The Diagnostic Odyssey in Myasthenia Gravis

Patient #1: Diagnosis of ocular MG

31-year-old-female

Case contributor and commentary:

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Age 29

Initial symptoms:

» Intermittent drooping of the right eyelid

Age 30

Symptom progression:

» 6 months later - Transient double vision on up and down gaze, most prominent when reading books or watching TV

PCP workup:

» Symptoms were initially considered by her primary care physician to result from infection in the eyelids

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Treatment:

» Received a course of antibiotics, which did not improve her symptoms

Referral to neuro-ophthalmologist:

» Considered myasthenia gravis given the fatigable nature of oculomotor function observed on exam

Antibody testing:

» Tests for AChR and MuSK antibodies were negative and she was referred for further evaluation, including single fiber (EMG)

Electrodiagnostic tests:

» Repetitive nerve stimulation (RNS) studies of hand and facial muscles were normal

The patient was referred to the neuromuscular clinic for further evaluation.

Overview of MG subgroups

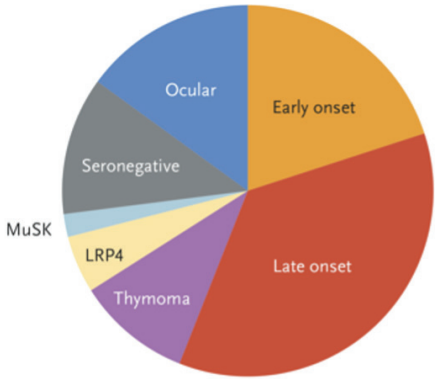

Table 1. Features of Myasthenia Gravis Subgroups.*

Subgroup	Antibody	Age at Onset
Early onset	Acetylcholine receptor	<50 yr
Late onset	Acetylcholine receptor	≥50 yr
Thymoma	Acetylcholine receptor	Any age
Muscle-specific kinase	Muscle-specific kinase	Any age
LRP4	LRP4	Any age
Seronegative	None detected	Any age
Ocular	Variable	Any age

* LRP4 denotes lipoprotein receptor–related protein 4.

Figure adapted from reference[1]

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The patient presented to neuromuscular clinic for evaluation of droopy eyelids:

Diagnostic evaluation

Reported symptoms:

» No limb weakness, shortness of breath or difficulty chewing, swallowing or speaking

Physical examination:

» Severe right and moderate left eyelid ptosis that became worse with upgaze
» Mild weakness of elevation of the left eye
» Eyelid closure and cheek puff were mildly impaired bilaterally
» Remainder of cranial nerve, motor and sensory examinations and deep tendon reflexes were normal
» No muscle atrophy

SFEMG:

» Single fiber EMG revealed increased jitter in the left frontalis, which confirmed the presence of abnormal neuromuscular transmission consistent with the diagnosis of myasthenia gravis

Commentary: The diagnosis of myasthenia gravis is frequently delayed when the first provider has low clinical suspicion for it. Negative serum antibody tests and normal repetitive nerve stimulation studies can result in a further delay in diagnosis.

Most patients with MG exhibit ocular symptoms initially, and symptoms remain limited to ocular muscles in about 15% of cases.[2] In patients with purely ocular weakness two years or more after the start of symptoms, the disease typically remains limited to the ocular muscles.

Antibodies to AChR, MuSK, and LRP4 are not found in approximately 50% of patients with ocular myasthenia[3] and repetitive nerve stimulation tests are normal in approximately 50% of patients.[4] Both tests are normal in approximately 33% of patients.

It took two years to establish the diagnosis in this patient. In patients like this, single fiber EMG plays an important role in making the diagnosis with high sensitivity.

Sensitivity of Electrodiagnostic Tests		
	RNS	SFEMG
Ocular MG	48%	97%
Generalized MG	76%	99%

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Management based on MG diagnosis

Recommended treatment regimen:

» Pyridostigmine 60mg three times per day

Outcome:

» Significant improvement of symptoms

Key learning points

» The diagnosis of MG can be significantly delayed when the clinical suspicion is low and serum antibody tests and repetitive nerve stimulation studies are normal

» Single fiber EMG plays an important role in establishing the diagnosis in MG patients with mild or purely ocular disease

References

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