435–446.
- [7] Lessel S, Lessel IM, Rizzo JF. Ocular neuromyotonia after radiation therapy. *Am J Ophthalmol* 1986;102:766–770.
- [8] Inoue T, Hirai H, Shimuzu T, et al. Ocular neuromyotonia treated by microvascular decompression: usefulness of pre-operative 3D imaging. *J Neurosurg* 2012;117:1166–1169.

Supplementary materials available online.