Test Definition: MUSK

MuSK Autoantibody, S

Overview

Useful For

Diagnosis of autoimmune muscle-specific kinase (MuSK) myasthenia gravis

Second-order test to aid in the diagnosis of autoimmune myasthenia gravis when first-line serologic tests are negative

Establishing a quantitative baseline value for MuSK antibodies that allows comparison with future levels if weakness is worsening

Testing Algorithm

See Myasthenia Gravis Evaluation with MuSK Reflex Algorithmin Special Instructions.

Special Instructions

- Myasthenia Gravis Evaluation with MuSK Reflex Algorithm

Method Name

Radioimmunoassay (RIA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Container/Tube:

Preferred: Red top

Acceptable: Serum gel

Specimen Volume: 1.5 mL

Forms

If not ordering electronically, complete, print, and send a Neurology Specialty Testing Client Test Request (T732) with the specimen.

Specimen Minimum Volume

1 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	28 days	
	Frozen	28 days	
	Ambient	72 hours	

Clinical and Interpretive

Clinical Information

Fatigable weakness due to impaired synaptic transmission at the neuromuscular junction is characteristic of myasthenia gravis (MG). The diagnosis is made by clinical and electromyographic criteria. Positive autoimmune serology must be interpreted in the clinical and electrophysiological context and response to anticholinesterase medication. Most cases are autoimmune and are caused by IgG autoantibodies binding to critical postsynaptic membrane molecules (nicotinic acetylcholine receptor or its interacting proteins).(1) Autoantibody detection frequency is lowest in patients with weakness confined to extraocular muscles (71% muscle acetylcholine receptor: AChR binding).(2) Mayo Clinic Laboratories' first-line serological evaluation detects muscle AChR antibody in 92% of nonimmunosuppressed patients with generalized weakness due to MG. Muscle-specific kinase (MuSK) antibody is detectable in more than one-third of those seronegative for muscle AChR antibody (less than 4% of all patients).(3) Physiologically, MuSK is involved in integrating and stabilizing AChR clusters in the motor endplate. MuSK is activated when the nerve-derived proteoglycan agrin binds to its receptor, lipoprotein-related protein 4 (LRP4). Antibodies to LRP4 itself have been described in rare patients.(1)

Six percent of nonimmunosuppressed patients with generalized MG lack demonstrable AChR or MuSK antibodies (double seronegative). Other rare autoantibodies no doubt remain to be discovered in such cases. However, as in autoimmune AChR MG and MuSK MG, testing for common organ-specific and nonorgan-specific autoantibodies is a valuable ancillary investigation in evaluating seronegative acquired generalized MG. General serological testing, coupled with family or personal history, will disclose autoimmune phenomena in 77% of those cases.(3) These disorders may include thyroid disease, type 1 diabetes, vitiligo, premature greying, rheumatoid arthritis, or lupus. Testing may also reveal antinuclear antibodies, glutamic acid decarboxylase (GAD65) antibodies, thyroperoxidase/thyroglobulin antibodies, or gastric parietal cell antibodies.(3) Objective improvement in strength following a therapeutic trial of plasmapheresis or intravenous immune globulin would justify consideration of long-term immunosuppression.

Females are generally affected by autoimmune MuSK MG more often than males. Onset can occur at any age (pediatric to elderly). Patients may derive limited benefit from anticholinesterase medication. The thymus is normal, and patients are generally not benefited by thymectomy. Antibody-lowering therapies are effective. Bulbar, facial, and respiratory weakness are prominent, and crises are common.(1,4)

Reference Values

< or =0.02 nmol/L

Interpretation

A positive result, in the appropriate clinical context, confirms the diagnosis of autoimmune muscle-specific kinase myasthenia gravis.

Seropositivity justifies consideration of immunotherapy.

Cautions

Immunosuppressant therapy is a common cause of false-seronegativity. It is, therefore, important to perform a comprehensive serological evaluation before initiating immunosuppressant therapy.

Interpretation of a patientÃ¢â‚¬â„¢s serological and clinical status is further complicated when characteristic signs of myasthenia gravis are obscured by a superimposed steroid-induced myopathy.

Clinical Reference

1. Li Y, Arora Y, Levin K: Myasthenia gravis: Newer therapies offer sustained improvement. Cleve Clin J Med 2013 Nov;80(11):711-721

2. Lennon VA: Serological profile of myasthenia gravis and distinction from the Lambert-Eaton myasthenic syndrome. Neurology 1997;48 (Suppl 5):S23-S27

3. Chan KH, Lachance DH, Harper CM, Lennon VA: Frequency of seronegativity in adult-acquired generalized myasthenia gravis. Muscle Nerve 2007 Nov;36(5):651-658

4. Skjei KL, Lennon VA, Kuntz NL: Muscle specific kinase autoimmune myasthenia gravis in children: A case series. Neuromuscul Disord 2013 Nov;23(11):874-882

Performance

Method Description

Duplicate aliquots of patient serum are incubated with I(125)-labeled recombinant human muscle-specific kinase. Immune complexes, formed by adding secondary (goat) antihuman immunoglobulin, are pelleted by centrifugation and washed. Gamma emission from the washed pellet is counted, and mean counts per minute (cpm) are compared with results yielded by high positive and negative control sera. Sera yielding cpm higher than the background cpm yielded by normal human serum are retested to confirm positivity and titrated as necessary to obtain a value in the linear range of the assay. The antigen binding capacity (nmol per liter) is calculated from the cpm precipitated at a dilution yielding a linear range value.(Lavrnic D, Losen M, Vujic A, et al: The features of myasthenia gravis with autoantibodies to MuSK. J Neurol Neurosurg Psychiatry 2005 Aug;76[8]:1099-1102)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Friday; 6 a.m.

Analytic Time

3 days

Maximum Laboratory Time

10 days

Specimen Retention Time

28 days

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification

This test was developed using an analyte specific reagent. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

83519

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
MUSK	MuSK Autoantibody, S	51716-9

Result ID	Test Result Name	Result LOINC Value
64277	MuSK Autoantibody, S	51716-9