American Journal of Ophthalmology Case Reports 12 (2018) 76–78

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.elsevier.com/locate/ajoc

Case report

Bilateral pseudo-internuclear ophthalmoplegia in a patient with myasthenia gravis

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ARTICLE INFO

Keywords:
Myasthenia gravis
Ocular myasthenia gravis
Pseudo internuclear ophthalmoplegia
False localizing signs

ABSTRACT

Purpose: To report a case of myasthenia gravis presenting with a false localizing sign, a bilateral pseudo internuclear ophthalmoplegia.

Observations: A 61 year-old male presented with a five-week history of painless binocular oblique diplopia that was associated with fatigue, vocal hoarseness and bilateral ptosis, the latter two of which worsened through the course of the day. Exam was remarkable for an apparent bilateral internuclear ophthalmoplegia (INO). MRI of the brain with and without contrast and MRA of the head and neck were within normal limits. Lab work was positive for anti-AChR binding, blocking, and modulating antibodies, as well as anti-striated muscle and anti-titin antibodies. The patient was initiated on therapy for myasthenia gravis.

Conclusion and importance: Although myasthenia gravis often presents with ptosis or diplopia, rarely patients may develop pseudo-INO secondary to extraocular muscle weakness. True INO occurs with damage to the medial longitudinal fasciculus, a myelinated tract of fibers that controls yoked horizontal eye movements. Clinicians should be suspicious of the false localizing sign of a pseudo-INO associated with myasthenia gravis when more common causes of INO have been excluded.

1. Introduction

Myasthenia gravis (MG) is an autoimmune disorder affecting the function of neuromuscular junctions (NMJ) at striated muscle fibers. The pathophysiology of this disease involves formation of auto-antibodies against postsynaptic acetylcholine receptors (AChR) at the NMJ. In ocular MG, a localized form of MG, the major target of anti-AChR antibodies are NMJs at the muscles that control eye and eyelid movement. As in generalized MG, ocular and orbital muscle weakness in ocular MG display both characteristic fatigability and variable presentation.

Over half of all MG patients initially present for evaluation of ptosis and/or diplopia.[1] Moreover, myasthenic involvement of extraocular muscles follows no particular pattern.[2,3] Any or all of the orbital muscles may be affected in ocular MG, resulting in comitant or incomitant binocular diplopias of the horizontal, vertical or oblique variety. Thus, the clinical presentation of ocular MG can mimic a range of neurological or neuromuscular conditions, including isolated cranial nerve palsies[4] and internuclear ophthalmoplegia (INO).[2,5–9]

INO is an abnormality of conjugate horizontal eye movement that occurs with damage to the medial longitudinal fasciculus (MLF), a myelinated tract of fibers responsible for yoked eye movements. Patients with bilateral INO display bilateral adduction deficits with contralateral abducting nystagmus. True INO is a sign classically associated with demyelination-induced dysfunction in multiple sclerosis (often bilateral INO)[10,11] or with ischemic damage to the MLF (often unilateral INO).[12] However, extraocular muscle weakness can rarely produce a pseudo-INO.[13] Reports of pseudo-INO and extraocular muscle weakness associated with MG first emerged fifty years ago.[7] It is now increasingly recognized that MG should be kept in the differential diagnosis of bilateral INO, particularly when CNS lesions have been ruled out.

2. Case report

A 61-year-old male presented with painless binocular oblique diplopia lasting five weeks. This was associated with bilateral ptosis, which worsened through the course of the day, and with fatigue and

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https://doi.org/10.1016/j.ajoc.2018.09.008
Received 20 May 2018; Received in revised form 12 September 2018; Accepted 16 September 2018
Available online 19 September 2018

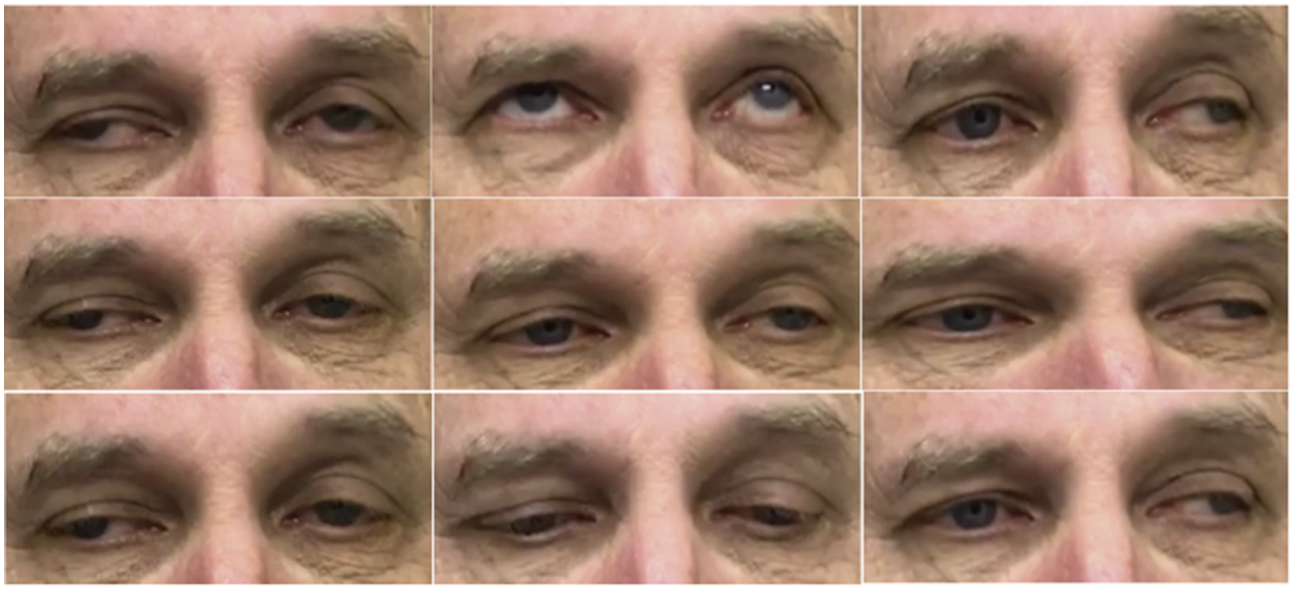

Fig. 1. Bilateral adduction deficits with contralateral abducting nystagmus.

vocal hoarseness, most prominent at the end of the day. He denied jaw claudication, scalp tenderness, loss of vision, bowel or bladder dysfunction, weakness, numbness, fever, headache, weight loss, rash, or joint pain. Past medical history was notable for prostate cancer (in remission for 3 years), arthritis, and depressed mood. Past surgical history was notable for a total hip arthroplasty. The patient was taking citalopram for depressed mood and no other medications.

Physical exam was remarkable for bilateral adduction deficits with contralateral abducting nystagmus consistent with a bilateral INO, as depicted (Fig. 1) (Video 1). This was accompanied by bilateral asymmetric fatigable ptosis (right side at 35 seconds, left side at 50 seconds) on upgaze, and by motor fatigue (hip flexors at 18–19 repetitions, and distal finger extensors at 14 repetitions). Recovery from this fatigable weakness was complete after one minute. MRI of the brain with and without IV contrast and MRA of the head and neck were within normal limits and did not reveal demyelinating lesions, a cerebrovascular accident, or an intracranial mass to explain the patient's diplopia. Lab work was positive for anti-AChR binding, blocking, and modulating antibodies, as well as anti-striated muscle and anti-titin antibodies. A CT chest was performed, which showed no evidence of a mediastinal mass.

Supplementary video related to this article can be found at https://doi.org/10.1016/j.ajoc.2018.09.008.

Due to indications of generalizing motor weakness and the severity of visual symptoms, the patient was treated with 60 mg of pyridostigmine TID, an induction dose of IVIG (total 2.1 g/kg) for four days, and steroids, which were begun on the second day of treatment and slowly increased to 30 mg every other day. After discharge, the patient was treated outpatient with mycophenolate mofetil, prednisone taper, and pyridostigmine. He continued to receive IVIG infusions every three weeks, which was ongoing at the time of this writing.

3. Discussion

The pathophysiology of MG is mediated by AChR antibodies that can bind, block, and/or modulate postsynaptic AChRs at NMJs of striated muscle. This initiates pathological immune responses against AChRs via complement-mediated destruction (for AChR binding antibody), impaired binding of ACh at the junction (for AChR blocking antibody), or AChR endocytosis (for AChR modulating antibody).[14] Our patient was seropositive for all three types of AChR antibodies, together resulting in significant functional impairment of muscular control.

Of note, the patient's additional lab work suggested a more severe disease course. Striated muscle antibodies have been detected in nearly half of all AChR seropositive, late-onset (≥50 years of age) MG cases[15] and recognize epitopes on three major muscle antigens, including titin, ryanodine receptor, and Kv1.4 (a subunit of voltage-gated potassium channel).[16] Both the presence of striated muscle antibodies and specifically titin antibody have been correlated with severe disease.[15–17]

The unusual feature of this case was the patient's presentation with a bilateral pseudo-INO, which could direct clinical consideration toward multiple sclerosis in patients younger than 50 years of age or ischemic damage to the MLF tracts in patients older than 50 years of age. Cases of MG presenting with an apparent bilateral INO have been noted previously but remain uncommon.[2,5–9] Our patient initially presented with the symptoms of hoarseness and eyelid drooping that distinctively worsened throughout the day – telltale indications to consider the diagnosis of MG. However, others have reported cases of MG presenting as bilateral pseudo-INO without accompanying muscular fatigability or diurnal variation.[5,6] Close examination of an apparent bilateral INO may reveal subtle clues that point to MG, including decreasing beat-to-beat amplitude of nystagmus or diminished amplitude of nystagmus on sustained lateral gaze (fatigability).[6] Although the mechanism is unknown, pseudo-INO associated with MG may arise from the combination of: (1) antibody-mediated peripheral disruption of neural signals to the extraocular muscles at the NMJ, producing adduction deficit[5] and (2) central overcompensation for the adduction deficit, producing dissociated contralateral nystagmus.[8,11,18]

4. Conclusions

MG often presents with complaints of ptosis or diplopia but can rarely manifest as a pseudo-INO bilaterally. Bilateral INO is classically associated with demyelination or ischemia of the MLF tracts, but autoimmune destruction of peripheral signaling to extraocular muscles may also produce a bilateral pseudo-INO. Thus, the differential diagnosis of an apparent bilateral INO should include MG, especially when more common causes have been excluded.

Patient consent

The patient consented to publication of this case in writing.

Funding

CKM is supported by the Robert and Janice McNair Foundation.

Conflicts of interest

The authors report no conflicts of interest.

Authorship

Each of the authors has contributed to, read and approved this manuscript. All authors attest that they meet the current ICMJE criteria for authorship.

Acknowledgements

None.

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