The Diagnostic Odyssey in Myasthenia Gravis

Patient #4: MuSK MG misdiagnosed as ALS

52-year-old-female

Case contributor and commentary:

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Age 46-52

At age 46, the patient began experiencing the following symptoms:

Initial symptoms:

- Difficulty swallowing
- Slurred speech and a nasal voice
- Mild eyelid drooping, initially on the right, which did not fluctuate
- Speech was worse after sustained speaking
- Face drooped at times and she had difficulty moving food around in her mouth with her tongue
- No blurred or double vision

The patient's symptoms resolved spontaneously over several months, but recurred after approximately two years.

Outside evaluation:

- MRI brain scan showed a small gliotic focus in the right basal ganglia, which was unchanged on follow-up MRI several months later
- EMG was interpreted as showing ongoing denervation in her tongue bilaterally

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Diagnosis:

- Patient was diagnosed as having ALS

Over the next several years, patient had progressive shrinking of her tongue. Her other symptoms remained relatively unchanged.

Age 52

She presented to the neuromuscular clinic for evaluation because of sustained disease course.

Diagnostic evaluation

Neurological exam:

- Mild bilateral ptosis and weakness of eyelid closure
- Tongue was "atrophied and sulcated" without visible fasciculations
- Sternocleidomastoid muscles were slightly weak bilaterally
- Strength, bulk and tone were normal in the rest of her muscles and there were no fasciculations
- Sensory examination was normal
- Tendon reflexes were normal (2+) throughout and her toes were down-going bilaterally

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EMG/Nerve conduction studies:

» Nerve conduction studies and repetitive nerve stimulation of the left abductor digiti minimi and left nasalis muscles were normal
» EMG of tongue showed no spontaneous activity, but there were many polyphasic and markedly unstable motor unit action potentials
» EMG of facial, cervical, thoracic and lumbosacral muscles was normal
» Single-fiber EMG showed markedly abnormal jitter and blocking in the frontalis and orbicularis oculi muscles and less severe abnormalities in the extensor digitorum, consistent with a neuromuscular junction disorder

Antibody testing:

» Acetylcholine receptor (AChR) antibodies were negative
» Muscle-specific kinase (MuSK) autoantibodies were positive

Patient was diagnosed with MuSK myasthenia gravis.

Overview of MuSK MG

Subtype	AChR MG	MUSK MG	LRP4 MG	LRP4 Seronegative MG
Relative prevalence[1,2]	80%	9%	2%	5%

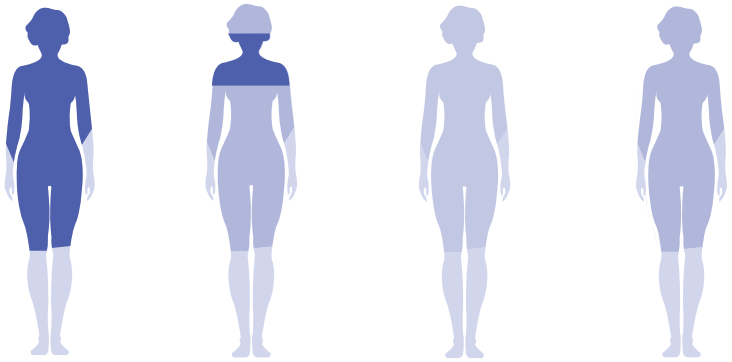

Figure adapted from reference.[1] Affected body sites indicated by blue highlighting, with dark blue representing the most affected areas

Anti-MuSK MG is a severe form of MG[3]

Anti-MuSK (Muscle Specific Kinase):
1/3 Seronegative MG (7% total)
4000 - 5000 patients in US

Age of onset:
» Females - 36.7 ± 18.7 years
» Males - 44.1 ± 17.0 years
In 64% of patients, onset was before 40 years of age.

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Management based on MG diagnosis

» High-dose daily prednisone and mycophenolate mofetil (MMF)

Follow up evaluations

» About 2-3 weeks after starting these medications, there was improvement in speech, chewing and swallowing and resolution of ptosis

» Prednisone and MMF were continued for 13 years with gradual resolution of most symptoms and tongue atrophy

» Prednisone dose was tapered to 20mg/day, but attempts at further reduction led to return of symptoms

Age 65

In 2017, 13 years after beginning immunosuppressive therapy, patient started new therapy.

Symptoms
Residual slurred speech

Management
Rituximab infusions

Outcome
» After 7 months, no longer "dragging her words"
» Prednisone was gradually reduced to the current dose of 12.5 mg/day

Currently, patient reports only mild eyelid drooping and that she has to stop and rest when brushing her hair.

Commentary: This case highlights the unique presentation of MuSK MG in comparison to AChR MG and how it may mimic other neuromuscular conditions such as ALS. Tongue atrophy may be prominent as in this case and this may be confused with the tongue atrophy seen in ALS. The presence of ocular weakness, even mild, should alert the clinician to the possibility of MG, as ocular weakness is rare in ALS. Furthermore, normal reflexes should dissuade the clinician from the diagnosis of ALS as hyperreflexia is usually seen with this disease. Single-fiber EMG may be useful in differentiating ALS from MG.

Key learning points

» MuSK MG may cause tongue atrophy and less pronounced ocular weakness than AChR MG
» A MuSK antibody assay should be performed in patients with a suspicion for MG whose AChR antibody test is negative
» Normal deep tendon reflexes should make the clinician question the diagnosis of ALS
» Single-fiber EMG may help distinguish MuSK MG from ALS

References

1. Gilhus NE, Verschuuren JJ. Myasthenia gravis: Subgroup classification and therapeutic strategies. The Lancet Neurology. 2015;14(10):1023-1036. doi:10.1016/S1474-4422(15)00145-3
2. Rivner MH, Pasnoor M, Barohn R, et al. MuSK and Myasthenia Gravis due to other antibodies. Neurol Clin. 2018;36(2):293-310. doi10.1016/j.ncl.2018.01.004.
3. Pasnoor M, Wolfe GI, Nations S, et al. Clinical findings in MuSK-antibody positive myasthenia gravis: a U.S. experience. Muscle and Nerve. 2010;41(3):370-374. doi:10.1002/mus.21533