Anti-MuSK Myasthenia Gravis Presenting With Purely Ocular Findings

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Background: Antibodies to a muscle-specific receptor tyrosine kinase (MuSK) have been found in approximately 40% of patients with generalized myasthenia gravis who are seronegative for the acetylcholine receptor antibody. Many of the patients with anti-MuSK antibodies have prominent oculobulbar symptoms or weakness of the neck and respiratory muscles, but patients with ocular myasthenia have not been described.

Objective: To report a case of ocular myasthenia due to anti-MuSK antibodies.

Results: Anti-MuSK antibody was detected by radioimmunoassay using highly purified MuSK recombinant antigen.

Conclusion: Ocular myasthenia gravis is a presentation of the anti-MuSK antibody syndrome.

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As many as 90% of patients with generalized myasthenia gravis (MG) have an elevated acetylcholine receptor (AChR) antibody titer.\(^1\) In 2001, Hoch et al\(^2\) reported that 17 (70%) of 24 patients with seronegative generalized MG (SNMG) had antibodies to a muscle-specific receptor tyrosine kinase (MuSK), a muscle membrane constituent necessary for the development of the neuromuscular junction. The frequency of this antibody was found to be 41% in a more representative sample of patients with SNMG.\(^3\) Other groups have reported from 38% to 47% of patients with SNMG to have elevated amounts of anti-MuSK antibodies.\(^4,5\) In ocular myasthenia, only 50% of patients were found to have anti-AChR antibodies,\(^1\) and of 38 patients with seronegative ocular MG, none showed elevated titers of the anti-MuSK antibody.\(^3,4,6\) The present report describes a patient presenting with ocular MG and having anti-MuSK antibodies.

Patient: A young woman with ocular myasthenia and antibodies to MuSK.

Results: Anti-MuSK antibody was detected by radioimmunoassay using highly purified MuSK recombinant antigen.

Conclusion: Ocular myasthenia gravis is a presentation of the anti-MuSK antibody syndrome.

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REPORT OF A CASE

An 18-year-old, left-handed woman developed intermittent ptosis of her left eye followed within a few weeks by diplopia. Her symptoms became more frequent over the next several weeks, and a diurnal pattern developed. Over the course of the day, her left lid would be open in the morning but completely shut by evening. She could improve her diplopia by tilting her head into certain positions. She was referred to an ophthalmologist, who diagnosed a partial left oculomotor nerve palsy. Magnetic resonance imaging of the brain with magnetic resonance angiography showed no abnormalities, and she was subsequently seen by a local neurologist for possible MG 3 months after the onset of symptoms.

She denied sensory symptoms, dysphagia, dysarthria, shortness of breath, or limb weakness. Her examination revealed spontaneous and fluctuating bilateral ptosis, more prominent on the left. She had subjective diplopia despite normal extraocular movements without obvious disconjugate gaze. She had no facial or jaw weakness and full strength throughout the neck and limbs without fatigability. Reflexes and sensation were normal. Thyroid findings, erythrocyte sedimentation rate, and rheumatoid factor and creatine kinase levels were normal; antinuclear antibody titer was positive at 1:160 with a speckled pattern. Her AChR antibody titer was determined by radioimmunoassay (LabCorp, Burlington, NC) and was within the normal range.

She started pyridostigmine and prednisone therapy but was unable to tolerate pyridostigmine owing to “shakiness” and stopped taking it before its effect was clear.
One month later, her diplopia had resolved and the ptosis had improved. Her prednisone dose was increased, and she was sent to Wake Forest University Baptist Medical Center for further evaluation. At that time, she was taking no medicines besides prednisone and had no significant medical, surgical, social, or family history.

On examination, she had equal bilateral ptosis covering the top third of her iris, which worsened with sustained up-gaze. Extraocular movements were normal, but cover/uncover testing revealed mild bilateral esotropia producing momentary diplopia. There was no weakness of eye closure or neck flexion or extension. Limb strength was full bilaterally without fatigability, and the remainder of her neurologic findings were normal. Repetitive stimulation testing recording from the left nasalis with 3-Hz stimulation did not reveal a decrement at baseline or after 1 minute of exercise.

Anti-MuSK antibody concentration was determined by radioimmunoassay using highly purified MuSK recombinant antigen (Athena Diagnostics, Worcester, Mass). The concentration of anti-MuSK antibodies was 31,435 pg/mL, with the low positive range beginning at 1949 pg/mL and the high positive range beginning at 28,554 pg/mL. Control values were 249 and 264 pg/mL.

Computed tomography of the chest with contrast enhancement revealed a normal-appearing thymus gland without thymoma. Her prednisone dose was increased to 40 mg/d, and she became asymptomatic from her myasthenia. She remained asymptomatic over the following year as her prednisone dose was tapered and at last observation was free of all myasthenia medicines for 4 months.

COMMENT

This report extends the clinical spectrum of anti-MuSK–positive MG to include ocular myasthenia. Our patient had purely ocular symptoms develop over several months prior to the initiation of immunosuppression, which may have affected disease progression, but she could develop generalized MG in the future. The anti-MuSK receptor antibody is directed against an extracellular portion of the muscle-membrane protein and may be pathogenic in SNMG. Anti-MuSK antibodies have not been found in 38 patients with ocular MG.

Demonstration of the anti-MuSK antibody is useful in these patients because it confirms the clinical diagnosis without requiring electrophysiologic testing, which can be uncomfortable and can usually be performed only at specialized centers. Younger children in particular may have difficulty tolerating repetitive stimulation testing and single-fiber electromyography.

The anti-MuSK MG syndrome tends to present with 1 of 3 patterns of clinical findings: severe oculobulbar syndrome; weakness of neck, shoulder, and respiratory muscles with late ocular involvement; or a presentation indistinguishable from typical generalized MG. While it is apparent that ocular MG is a less common presentation, it may now be reasonable to check for anti-MuSK antibodies in all seronegative patients regardless of the clinical presentation.

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REFERENCES