Voltage-Gated Potassium Channel Antibody Disorders

Voltage-gated potassium channel antibody disorders include limbic encephalitis, faciobrachial dystonic seizures, and peripheral nerve hyperexcitability disorders that may occur following immunotherapy and/or plasmapheresis.

Disease Overview

Incidence
Unknown

Symptoms
- Limbic encephalitis (mainly LGI1 antibodies):
  - Amnesia
  - Seizures
  - Disorientation
  - Psychiatric disturbance
  - Peripheral nerve hyperexcitability
  - Neuromyotonia
  - CSF usually normal
- Morvan syndrome (mainly CASPR2 antibodies):
  - Limbic encephalitis
  - Neuromyotonia
  - Confusion
  - Amnesia
  - Insomnia
  - Pain
  - Autonomic dysfunction: hyperhidrosis, constipation, urinary incontinence

Diagnostic Issues
Antibody testing may aid in diagnosis.

- Testing should be performed only when neuromuscular and/or neurological symptoms are present.
- Anti-VGKC disorders are rare and present with symptoms similar to those of other encephalitic disorders.
- Antibody testing should not be used for screening.
- Antibodies may be associated with paraneoplastic (autoimmune) or nonparaneoplastic neurological disorders.
- Not all neurological disorders or antibodies are associated with tumors.
  - In most antibody-mediated, non-neoplastic-associated diseases, individuals improve substantially with immunotherapy.
  - It is important to diagnose these illnesses due to therapeutic responsiveness.

Physiology
- VGKC autoantibodies:
  - Directed against a protein that is complexed with potassium channels in both the peripheral nervous system and CNS
    - CASPR2:
      - Present in ~50% of individuals with neuromyotonia

Tests to Consider

Voltage-Gated Potassium Channel Antibody with Reflex to LGI1 and CASPR2 Screen and Titer, Serum 2009463
Method: Quantitative Radioimmunoassay/Semi-Quantitative Indirect Fluorescent Antibody
- Screening test for VGKC antibody receptor complex-associated autoantibodies
- Reflexes to CASPR2 and LGI1 antibodies

Voltage-Gated Potassium Channel (VGKC) Complex Antibody Panel with Reflex to Titer, CSF 3001996
Method: Quantitative Radioimmunoassay/Semi-Quantitative Indirect Fluorescent Antibody
Screening test for VGKC antibody receptor complex-associated autoantibodies

Voltage-Gated Potassium Channel (VGKC) Antibody, Serum 2004890
Method: Quantitative Radioimmunoassay
Screening test for VGKC antibody receptor complex-associated autoantibodies

Voltage-Gated Potassium Channel (VGKC) Antibody, CSF 3001387
Method: Quantitative Radioimmunoassay
Screening test for VGKC antibody receptor complex-associated autoantibodies

Leucine-Rich, Glioma-Inactivated Protein 1 Antibody, IgG with Reflex to Titer, Serum 2009456
Method: Semi-Quantitative Indirect Fluorescent Antibody
Aids in diagnosis of LGI1 disorders

Leucine-Rich, Glioma-Inactivated Protein 1 Antibody, IgG with Reflex to Titer, CSF 3001992
Method: Semi-Quantitative Indirect Fluorescent Antibody
Aids in diagnosis of LGI1 disorders

Contactin-Associated Protein-2 Antibody, IgG with Reflex to Titer, Serum 2009452
Method: Semi-Quantitative Indirect Fluorescent Antibody
Aids in diagnosis of CASPR2 disorders

Contactin-Associated Protein-2 Antibody, IgG with Reflex to Titer, CSF 3001986
Method: Semi-Quantitative Indirect Fluorescent Antibody
Aids in diagnosis of CASPR2 disorders
- CASPR2 antibodies are common in individuals with thymic malignancies.
  - LGI1:
    - Not directed against the potassium channels
    - Associated with limbic encephalitis, faciobrachial dystonic seizures, hyponatremia, and myoclonic movements
    - Disorders are rarely associated with tumors
- VGKC radioimmunoassay (RIA) tests can be used as a general screen for VGKC-complex antibodies directed against:
  - LGI1
  - CASPR2
  - Other unidentified targets

**Test Interpretation**

**Results**

**VGKC Antibody, Serum**
- Positive: >88 pmol/L
  - Suggests VGKC antibody-related disease
- Indeterminant: 32-87 pmol/L
  - Retest in 2-4 weeks
- Negative: 0-31 pmol/L
  - Likelihood of VGKC antibody-related disease is reduced but not necessarily eliminated

**VGKC Antibody, CSF**
- Positive: >1.1 pmol/L
  - Suggests VGKC antibody-related disease
- Negative: 0.0-1.1 pmol/L
  - Likelihood of VGKC antibody-related disease is reduced but not necessarily eliminated

**LGI1 Antibody, Serum**
- Positive: ≥1:10
  - Suggests LGI1 antibody-related disease
- Negative: <1:10
  - Does not rule out disorders associated with VGKC complex antibodies

**CASPR2 Antibody, Serum**
- Positive: ≥1:10
  - Suggests CASPR2 antibody-related disease
- Negative: <1:10
  - Does not rule out disorders associated with VGKC complex antibodies

**Limitations**

**VGKC Antibody**
- Presence of VGKC antibodies should be used in conjunction with clinical manifestations for:
  - Neuromyotonia spectrum of disorders
  - VGKC antibody-associated limbic encephalitis
- Should not be used as the sole criterion for diagnosis
- VGKC receptor-complex proteins may be coprecipitated by anti-VGKC antibodies, including:
  - LGI1
  - CASPR2
  - Other unidentified targets

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**Leucine-Rich, Glioma-Inactivated Protein 1 Antibody, IgG and Contactin-Associated Protein-2 Antibody, IgG with Reflex to Titers, Serum 2009460**

**Method:** Semi-Quantitative Indirect Fluorescent Antibody

Aids in diagnosis of LGI1 and CASPR2 disorders

**Autoimmune Encephalitis Extended Panel, Serum 3001431**

**Method:** Semi-Quantitative Indirect Fluorescent Antibody/Quantitative Radioimmunoassay/Semi-Quantitative Enzyme-Linked Immunosorbent Assay

- Differential evaluation of encephalitis of unknown origin with subacute onset of seizures, confusion, memory loss, and/or behavioral change
- For adults and patients with suspicion of cancer, additional evaluation of paraneoplastic autoantibodies is recommended
- Individual tests in the panel may also be ordered separately.

See the Anti-NMDA Receptor (NR1) IgG Antibodies Test Fact Sheet for more information on the evaluation of NMDA antibodies in autoimmune encephalitis.

**Autoimmune Neuromuscular Junction Reflexive Panel 3003017**

**Method:** Quantitative Radioimmunoassay/Qualitative Radiobinding Assay/Semi-Quantitative Flow Cytometry/Semi-Quantitative Indirect Fluorescent Antibody

- Acceptable reflexive panel for the differential diagnosis of acquired neuromuscular junction disorders
- Panel includes acetylcholine receptor binding, blocking, and modulating antibodies; ganglionic acetylcholine receptor antibodies; P/Q-type and N-type voltage-gated calcium channels; voltage-gated potassium channels; titin antibody; striated muscle antibodies; leucine-rich glioma-inactivated protein 1 antibody; and contactin-associated protein-2 antibody IgG with reflex to titers.

See Related Tests.
Related Information

N-methyl-D-Aspartate (NMDA)-Type Glutamate Receptor Autoantibody Disorders - Anti-NMDA-Receptor Encephalitis
Paraneoplastic Neurologic Syndromes and Associated Disorders - PNS
Paraneoplastic Neurologic Syndromes Testing Algorithm - Serum

Related Tests

Autoimmune Encephalitis Reflexive Panel, CSF 3002787
Method: Semi-Quantitative Indirect Fluorescent Antibody/Quantitative Radioimmunoassay/Semi-Quantitative Enzyme-Linked Immunosorbent Assay

N-methyl-D-Aspartate Receptor Antibody, IgG, Serum with Reflex to Titer 2004221
Method: Semi-Quantitative Indirect Fluorescent Antibody

N-methyl-D-Aspartate Receptor Antibody, IgG, CSF with Reflex to Titer 2005164
Method: Semi-Quantitative Indirect Fluorescent Antibody

Glutamic Acid Decarboxylase Antibody 2001771
Method: Semi-quantitative Enzyme-Linked Immunosorbent Assay

Glutamic Acid Decarboxylase Antibody, CSF 3002788
Method: Semi-quantitative Enzyme-Linked Immunosorbent Assay

Aquaporin-4 Receptor Antibody 2003036
Method: Semi-quantitative Enzyme-Linked Immunosorbent Assay

Aquaporin-4 Receptor Antibody, IgG by IFA with Reflex to Titer, Serum 2013320
Method: Semi-Quantitative Indirect Fluorescent Antibody

Alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic Acid (AMPA) Receptor Antibody, IgG by IFA with Reflex to Titer, Serum 3001260
Method: Semi-Quantitative Indirect Fluorescent Antibody

Gamma Aminobutyric Acid Receptor, Type B (GABA-BR) Antibody, IgG by IFA with Reflex to Titer, Serum 3001270
Method: Semi-Quantitative Indirect Fluorescent Antibody

Myelin Oligodendrocyte Glycoprotein (MOG) Antibody, IgG by IFA with Reflex to Titer, Serum 3001277
Method: Semi-Quantitative Indirect Fluorescent Antibody

PCCA/ANNA by IFA with Reflex to Titer and Immunoblot 2007961
Method: Semi-Quantitative Indirect Fluorescent Antibody/Qualitative Immunoblot

Antinuclear Antibody (ANA) with HEp-2 Substrate, IgG by IFA 3000082
Method: Semi-Quantitative Indirect Fluorescent Antibody

ANCA-Associated Vasculitis Profile (ANCA/MPO/PR3) 3003745
Method: Semi-Quantitative Indirect Fluorescent Antibody/Semi-Quantitative Multiplex Bead Assay

Antiphospholipid Syndrome Reflexive Panel 2003222
Method: Electromagnetic Mechanical Clot Detection/Semi-Quantitative Enzyme-Linked Immunosorbent Assay

Dipeptidyl Aminopeptidase-Like Protein 6 (DPPX) Antibody, IgG by IFA With Reflex to Titer, Serum 3004359
Method: Semi-Quantitative Indirect Fluorescent Antibody