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

TESTS TO CONSIDER

Voltage-Gated Potassium Channel (VGKC) Antibody with Reflex to LGI1 and CASPR2 Screen and Titer 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) 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 2009456
Method: Semi-Quantitative Indirect Fluorescent Antibody
Aid in diagnosis of LGI1 disorders

Contactin-Associated Protein-2 Antibody, IgG with Reflex to Titer 2009452
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 Titers 2009460
Method: Semi-Quantitative Indirect Fluorescent Antibody
Aid in diagnosis of LGI1 and CASPR2 disorders
**Autoimmune Encephalitis Reflexive Panel 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, AQP4 antibody, and LGI1 and CASPR2 antibodies.
- 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 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
- Testing for LGI1 and CASPR2 antibodies always performed.
- Panel includes NMDA receptor antibody, VGKC antibody, GAD65 antibody, AQP4 antibody, and LGI1 and CASPR2 antibodies.
- 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 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

**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

- 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

**CASPR2**

- Present in ~50% of individuals with neuromyotonia

**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

**Autoimmune Encephalitis Reflexive Panel 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, AQP4 antibody, and LGI1 and CASPR2 antibodies.
- 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 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
- Testing for LGI1 and CASPR2 antibodies always performed.
- Panel includes NMDA receptor antibody, VGKC antibody, GAD65 antibody, AQP4 antibody, and LGI1 and CASPR2 antibodies.
- For adults and patients with suspicion of cancer, additional evaluation of paraneoplastic autoantibodies is recommended
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**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
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-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

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

ARUP Laboratories is a nonprofit enterprise of the University of Utah and its Department of Pathology.
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