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
  - Quantitative radioimmunoassay (RIA)/semiquantitative flow cytometry
  - 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
  - Quantitative RIA/semiquantitative enzyme-linked immunosorbent assay (ELISA)/semiquantitative indirect fluorescent antibody (IFA)/semiquantitative flow cytometry
  - 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
  - Quantitative RIA/qualitative radiobinding assay/semiquantitative flow cytometry/semiquantitative IFA
  - 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
- Muscle-Specific Receptor Tyrosine Kinase (MuSK) Antibody by RIA
  - Quantitative RIA
- Acetylcholine Receptor Binding Antibody
  - Quantitative RIA
- Acetylcholine Receptor Blocking Antibody
  - Semiquantitative flow cytometry
- Acetylcholine Receptor Modulating Antibody
  - Semiquantitative flow cytometry

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 2012420
- Acetylcholine Receptor Binding Antibody 0080009
- Acetylcholine Receptor Blocking Antibody 0099580
- Acetylcholine Receptor Modulating Antibody 0099521

Related tests

Secondary diagnostic testing for MG

- Order if the primary tests are negative
  - Striated Muscle Antibodies, IgG with Reflex to Titer 0050746
  - 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
      - 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
  - Neither the presence nor 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

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