Apraxia of lid opening in multiple sclerosis

Apraxia of lid opening (ALO) is a nonparetic, nonrestrictive lid-opening abnormality that manifests as an inability to open the eyelid on command. The levator palpebra superioris muscle, the third cranial nerve, and the orbicularis oculi (OOc) are all normal in ALO. ALO is believed to be the result of supranuclear involuntary levator palpebrae inhibition versus stimulation (contraction) of the pretarsal OOc muscle. The underlying pathophysiology of ALO is still unknown, but it is associated with progressive supranuclear palsy, multiple system atrophy, parkinsonism, and other extrapyramidal-like syndromes.[1]

Multiple sclerosis (MS) is an autoimmune disorder characterized by demyelinating plaques in the CNS. We report a case of eyelid apraxia in a patient with MS described in the neurologic literature only once before.[2] To our knowledge, this is the first case of ALO in a patient with MS reported in the English-language ophthalmic literature.

A 62-year-old white female presented with intermittent "ptosis." She had a history of relapsing-remitting MS for 18 years that was treated with teriflunomide. She described her lid abnormality as transient difficulty in opening one or both eyes that would last minutes to days and then improve spontaneously. The passively closed eyelid would occur on awakening and could affect either the left or right eyelid. There was no blepharospasm or hemifacial spasm noted by history or on examination. Passive elevation of the lids manually would resolve the "ptosis" OU. Medications included teriflunomide, pramipexole, baclofen, atenolol, gabapentin, and omeprazole. Her last recorded MS exacerbation was 5 months prior to the neuro-ophthalmic visit. Electromyography and serologic testing for myasthenia gravis were negative. Repeat magnetic resonance imaging of the brain 4 months prior to the initial visit showed multifocal inactive and nonenhancing demyelination, and there were no white matter hyperintensities in the areas involving the brainstem motor nuclei, basal ganglia, or thalamus. Cervical spine magnetic resonance imaging showed multilevel cervical disc degenerative changes.

During her neuro-ophthalmology visit, the patient was asymptomatic with a completely normal eye examination. External, lid, and extraocular motility examinations were normal OU. The patient reported that her "ptosis" OU at home would resolve after manually raising the affected eyelid or with active voluntary "lifting of her eyebrows." The patient took photographs of her "ptosis" that were consistent with ALO (**Figs. 1** and **2**).

ALO is a diagnosis of exclusion, and the levator palprebra superioris, third cranial nerve, and OOc should be normal. Normal lid opening is voluntary and requires supranuclear innervation to both levator muscles via the third nerve nucleus and single caudal subnucleus. Normal voluntary lid closure requires supranuclear input to the OOc. Patients with ALO, as in our case, often can open their eyes following reflex blinking or by certain other facial motor manoeuvres (e.g., massaging the eyelids or manual elevation of the lids). ALO differs from benign essential blepharospasm (BEB), which is also a focal dystonia involving the eyelid that, interestingly, is commonly associated with ALO. BEB is bilateral, and thus ALO in BEB is typically bilateral and supranuclear.

Isolated ALO without BEB is much less common.[1,3] In some cases, diagnosis of ALO is unmasked with persistence of eye closure after therapeutic botulinum toxin injection into the OOc to treat BEB. Unlike BEB, however, ALO can be treated with botulinum toxin injection into the pretarsal OOc muscle, suggesting that pretarsal stimulation and not levator inhibition alone is the mechanism for ALO. Supranuclear inhibition of the levator in dorsal midbrain syndrome produces bilateral lid retraction (Collier lid retraction sign), and supranuclear stimulation of the unpaired central caudal nucleus of the levator in the third nerve nucleus also would be expected to be bilateral. Unilateral or alternating cases of ALO suggest that the focal dystonia mechanism is with OOc activation rather than central levator inhibition. Systemic extrapyramidal treatments, however, like levodopa have shown limited efficacy in ALO.[1]

To our knowledge, there is only 1 other case of apraxia of the eyelid in MS. This case appeared in the Italian neurologic literature—the patient had apraxia of eyelid *closure* concurrent with MS. That patient also had preserved reflexive blinking, a common finding in both apraxia of eyelid closure and ALO.[2,4]

Some patients develop a form of "sensory trick" that can reverse or block the ALO. One commercial device (PressOp, Dystonia UK, London, UK) can help maintain an elevated eyelid in ALO patients. The mechanism for how manual elevation of the eyebrows or eyelids works to reduce ALO remains ill-defined. The PressOp applies pressure around the periorbit and is adjusted to the right position. Some patients with severe symptoms who fail botulinum toxin and other conservative measures may require surgical treatment (e.g., frontalis suspension surgery).[5] Oculoplastic consultation and information about PressOp were given to our patient, but currently no treatment modality has been pursued.

In summary, clinicians should be aware that passive closure of the eyelids can mimic neurogenic ptosis. The inability to voluntarily open the eyelids in the absence of pathology in the eyelid, the levator muscle, the third cranial nerve, or the neuromuscular junction (e.g., myasthenia gravis) suggests ALO. Pretarsal OOc stimulation rather than levator inhibition is a more likely mechanism for ALO cases like ours that are unilateral or alternating because bilateral BEB and bilateral ALO are supranuclear and the

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Fig. 1—Side-by-side eyelid comparison. Top shows "ptosis" of the bilateral eyelids before manual elevation. There is no indication of spasming or contraction of the surrounding OOc muscle or forceful eyelid closure, as expected with blepharospasm. Bottom shows absence of upper lid laxity of the left eyelid after manual elevation.

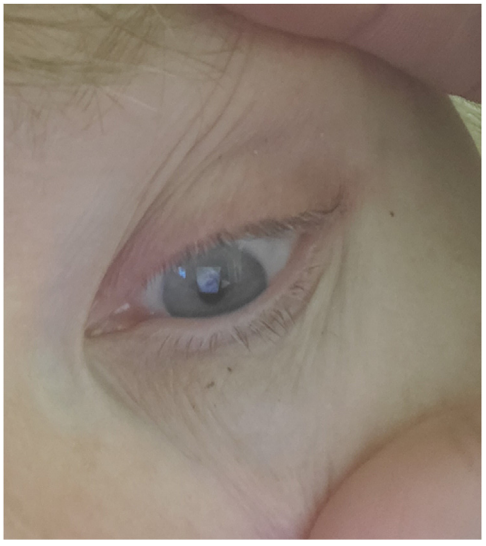

Fig. 2—Shows the manual eyelid elevation technique performed by the patient to improve the "ptosis."

levator subnucleus is unpaired (central caudal subnucleus in third nerve nucleus). Botulinum toxin can be used to treat ALO, but myasthenia gravis and true neurogenic ptosis should be excluded prior to administering any agents that could worsen neuromuscular blockade. MS is a very uncommon cause of ALO; the subtleness of ALO makes it often go undetected, presumably more so in the context of an uncharacteristic presentation in conjunction with a relapsing and remitting disease.[1,3] An alternating and unilateral presentation of ALO without BEB association may be typical of ALO in MS, and we believe that this case may be useful for further hypothesis generation on the mechanisms for ALO. Unilateral cases might support the hypothesis that stimulation of the pretarsal OOc rather than inhibition of the levator muscle as the mechanism for ALO in some cases.

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Footnotes and Disclosure

The authors have no proprietary or commercial interest in any materials discussed in this correspondence.