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

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
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

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

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 - 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
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