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 B_{12}
- 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 panels 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

- Aids 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

- Aids 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

- Aids in diagnosis of combined motor/sensory neuropathy with suspicion for plasma cell dyscrasia or suspicion for other malignancy

Motor Neuropathy Panel 0051225

- Aids in diagnosis of motor neuropathy with suspicion for plasma cell dyscrasia

Antibody Components
Primary Tests for Autoimmune Neuropathies

Antibody	2007965 Sensory Antibody Panel	2007966 Motor & Sensory	2007967 Motor & Sensory with IFE	0051225 Motor Panel
Purkinje cell/neuronal nuclear IgG	✓	✓	✓	
Purkinje cell antibody titer	✓	✓	✓	
Neuronal nuclear (Hu, Ri, and Yo, and Tr/DNER) IgG	✓	✓	✓	
Neuronal nuclear antibody (ANNA) IgG titer	✓	✓	✓	
MAG IgM	✓	✓	✓	✓
SGPG IgM	✓	✓	✓	✓
Asialo-GM1 IgG and IgM		✓	✓	✓
IgG and IgM for GM1, GD1a, GD1b		✓	✓	✓
GQ1b antibodies		✓	✓	✓
Total protein electrophoresis, serum			✓	✓
Albumin			✓	✓
Alpha-1 and alpha-2 globulins			✓	✓
Beta globulins			✓	✓
Gamma globulins			✓	✓
Immunoglobulins A, G, M			✓	✓

Related Tests

Paraneoplastic Reflexive Panel 3002929

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, GD1a, GD1b, and GQ1b) Antibodies 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 on next page

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

- Dalmau J, Rosenfeld MR. Paraneoplastic syndromes of the CNS. Lancet Neurol. 2008 Apr;7(4):327-40. PubMed
- Graus F, Delattre JY, Antoine JC, Dalmau J, Giometto B, Grisold W, Honnorat J, Smitt PS, Vedeler Ch, Verschuuren JJ, Vincent A, Voltz R. Recommended diagnostic criteria for paraneoplastic neurological syndromes. J Neurol Neurosurg Psychiatry. 2004 Aug;75(8):1135-40. PubMed
- Ohst C, Saschenbrecker S, Stiba K, et al. Reliable Serological Testing for the Diagnosis of Emerging Infectious Diseases. Adv Exp Med Biol. 2018;1062:19-43.
- Vernino S, Wolfe GI. Antibody testing in peripheral neuropathies. Neurol Clin. 2007 Feb;25(1):29-46. Review. PubMed
- Willison HJ. Biomarkers in experimental models of antibody-mediated neuropathies. J Peripher Nerv Syst. 2011 Jun;16 Suppl 1:60-2. PubMed

Table 1

Nonparaneoplastic Antibody Markers and Associated Disorders/Syndromes/Diseases	
Antibody	**Associated neuropathic disorder/syndrome/disease**
GM1	Motor – GBS, MMN, multiple sclerosis (MS)
GM2	Motor – GBS-variants, MMN, MS
	Sensory – demyelinating sensory neuropathy
GD1a	Motor – GBS-like syndrome (acute motor & axonal), MMN, demyelinating motor neuropathy (with IgM M-protein)
	Combined – demyelinating sensory-motor neuropathy
GD1b	Motor – cranial nerve neuropathy
	Combined – sensory-motor neuropathy (ataxic)
GQ1b	Motor – Miller-Fisher syndrome, GBS with ataxia or ophthalmoplegia
	Combined – sensory-motor neuropathy (ataxic)
Myelin-associated glycoprotein (MAG) and sulfate-3-glucuronyl paragloboside (SGPG)	Motor – multifocal motor neuropathy with conduction block (SGPG only); IgM-related neuropathy
	Combined – chronic demyelinating sensory-motor polyneuropathy (MAG and SGPG); axonal sensory-motor neuropathy (SGPG only)
Sulfatide	Sensory – axonal, demyelinating
	Combined – GALOP syndrome (gait disorder, antibody, late-age onset polyneuropathy)
Vernino, 2007; Willison, 2011	

Table 2

Paraneoplastic Antibody Markers and Associated Disorders/Syndromes/Diseases		
Antibody	**Associated neuropathic disorder/syndrome/disease**	**Associated tumor/cancer**
Hu (ANNA-1)	Sensory neuronopathy, encephalomyelitis, limbic encephalitis, opsoclonus-myoclonus, subacute cerebellar degeneration, autonomic neuropathy, enteric neuropathy (GI dysmotility)	Small-cell lung cancer (SCLC), neuroblastoma
Ri (ANNA-2)	Opsoclonus-myoclonus, brainstem encephalitis, cerebellar degeneration	SCLC, breast, ovary
Yo (PCA-1)	Subacute cerebellar degeneration, occasional GI dysmotility, chorea	Ovary, breast
CV2/CRMP5	Encephalomyelitis, chorea, limbic encephalitis, sensory neuronopathy, sensorimotor neuropathy, optic neuropathy (retinitis, optic neuritis, uveitis), subacute cerebellar degeneration, autonomic neuropathy, GI dysmotility	SCLC, thymoma
Tr(DNER)	Subacute severe ataxia, cerebellar degeneration	Hodgkin lymphoma
Dalmau 2008; Graus, 2004; Ohst, 2018		