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
- 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
  - Important to diagnose these illnesses due to therapeutic responsiveness

Physiology

- VGKC autoantibodies
  - Directed against a protein that is complexed with potassium channels in both peripheral nervous system and CNS
    - CASPR2
      - Present in ~50% of individuals with neuromyotonia
      - 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 RIA test can be used as a general screen for VGKC-complex antibodies directed against
    - LGI1
    - CASPR2
    - Other unidentified targets

TESTS TO CONSIDER

Voltage-Gated Potassium Channel (VGKC) 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

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
Aid 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
Aid in diagnosis of LGI1 disorders

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

Contactin-Associated Protein-2 Antibody, IgG with Reflex to Titer, CSF 3001986
Method: Semi-Quantitative Indirect Fluorescent Antibody
Aid in diagnosis of CASPR2 disorders

Leucine-Rich, Glioma-Inactivated Protein 1 Antibody, IgG and Contactin-Associated Protein-2 Antibody, IgG with Reflex to Titer, Serum 2009460
Method: Semi-Quantitative Indirect Fluorescent Antibody
Aid in diagnosis of LGI1 and CASPR2 disorders

Autoimmune Encephalitis Reflexive Panel, Serum 2013601
Method: Semi-Quantitative Indirect Fluorescent Antibody/Semi-Quantitative Enzyme-Linked Immunosorbent Assay/Quantitative Radioimmunoassay
  - Differential evaluation of encephalitis of unknown origin with subacute onset of seizures, confusion, memory loss, and/or behavioral change
  - Panel includes NMDA receptor antibody, VGKC antibody, GAD65 antibody,
For adults and patients with suspicion of cancer, additional evaluation of paraneoplastic autoantibodies is recommended. Individual tests in panel may also be ordered separately.

**Autoimmune Encephalitis Extended Panel, Serum 3001431**
- Differential evaluation of encephalitis of unknown origin with subacute onset of seizures, confusion, memory loss, and/or behavioral change
- Testing for LGI1 and CASPR2 antibodies always performed.
- Panel includes NMDA receptor antibody, VGKC antibody, GAD65 antibody, AQP4 antibody.
- For adults and patients with suspicion of cancer, additional evaluation of paraneoplastic autoantibodies is recommended
- Individual tests in panel may also be ordered separately.

See **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 2005640**
- Acceptable reflexive panel for the differential diagnosis of acquired neuromuscular junction disorders
- Panel includes acetylcholine receptor binding, blocking, and modulating antibodies; VGKC antibody; VGCC antibody; titin antibody; striated muscle antibody; and LGI1 and CASPR2 antibodies

See **Related Tests**

**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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**RELATED INFORMATION**

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

**RELATED TESTS**

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

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-isoxazolopropionic 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

Paraneoplastic Antibodies (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) with Reflex to ANCA Titer 2006480
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