Autoimmune Neuropathies

Indications for Ordering

Evaluation of autoimmune neuropathies

Test Description

- Semiquantitative indirect fluorescent antibody (IFA)
  - Neuronal nuclear antibody (ANNA-1 and ANNA-2)
  - Purkinje cell cytoplasmic antibody-1 (PCCA-1)
- Qualitative immunoblot assay
  - Neuronal nuclear antibodies (Hu, Ri, and Yo)
- Semiquantitative enzyme-linked immunosorbent assay
  - Myelin-associated glycoprotein (MAG) antibodies
  - Sulfate-3-glucuronyl paragloboside (SGPG)
  - Ganglioside (Asialo-GM1, GM1, GM2, GD1a, GD1b, and GQ1b) antibodies

Tests to Consider

Typical testing strategy

Initial testing to rule out other, more common diseases
- Infectious
  - Complete blood count
  - Cerebral spinal fluid testing for protein, cell count, glucose, and culture
- Metabolic
  - Electrolytes
  - Vitamin B12
- Inflammatory
  - Erythrocyte sedimentation rate or C-reactive protein
  - Elevations in either might suggest connective tissue disease or vasculitis evaluation (eg, ANA, ANCA)
- Other testing based on individual presentation
  - Campylobacter jejuni (stool specimen)
  - Mycoplasma pneumoniae
  - Hepatitis virus
  - HIV

Neuronal marker testing
- Choice of panel – based on clinical manifestations
  - Sensory only (typical)
  - Sensorimotor
  - Motor predominant
- Age – aids in decision about whether to test for underlying cancer/tumor
- Risk or presence of specific malignancy – may determine appropriate antibody tests

Primary tests

Sensory Neuropathy Antibody Panel with Reflex to Titer and Neuronal Immunoblot 2007965
- Aid in diagnosis of a sensory neuropathy when malignancy, other than plasma cell dyscrasia, is suspected

Motor and Sensory Neuropathy Evaluation with Reflex to Titer and Neuronal Immunoblot 2007966
- Aid in diagnosis of combined motor/sensory neuropathy when malignancy, other than plasma cell dyscrasia, is suspected

Motor and Sensory Neuropathy Evaluation with Immunofixation Electrophoresis and Reflex to Titer and Neuronal Immunoblot 2007967
- Aid in diagnosis of combined motor/sensory neuropathy with suspicion for plasma cell dyscrasia or suspicion for other malignancy

Motor Neuropathy Panel 0051225
- Aid in diagnosis of motor neuropathy with suspicion for plasma cell dyscrasia

<table>
<thead>
<tr>
<th>Antibody Components</th>
<th>Primary Tests for Autoimmune Neuropathies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibody</td>
<td>2007965 Sensory Antibody Panel</td>
</tr>
<tr>
<td>Purkinje cell/neuronal nuclear IgG</td>
<td>✓</td>
</tr>
<tr>
<td>Purkinje cell antibody titer</td>
<td>✓</td>
</tr>
<tr>
<td>Neuronal nuclear (Hu, Ri, and Yo) IgG</td>
<td>✓</td>
</tr>
<tr>
<td>Neuronal nuclear antibody (ANNA) IgG titer</td>
<td>✓</td>
</tr>
<tr>
<td>MAG IgM</td>
<td>✓</td>
</tr>
<tr>
<td>SGPG IgM</td>
<td>✓</td>
</tr>
<tr>
<td>Asialo-GM1 IgG and IgM</td>
<td>✓</td>
</tr>
<tr>
<td>IgG and IgM for GM1, GD1a, GD1b</td>
<td>✓</td>
</tr>
<tr>
<td>GQ1b antibodies</td>
<td>✓</td>
</tr>
<tr>
<td>Total protein electrophoresis, serum</td>
<td>✓</td>
</tr>
<tr>
<td>Albumin</td>
<td>✓</td>
</tr>
<tr>
<td>Alpha-1 and alpha-2 globulins</td>
<td>✓</td>
</tr>
<tr>
<td>Beta globulins</td>
<td>✓</td>
</tr>
<tr>
<td>Gamma globulins</td>
<td>✓</td>
</tr>
<tr>
<td>Immunoglobulins A, G, M</td>
<td>✓</td>
</tr>
</tbody>
</table>
### Related Tests
- Paraneoplastic Reflexive Panel 2013955
- Paraneoplastic Antibodies (PCCA/ANNA) by IFA with Reflex to Titer and Immunoblot 2007961
- Myelin Associated Glycoprotein (MAG) Antibodies, IgM and Sulfate-3-Glucuronyl Paragloboside (SGPG) Antibodies, IgM 2004412
- Ganglioside (Asialo-GM1, GM1, GM2, GD1α, GD1b, and GQ1b) Antibodies, IgG and IgM 0051033
- Sulfate-3-Glucuronyl Paragloboside (SGPG) Antibody, IgM 0051284
- Myelin Associated Glycoprotein (MAG) Antibody, IgM 0051285
- Ganglioside (GM1) Antibodies, IgG and IgM 0050591
- Ganglioside (GM1, GD1b, and GQ1b) Antibodies, IgG and IgM 2004998
- CV2.1 Screen by IFA with Reflex to Titer 2013956
- Amphiphysin Antibody 2008893

### Disease Overview

**Classification**
- Monoclonal gammopathy associated
- Polyclonal inflammatory polyneuropathy
- Guillain-Barré syndrome (GBS)
- Chronic inflammatory demyelinating polyneuropathy
- Multifocal motor neuropathy (MMN)
- Paraneoplastic neuropathy (PNS)

**Antibody markers associated with syndromes**
See Tables 1 and 2

**Symptoms**
- Motor symptoms are often mild and diagnosed only with electromyography
  - Isolated sensory symptoms are not uncommon
  - Paresthesias, dysesthesias, and pain predominate
  - Symptoms depend on type of syndrome
  - May have rapid onset and include respiratory muscles

**Diagnostic issues**
- Overlap of symptoms among syndromes often makes diagnosis difficult
- Antibody testing may aid in clarification of diagnosis, but cannot be used as sole diagnostic tool

### Test Interpretation

**Results**
- Positive – marker(s) detected
  - In context of appropriate clinical setting, may suggest the presence of disease
  - Close clinical correlation is recommended
  - Suggests antibody-mediated neuropathy
- Negative – marker(s) not detected
  - Does not rule out disease and/or cancer

**Limitations**
Some antibodies may be associated with more than one disease and/or cancer

### References

### Table 1

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Associated neuropathic disorder/syndrome/disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>GM1</td>
<td>Motor – GBS, MMN, multiple sclerosis (MS)</td>
</tr>
<tr>
<td>GM2</td>
<td>Motor – GBS-variants, MMN, MS</td>
</tr>
<tr>
<td>GD1α</td>
<td>Sensory – demyelinating sensory neuropathy</td>
</tr>
<tr>
<td>GD1b</td>
<td>Motor – GBS-like syndrome (acute motor &amp; axonal), MMN, demyelinating motor neuropathy (with IgM M-protein)</td>
</tr>
<tr>
<td>GD1b</td>
<td>Combined – demyelinating sensory-motor neuropathy</td>
</tr>
<tr>
<td>GQ1b</td>
<td>Motor – cranial nerve neuropathy</td>
</tr>
<tr>
<td>GQ1b</td>
<td>Combined – sensory-motor neuropathy (ataxic)</td>
</tr>
<tr>
<td>Myelin-associated glycoprotein (MAG) and sulfate-3-glucuronyl paragloboside (SGPG)</td>
<td>Motor – multifocal motor neuropathy with conduction block (SGPG only); IgM-related neuropathy</td>
</tr>
<tr>
<td></td>
<td>Combined – chronic demyelinating sensory-motor polyneuropathy (MAG and SGPG); axonal sensory-motor neuropathy (SGPG only)</td>
</tr>
<tr>
<td>Sulfatide</td>
<td>Sensory – axonal, demyelinating</td>
</tr>
<tr>
<td></td>
<td>Combined – GALOP syndrome (gait disorder, antibody, late-age onset polyneuropathy)</td>
</tr>
</tbody>
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Vernino, 2007; Willison, 2011
<table>
<thead>
<tr>
<th>Antibody</th>
<th>Associated neuropathic disorder/syndrome/disease</th>
<th>Associated tumor/cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hu (ANNA-1)</td>
<td>Sensory neuronopathy, encephalomyelitis, limbic encephalitis, opsoclonus-myoclonus, subacute cerebellar degeneration, autonomic neuropathy, enteric neuropathy (GI dysmotility)</td>
<td>Small-cell lung cancer (SCLC), neuroblastoma</td>
</tr>
<tr>
<td>Ri (ANNA-2)</td>
<td>Opsoclonus-myoclonus, brainstem encephalitis, cerebellar degeneration</td>
<td>SCLC, breast, ovary</td>
</tr>
<tr>
<td>Yo (PCA-1)</td>
<td>Subacute cerebellar degeneration, occasional GI dysmotility, chorea</td>
<td>Ovary, breast</td>
</tr>
<tr>
<td>CV2/CRMP5</td>
<td>Encephalomyelitis, chorea, limbic encephalitis, sensory neuronopathy, sensorimotor neuropathy, optic neuropathy (retinitis, optic neuritis, uveitis), subacute cerebellar degeneration, autonomic neuropathy, GI dysmotility</td>
<td>SCLC, thymoma</td>
</tr>
</tbody>
</table>

Dalmau 2008; Graus, 2004