

Clinical Signs in Neuro-Ophthalmology: Eye Signs in Myasthenia Gravis

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Abstract

A hallmark of myasthenia gravis (MG) is the variability and fatigability of striated muscles. The majority of people with MG have eye symptoms of ptosis and diplopia. This paper outlines the eye signs in MG, including practical tips on the examination technique relevant to MG, and pitfalls to avoid.

Keywords: Clinical signs, myasthenia gravis, neuro-ophthalmology, ocular

INTRODUCTION

Myasthenia gravis (MG) is an autoimmune condition affecting the neuromuscular junction. A hallmark of this condition is fatigability and variability of muscle weakness. This paper will focus on the eye signs in MG.

The pathognomonic features of MG are the variability and fatigability of striated muscles. This typically starts at the levator palpebrae superioris (LPS), orbicularis oculi, and one or more extraocular muscles (EOMs). In ocular myasthenia gravis (OMG), these are the only muscles symptomatically affected.^[1]

EYELIDS

Ptosis is possibly the most common symptom in MG.^[1] The muscle affected is the LPS. Ptosis can be missed if the patient is compensating for the LPS weakness by using the frontalis muscle. Therefore, it is recommended that the methodical assessment for the presence of ptosis includes the stabilization of the eyebrows against the brow bone [Figure 1].

In suspected MG with no apparent ptosis on initial assessment, it can be helpful to provoke ptosis by fatiguing the LPS. This is brought out by persistent up gaze while the frontalis muscle is inactivated as described above. In my experience, the fatigue of LPS to provoke ptosis (in the absence of initial ptosis) is often seen from approximately 40 s. Therefore, a persistent up gaze of at least 45–60 s is recommended.

Documenting the position of the upper lid in the primary position after persistent up gaze is a helpful quantitative measure. Examples of how to annotate this include noting the palpebral aperture, i.e., the distance between the upper and lower lid; or the upper margin reflex distance, i.e., the distance between the upper lid and the center of the pupil.

The variability of levator excursion, i.e., the range of lid movement from downgaze to up gaze position,

can also be a helpful measure to show the variability of LPS weakness.

In the presence of LPS weakness, the Cogan's lid twitch is characteristic for MG. A word of caution: avoid confusing this with eyelid overshoot from refixation in non-ptotic lids. In the presence of ptosis, the Cogan's lid twitch is brought out after a short period of rest (approximately 10–15 s) in the downgaze position. When the patient then refixates in the primary position, there is a “twitch” seen as the eyelid overshoots on an upward gaze.

Another useful clinical sign, that is not specific to MG but relates to ptosis (of any cause), is the enhanced ptosis sign (sometimes described as the “curtain sign”).^[2] This relates to Hering's law of equal innervation, where both lids receive the same amount of drive to open their eyes. In the presence of asymmetrical ptosis, lifting the ptotic lid brings out any underlying ptosis in the contralateral lid. This is therefore a useful test in patients with suspected MG, to determine if the contralateral lid is also affected.

Conversely, patients who have unilateral ptosis may not present with this symptom or sign but instead present with retraction of the contralateral eyelid. The apparent retraction resolves on lifting (and therefore unmasking) the eye with underlying

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ptosis. This compensatory retraction of the contralateral upper lid in unilateral ptosis was first described by Walsh as Hering’s law for eyelids.^[3,4]

Extraocular muscles

A careful examination of the EOMs is important to determine the patterns of deficit in MG, i.e., different muscles or variable deficits over time. This is particularly useful in the diagnostic process for seronegative OMG.

Comparing the examination of pursuit eye movements in versions (i.e., with both eyes open) and ductions (i.e., with one eye open at a time) can clarify the degree of deficits present in all EOM. This can be particularly helpful when many EOMs are affected, when fixation may change between the eyes during the examination, or if there is a history of congenital squint. Figure 2 shows the vector of maximum action of the respective EOMs.

In the presence of severe ophthalmoplegia, saccadic examination with small amplitude movement may bring out a “twitch,” or so-called “quiver” movement. These appear as hypermetric saccades with high initial velocities, likely due to the relative sparing of twitch fibers that generate rapid saccadic

movements when muscle fibers responsible for maintenance of eccentric gaze (tonic fibers) are severely affected.^[5,6]

As with the provocation for lid fatigue described earlier, the provocation for diplopia with sustained gaze can also be helpful. This is also called the Simpson’s sign, described by him with the provocation of diplopia or ptosis by sustained up gaze or lateral gaze.^[1,7]

Orbicularis oculi

Weakness of the orbicularis oculi is often noted in MG, and at its most severe though not often seen, it can limit complete eye closure.

The ice, rest, and sleep tests as alternatives to the edrophonium test

The edrophonium (Tensilon^[8]) test has long been established as a diagnostic test for OMG. However, with the lack of availability of edrophonium and the need for cardiac monitoring, other bedside tests such as the ice,^[9,10] rest, or sleep^[11] tests can be helpful.

The application of ice on a ptotic lid for 2–5 min, can improve myasthenic ptosis. In practice, this can be done using ice on glove with a paper towel to prevent water dripping down the patient’s face, and advising the patient to hold it against a closed eye. A positive test shows an improvement of 2 or more millimeters. The improvement is in part caused by rest, although the cold significantly improves ptosis more than rest alone.^[12] The ice test has been shown to be specific and relatively sensitive for myasthenic ptosis, although the sensitivity decreases in patients with complete ptosis.^[13]

The ice test has also been tested for diplopia. Application of an ice pack for up to 5–10 min may partially improve the degree of EOM deficits in myasthenic diplopia.^[14,15]



Figure 1: Holding the eyebrow against the brow bone inactivates the action of the frontalis muscle during assessment for ptosis

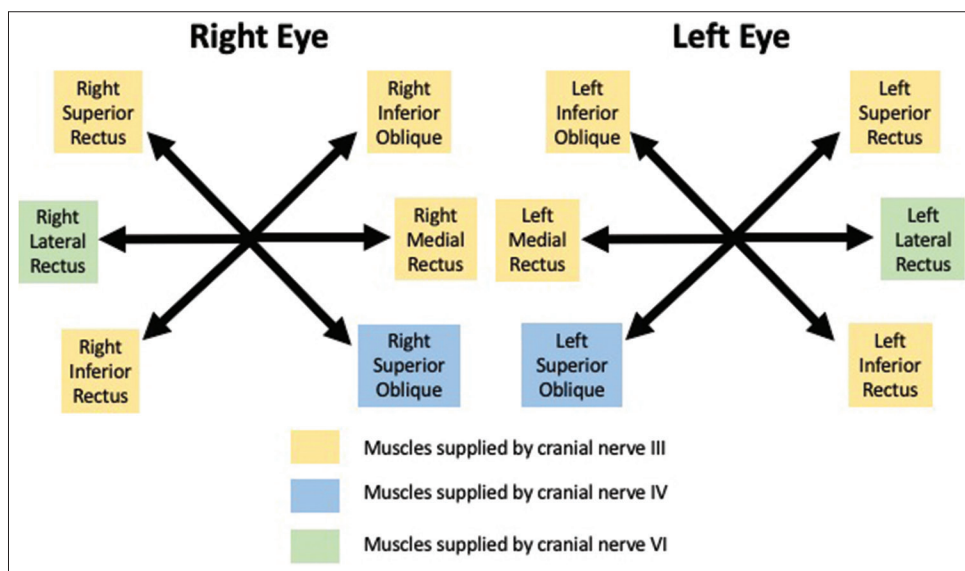


Figure 2: The maximum vector of action for the extraocular muscles (EOMs). Examining the pursuit eye movements in versions (both eyes open) and ductions (one eye open at a time) can be helpful to clarify the EOMs affected in MG. Be on alert for alternative differential diagnoses affecting the cranial nerves

The sleep test has also been proposed as a method of observing changes in myasthenic ptosis,^[11] although its specificity in MG has not been tested. The resolution of ptosis or ophthalmoparesis immediately after a 30-min sleep and the reappearance of myasthenic signs over the next 30 s to 5 min adds further confirmation.^[11]

Pitfalls to avoid

A few pitfalls to consider in the differential diagnoses for eyes signs in MG include the following:

- Cranial nerve deficits that affect different EOMs, for example, III nerve palsy, or cavernous sinus syndrome.
- Pupils should be normal in MG. III nerve palsy can cause dilated pupils, and Horner's syndrome can cause ptosis and miosis.
- The pathology in MG is at the level of the neuromuscular junction. Therefore, there should not be improvement with the doll's eye maneuver, as one may see in supranuclear gaze palsies.
- Mechanical ptosis such as levator disinsertion results in a higher lid crease on the affected side. In severe cases where patients compensate using frontalis muscle to manage their mechanical ptosis, they may also report worsening later in the day.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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