Acetylcholine Receptor Antibodies

Indications for Ordering

• Confirmation of clinical diagnosis of myasthenia gravis (MG)
• Assessment and management of individual with MG following immunomodulatory treatment or plasmapheresis
• Prognostic predictor of thymoma in individual with acetylcholine receptor (AChR) antibody-positive MG

Test Description

• Acetylcholine Receptor Antibody Reflexive Panel
  o Quantitative radioimmunoassay (RIA)/semiquantitative flow cytometry
  o Reflex pattern
    ▪ If binding antibody result is >0.4 mmol/L or blocking antibody result is >26%, modulating antibody will be added
• Acetylcholine Receptor Antibodies and Striated Muscle Antibodies Reflexive Panels, and Titin Antibody
  o Quantitative RIA/semiquantitative enzyme-linked immunosorbent assay (ELISA)/semiquantitative indirect fluorescent antibody (IFA)/semiquantitative flow cytometry
  o Reflex pattern
    ▪ If binding antibody result is >0.4 mmol/L or blocking antibody result is >26%, modulating antibody will be added
    ▪ If striated muscle antibody is detected, titer will be added
• Autoimmune Neuromuscular Junction Reflexive Panel
  o Quantitative RIA/qualitative radiobinding assay/semiquantitative flow cytometry/semiquantitative IFA
  o Reflex pattern
    ▪ If binding antibody result is >0.4 mmol/L or blocking antibody result is >26%, modulating antibody will be added
    ▪ If striated muscle antibody is detected, titer will be added
    ▪ If voltage-gated potassium channel antibody is indeterminate or positive, LGI1 antibody IgG and CASPR2 antibody IgG will be added
    ▪ If LGI1 antibody IgG is positive, titer will be added
    ▪ If CASPR2 antibody IgG is positive, titer will be added

Tests to Consider

Testing strategy
Acetylcholine receptor antibody reflexive panel tests for binding and blocking antibodies and reflexes to modulating antibody
• Most cost-effective testing algorithm for diagnosis of MG

Primary tests
Initial diagnostic testing for MG
• Acetylcholine Receptor Antibody Reflexive Panel 2001571
• Acetylcholine Receptor Antibodies and Striated Muscle Antibodies Reflexive Panels, and Titin Antibody 2005639
• Autoimmune Neuromuscular Junction Reflexive Panel 2005640
• Muscle-Specific Receptor Tyrosine Kinase (MuSK) Antibody by RIA
  o Quantitative RIA
• Acetylcholine Receptor Binding Antibody
  o Quantitative RIA
• Acetylcholine Receptor Blocking Antibody
  o Semiquantitative flow cytometry
• Acetylcholine Receptor Modulating Antibody
  o Semiquantitative flow cytometry

Related tests
Secondary diagnostic testing for MG
• Order if the primary tests are negative
  o Striated Muscle Antibodies, IgG with Reflex to Titer 0050746
  o Titin Antibody 2005636

Disease Overview

Incidence – 2/million/year
Prevalence – 0.5-14.2/100,000
**Age of onset**
- Mean age of onset
  - Females – 28 years
  - Males – 42 years
- Female predominance of MG in individuals <50 years
- No gender predominance in individuals >60 years
- Incidence rate increases with age for both genders

**Symptoms**
- Sporadic, fatigable muscle weakness
  - Begins with mild weakness in limited muscle groups
    - Ocular and bulbar muscles, initially
      - Ocular muscles only – 40%
        - Most severely affected muscles
      - Exclusively ocular – 16%
    - Almost always progresses to weakness of multiple muscle groups within first year
      - Exclusively ocular – 16%
    - Most serious condition results when respiratory muscles are affected
      - Myasthenic crisis can result

**Diagnostic issues**
- MG is an autoimmune disease – presence of antibodies aids in disease confirmation
- AChR antibodies are specific for MG
  - ~85% of individuals confirmed to have MG have detectable levels of anti-AChR antibodies
  - AChR antibodies are not detected in healthy individuals or in those with other autoimmune or neuromuscular disorders
  - ~15% of individuals with MG fail to demonstrate any AChR antibodies (seronegative MG [SNMG])
    - Predominantly female
    - Respiratory and bulbar muscles frequently involved
    - Individuals with SNMG often have antibodies against other neuromuscular junction proteins
      - Muscle-specific kinase (MuSK) – ~6%
      - Titin
    - Either the presence or the absolute concentration of AChR antibodies correlates with disease severity in any individual
- Thymic pathology in MG
  - ~75% of individuals with MG demonstrate abnormal thymic pathology
    - Hyperplasia
    - Thymic epithelial neoplasia
    - Thymoma
      - ~15% of individuals with MG have thymoma or other neoplasm
      - ~30% of individuals with thymoma have MG
      - Titin and/or striated muscle antibodies
        - Presence of antibodies is characteristic, but not diagnostic, of MG
        - One or both are found in ~13% of individuals with Lambert-Eaton myasthenic syndrome (LEMS)
        - Relatively high association with titin antibodies and thymic epithelial tumors
          - Predominantly thymoma
        - Antibodies are not specific for MG and have been identified in
          - Rheumatoid arthritis
          - Systemic lupus erythematosus
          - LEMS
          - Following myocardial infarction or cardiomytomy (striated only)
        - Antibodies may be useful in conjunction with AChR antibodies in the management of individuals with MG and/or AChR antibody-negative MG
        - Presence of titin antibodies in early onset MG indicates ~95% likelihood of underlying thymoma
        - May also be useful for individuals with MG
          - <50 years of age
          - Especially those with AChR-modulating antibodies

**Test Interpretation**

**Sensitivity**
- Binding>modulating>blocking
  - Combination of binding and blocking AChR antibody testing
    - Identifies 99.6% of population possessing AChR antibodies
    - Positive in up to 90% of individuals with generalized MG
    - Positive in 50-70% of individuals with purely ocular MG

**Results**

Positive
- Paraneoplastic disease is likely when positive AChR modulating antibody is in conjunction with
  - Striated muscle antibody titer – ≥1:80
  - Titin antibody index value – 0.72
  - Or both
    - Usually thymoma

**Limitations**

Absence of AChR antibody does not rule out diagnosis of MG