Test Definition: HMGCR

3-Hydroxy-3-Methylglutaryl Coenzyme-A (HMG-CoA) Reductase, Serum

Overview

Useful For

Evaluating patients with suspected necrotizing autoimmune myopathy

Measuring 3-hydroxy-3-methylglutaryl-CoA reductase antibodies

Method Name

Chemiluminescence Immunoassay (CIA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

NMS1 / Necrotizing Myopathy Evaluation, Serum is the preferred first tier test for identification of antibodies specific for necrotizing autoimmune myopathy (HMGCOA-IgG and SRP-IgG). This initial evaluation includes signal recognition particle (SRP) antibodies performed using tissue indirect immunofluorescence, which increases the clinical sensitivity as compared to SRP immunoblot methodologies.

Specimen Required

Collection Container/Tube:
Preferred: Red top
Acceptable: Serum gel
Submission Container/Tube: Plastic vial
Specimen Volume: 2 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

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	
	Ambient	72 hours	
	Frozen	28 days	

Clinical & Interpretive

Clinical Information

Necrotizing autoimmune myopathy (NAM) is a serious but rare muscle disease strongly associated with autoantibodies to either signal recognition protein (SRP) or 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR).(1) NAM typically manifests with subacute proximal limb muscle weakness and persistently elevated serum creatine kinase (CK) concentrations, but slower onset can occur and complicate diagnosis. Muscle biopsies in affected patients can demonstrate necrotic and regenerating myofibers without inflammatory infiltrates, suggesting the diagnosis.(2) However, sampling issues and lack of access to persons having expertise in obtaining, preparing, and interpreting muscle biopsy specimens may delay a diagnosis.(3)

Early identification of NAM and subsequent aggressive immune-modulating therapy is critical.(1,3) Discovery of SRP- or HMGCR-IgG autoantibodies can aid in establishing an earlier diagnosis and treatment initiation. In addition, the discovery of SRP or HMGCR autoantibodies should prompt a search for an underlying malignancy.(4) Serial testing for these autoantibodies can delay diagnosis with the discovery of either antibody aiding in establishing an earlier diagnosis and treatment initiation.(1,3)

The clinical onsets are not specific to NAM, consisting of proximal limb weakness in association with an elevated serum creatinine kinase, with or without exposure to lipid-lowering statin medications.(1,3-9) The clinical presentation can be confused with forms of inflammatory (dermatomyositis, polymyositis), toxic, metabolic, or even neurodegeneration (ie, muscular dystrophy) and the diagnosis delayed without serological testing by SRP- or HMGCR-autoantibody testing. Panel testing of both HMGCR and SRP autoantibodies is the preferred strategy for the best patient care.

Reference Values

<20.0 CU

Interpretation

Seropositivity for 3-hydroxy-3-methylglutaryl-CoA reductase autoantibodies supports the clinical diagnosis of necrotizing autoimmune myopathy (NAM). Confirmation with muscle biopsy is recommended. A paraneoplastic basis should be considered, according to age, sex, and other risk factors.(4) In cases of NAM, immune therapy is required and often multiple simultaneously utilized immunotherapies are needed to successfully treat patients.

Cautions

Negative results do not exclude the diagnosis of necrotizing autoimmune myopathy (NAM). Only approximately 35% of

cases of NAM are associated with autoantibodies against 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR). The remainder of cases are either positive for signal recognition protein autoantibodies (approximately 20%-30%) or are seronegative (approximately 35%).

Very rarely HMGCR antibodies can be detected in diseases other than NAM. A muscle biopsy is recommended.

Clinical Reference

1. Kassardjian CD, Lennon VA, Alfugham NB, Mahler M, Milone M. Clinical features and treatment outcomes of necrotizing autoimmune myopathy. JAMA Neurol. 2015;72(9):996-1003
2. Emslie-Smith AM, Engel AG. Necrotizing myopathy with pipestem capillaries, microvascular deposition of the complement membrane attack complex (MAC), and minimal cellular infiltration. Neurology. 1991;41(6):936-939
3. Ramanathan S, Langguth D, Hardy T, et al. Clinical course and treatment of anti-HMGCR antibody-associated necrotizing autoimmune myopathy. Neurol Neuroimmunol Neuroinflamm. 2015;2(3):e96
4. Allenbach Y, Keraen J, Bouvier AM, et al. High risk of cancer in autoimmune necrotizing myopathies: usefulness of myositis specific antibody. Brain. 2016;139(Pt 8):2131-2135
5. Christopher-Stine L, Casciola-Rosen L, Hong G, Chung T, Corse AM, Mammen AL. A novel autoantibody recognizing 200-kd and 100-kd proteins is associated with an immune-mediated necrotizing myopathy. Arthritis Rheum. 2010;62(9):2757-2766
6. Mammen AL, Chung T, Christopher-Stine L, et al. Autoantibodies against 3-hydroxy-3-methylglutaryl-coenzyme A reductase in patients with statin-associated autoimmune myopathy. Arthritis Rheum. 2011;63(3):713-721
7. Hengstman GJ, ter Laak HJ, Vree Egberts WT, et al. Anti-signal recognition particle autoantibodies: marker of a necrotising myopathy. Ann Rheum Dis. 2006;65(12):1635-1638
8. Miller T, Al-Lozi MT, Lopate G, Pestronk A. Myopathy with antibodies to the signal recognition particle: clinical and pathological features. J Neurol Neurosurg Psychiatry. 2002;73(4):420-428
9. Watanabe Y, Uruha A, Suzuki S, et al. Clinical features and prognosis in anti-SRP and anti-HMGCR necrotising myopathy. J Neurol Neurosurg Psychiatry. 2016;87(10):1038-1044

Performance

Method Description

IgG antibodies to 3-hydroxy-3- methylglutaryl coenzyme A reductase (HMGCR) are detected by a chemiluminescent assay using the Inova BIO-FLASH instrument. HMGCR antigen is coated on to paramagnetic beads, which are stored in the reagent cartridge lyophilized. When the assay cartridge is ready to be used for the first time, a buffer solution is added to the tube containing the beads, and the beads are resuspended with the buffer. The reagent cartridge is then loaded onto the BIO-FLASH instrument. A patient serum sample is diluted 1:17 by the instrument in a disposable plastic cuvette. An aliquot of the diluted patient serum, HMGCR-coupled beads, and assay buffer are combined into a second cuvette and mixed. This cuvette is incubated at 37 degrees C. The beads are then magnetized and washed several times. Isoluminol conjugated anti-human IgG antibody is then added to the cuvette and incubated at 37 degrees C. Again, the beads are magnetized and washed repeatedly. The isoluminol conjugate produces a luminescent reaction when "trigger" reagents are added to the cuvette. The light produced from this reaction is measured as relative light units (RLU) by the BIO-FLASH optical system. RLU values are proportional to the amount of bound isoluminol conjugate, which in turn is proportional to the amount of anti-HMGCR antibodies bound to the antigen on the beads. The QUANTA Flash HMGCR

assay utilizes a predefined lot specific master curve that is uploaded into the instrument through the reagent cartridge barcode. Based on the results obtained by running two calibrators, an instrument specific working curve is created, which is used by the software to calculate chemiluminescent units from the RLU value obtained for each sample.(Package insert: QUANTA Flash HMGCR 701333. Inova Diagnostics, Inc; V04, 09/2018)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
2 to 4 days

Specimen Retention Time
2 days

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & 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 account representative. For assistance, contact Customer Service.

Test Classification
This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information
82397

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
HMGCR	HMG-CoA Reductase Ab, S	93493-5

Result ID	Test Result Name	Result LOINC® Value
607414	HMG-CoA Reductase Ab, S	93493-5