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
      - CASPR2 antibodies are common in individuals with thymic malignancies.
    - LGI1:
      - Not directed against the potassium channels
Aids in diagnosis of LGI1 and CASPR2 disorders

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.

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

Related Information

- Leucine-Rich, Glioma-Inactivated Protein 1 Antibody, IgG CBA-IFA and Contactin-Associated Protein-2 Antibody, IgG CBA-IFA with Reflex to Titers, Serum 2009460
  - Method: Semi-Quantitative Cell-Based Indirect Fluorescent Antibody
  - Aids in diagnosis of LGI1 and CASPR2 disorders

- 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
  - 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
  - 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 gliala inactivated protein 1 antibody; and contactin-associated protein-2 antibody IgG with reflex to titers.

See Related Tests.
Autoimmune Encephalitis Reflexive Panel, CSF 3002787
Method: Semi-Quantitative Cell-Based Indirect Fluorescent Antibody/Quantitative Radioimmunoassay/Semi-Quantitative Enzyme-Linked Immunosorbent Assay

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

N-methyl-D-Aspartate Receptor Antibody, IgG CBA-IFA, CSF with Reflex to Titer 2005164
Method: Semi-Quantitative Cell-Based 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 Antibody, IgG by CBA-IFA with Reflex to Titer, Serum 2013320
Method: Semi-Quantitative Cell-Based Indirect Fluorescent Antibody

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

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

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

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

Dipeptidyl Aminopeptidase-Like Protein 6 (DPPX) Antibody, IgG by CBA-IFA With Reflex to Titer, CSF 3004512
Method: Semi-Quantitative Cell-Based Indirect Fluorescent Antibody