RESIDENT & FELLOW SECTION

Pearls & Oy-sters: Ocular Myasthenia Gravis

Central Ocular Motor Signs and Unilateral Visual Loss Caused by the Great Neuro-Ophthalmologic Impersonator

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Abstract

Myasthenia gravis (MG) has been described as a great mimicker of other neurologic and ocular motility disorders, including centrally mediated ophthalmoplegia. For example, ocular myasthenia gravis (ocular MG) may cause impaired binocular visual acuity for near vision due to reduced accommodation or for distance vision due to accommodative excess. Notably, accommodative excess due to ocular MG is rare, but may occur with exotropia, with or without diplopia. We report 2 cases of ocular MG: First, a 32-year-old man with exotropia, bilateral hypometric and slowed adducting saccades with dissociated abducting nystagmus, miosis, and decreased distance vision in his right eye; second, a 45-year-old man with similar ocular motor deficits, miosis, and myopia. Both patients showed ocular motor deficits which appeared to localize to the pons but were instead due to ocular MG. Ocular MG should be considered in patients who present with reduced visual acuities due to any disruption in accommodation. Any ocular motor deficit, even if appearing to be centrally mediated or occurring without ptosis, may be caused by ocular MG.

Pearls

- Pseudo-internuclear ophthalmoplegia or one-and-a-half syndrome can be the presenting clinical feature of ocular myasthenia gravis.
- Abnormal accommodation can cause impaired visual acuity in ocular myasthenia gravis due to either accommodative insufficiency or accommodative excess.

Oy-sters

- The absence of ptosis in individuals presenting with diplopia does not preclude the diagnosis of ocular myasthenia gravis, even in those with pseudo-internuclear ophthalmoplegia.
- Do not rule out ocular myasthenia gravis as a primary cause of binocular or monocular visual loss in the presence of refractive errors.

Case Report

Case 1

A 32-year-old man reported intermittent diplopia lasting 10–15 minutes on awakening. Examination showed uncorrected visual acuities of 20/20 in both eyes (OU). Pupils measured 2.0 mm OU with normal reactivity. He had bilateral, hypometric, slowed adducting saccades with dissociated abducting nystagmus, exotropia, and diminished convergence. MRI with and without contrast was negative for lesions involving orbits or brainstem, including demyelination, or space-occupying lesions such as tumor, hemorrhage, cysts, or infection. Because clinically isolated syndrome presenting with circumscribed brainstem findings may not have an MRI correlate, he was presumed to have demyelinating disease and was treated with high dose oral steroids followed by a taper. Three weeks later, he had a small residual left adduction deficit

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with normal convergence and 4.0-mm pupils OU. Two months later, he re-presented with complete right ptosis and progressive visual blurring in the right eye. At distance, uncorrected visual acuities measured 20/100 in the right eye (OD) and 20/20 in the left eye (OS). Distance acuity in the right eye improved to 20/25 with a −2.25 lens and to 20/20 with cycloplegia. Pupils measured 3.0 mm OU. He had complete right ptosis with positive curtain sign and ice pack test and negative Cogan lid twitch. There was re-emergence of the bilateral adduction deficit, with exotropia measuring 30 prism diopters at distance. Binocular viewing after eye closure prompted brisk, small, convergent movements and miosis (Video 1). After resting with eyes closed, the acuity in the right eye recovered to 20/20 for near and distance, but distance vision decreased to 20/60 after 60 seconds of reading. Positive acetylcholine receptor antibody titers and single fiber EMG confirmed the diagnosis of myasthenia gravis (MG).

Case 2

A 45-year-old man presented with intermittent ptosis of either eyelid, without diplopia. Acetylcholine receptor antibody titers were elevated and ptosis improved with pyridostigmine. On examination, visual acuities measured 20/25- OU with his chronic myopic correction (−4.00 OU), improving to 20/20 OU with additional −0.50 lenses. Pupils were pinpoint but reactive to light. He had variable left ptosis and positive Cogan lid twitch. Upward saccades were hypometric and slowed in both eyes with hypometria and slowing of saccades on right adduction and left abduction, and left adduction. Right abducting saccades were normal. Convergence was diminished. He had right hypertropia and exotropia in the primary position at near and at distance. The exotropia measured 25 prism diopters at distance. He was examined 4 months after initial presentation, having noted subjective improvement in ocular mobility after being started on azathioprine by his primary neurologist. He continued to have intermittent ptosis responsive to pyridostigmine. His examination (Video 2) showed full right adduction. Right abducting saccades were hypometric but of normal velocity. Left adduction and abduction remained variably slow and hypometric. The exotropia measured 25 prism diopters at distance. Pupils measured 2 mm OU with normal reactivity.

Discussion

Myasthenia gravis is a disorder of neuromuscular junction transmission known to mimic other neurologic conditions, particularly when signs and symptoms are confined to the ocular motor system. Variability in clinical findings due to weakness that worsens with exertion and recovers with rest cause the characteristic signs of fluctuating external ophthalmoplegia, ptosis, and weakness of eye closure, which are considered diagnostic.[1] However, this constellation of findings is not always present and any pattern of ocular motor deficit can occur, ranging from paresis of a single ocular muscle to complete external ophthalmoplegia. Ocular motor deficits which appear to be centrally mediated, including internuclear ophthalmoplegia (INO)[2-4] and one-and-a-half syndrome,[5] have been reported. Centrally mediated INO typically results from a medial longitudinal fasciculus lesion disrupting signals for horizontal saccades between one abducens nucleus in the pontine tegmentum and the opposite medial rectus subnucleus in the midbrain. Saccades are defined by 3 metrics: initiation, accuracy, and velocity. A saccade can be slow, but not hypometric; or it can be hypometric but not slowed. In these cases, as in true INO, saccades were both slow and hypometric. Case 1 showed bilateral slowing of adducting saccades with dissociated abducting nystagmus and exotropia which appeared consistent with wall-eyed binocular INO (WEBINO), but which proved to be pseudo-INO due to ocular MG. Case 2 showed ocular motor findings of unilateral gaze palsy and contralateral INO (again pseudo-INO) with exotropia, which also appeared consistent with another centrally mediated eye movement abnormality—paralytic pontine exotropia, which is a variant of one-and-a-half syndrome.[6] Failure of adduction and exotropia is common in ocular MG because medial rectus muscles are preferentially affected.[7] Abducting nystagmus in the other eye occurs due to Hering's law of equal innervation, and is adaptive, also occurring in true INO. Hering's law describes the conjugacy of movement of the eyes as being fundamental, with equal innervation going to muscles in a yoked pair. Case 2 had intermittent ptosis and had already been diagnosed with ocular MG, but the emergence of ptosis was delayed in the first patient, making the diagnosis of centrally mediated WEBINO plausible.

It is unusual for ocular MG to present without ptosis. 40% of patients with MG will present with diplopia or ptosis or both, with an additional 25% presenting with ocular involvement accompanied by bulbar, axial, or appendicular weakness.[7] In fact, Finelli and Hoyt concluded that ptosis always accompanied myasthenic pseudo-INO except when there was associated hyperthyroidism.[3] In a brief review of 64 patients presenting to our institution with ocular MG, only 15.6% had external ophthalmoplegia without ptosis. There was no gender effect, but those who presented without ptosis were significantly younger than those with ptosis (mean age without ptosis 58 years (SD 15.5); mean age with ptosis 70 years (SD 14.9); $p = 0.021$).

Diminished accommodation attributed to fatigable weakness of the ciliary muscle in MG has been well reported[8-12] dating back to the description of the original 60 cases in 1900.[8] However, the reduction in distance visual acuities seen in our cases was not due to *diminished* accommodation, but the opposite. In Case 1, improvement with rest, minus lens and cycloplegia, was consistent with accommodation excess and pseudomyopia. Pseudomyopia or "false myopia" is diagnosed when there is excessive contraction of the ciliary muscle causing the lens to become more spherical and increasing its refractive power for near (accommodation). Cycloplegic eye drops paralyze the ciliary muscle, reducing the power of the lens and decreasing the myopia. Pseudomyopia can also be improved by increasing minus lenses, as in true myopia. In Case 2, pinpoint pupils indicated increased convergence

effort; although already corrected for myopia, his acuity improved with increased minus correction. Accommodation excess in ocular MG is far less common than accommodation deficiency, having been previously reported in only 3 individuals.[13] Although accommodation and convergence may act separately, responses must be simultaneous and image disparity is the primary cue for both.[14] Diplopia is not required to cause this phenomenon; rather, the degree of either vergence or accommodation will depend on the emphases the individual places on the stimuli which drive the near response.[14] The degree of accommodation relative to vergence in response to disparity is almost impossible to measure at the bedside, but it is unlikely that our patients had spasm of accommodation. It is more likely that image disparity provoked both convergence and accommodation appropriately, but the convergence response could not be observed because of weakness of medial rectus muscles, and the accommodative response was sufficient to evoke pseudomyopia. Our first patient had unilateral pseudomyopia affecting only the right eye. While pseudomyopia is typically bilateral, it can be asymmetrical because accommodation can be elicited independently in each eye.[14] True unilateral accommodative spasm has been reported with normal ocular mobility and alignment, although it is more common with disruption of binocular vision.[15]

These 2 cases reinforce the fact that ocular MG can imitate any central ocular motor disorder, and even pseudointernuclear ophthalmoplegia can occur without ptosis. The absence of ptosis is less frequent in ocular MG on presentation, but when it does occur, it is more likely in a younger patient. Reduced visual acuity, especially in young patients, is unexpected in ocular MG and should prompt concerns about other unrelated causes of visual loss. However, in the absence of other causes, reduced visual acuity in ocular MG may be due to accommodative insufficiency from paresis of the ciliary muscles. Although rare, decreased distance acuity may be the result of enhanced accommodation causing pseudomyopia and may be asymmetric or monocular. Induction of the components of the near reflex occurs because of image disparity in the presence of exotropia but does not require subjective diplopia.

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