

Detection of Amphiphysin IgG Antibodies Associated with Paraneoplastic Neurological Syndromes (PNS)

IMMUNOBLOT ASSAY FOR THE DETECTION OF AMPHIPHYSIN IgG ANTIBODIES

Test Highlight

Amphiphysin-specific assay is available through ARUP.

Disease Overview

- Paraneoplastic syndromes (PNS) are diseases associated with remote effects of tumors, of which small-cell lung cancer (SCLC), ovarian cancer, breast cancer, thymoma, Hodgkin lymphoma, and testicular cancer are the most common.
- Stiff-person syndrome (SPS) is a rare neurological disorder characterized by stiffness of skeletal muscles with superimposed spasms, which can have an idiopathic or paraneoplastic component.
- First described in women with breast cancer and SPS, amphiphysin antibodies have been reported in patients with diverse paraneoplastic neurological disorders, and cancers.
- Amphiphysin antibodies are considered diagnostic for paraneoplastic neurological syndromes and can direct the search for an occult tumor, recurrence of tumor, or second tumor.

Pathophysiology

- Amphiphysin antibodies are directed against a 128 kD antigen found in synaptic vesicles of nerve terminals.
- A pathogenic role of amphiphysin antibodies has been demonstrated by passive IgG transfer and induction of SPS in rats.
- Mechanism of disease induction is unknown.

Indications for Ordering

- Individuals with stiff-person syndrome, paraneoplastic encephalomyelitis (PEM), and sensory neuronopathy (SN).
- Clinical presentation of amphiphysin antibody-positive patients is not uniform.
- Characteristic clinical features and symptoms may be atypical, psychiatric, or fluctuating.

Interpretation

- The presence of amphiphysin antibodies does not necessarily indicate the presence of a tumor. Absence of these antibodies does not rule out PNS.
- Imaging studies, such as computer tomography scan of the thorax, abdomen, pelvis, 18F-fluoro-2-deoxyglucose-positron emission tomography, FDG-PET scan, and magnetic resonance imaging (MRI) of the brain are recommended in the evaluation of patients suspected of having PNS.
- Follow-up testing on a case-by-case basis may be clinically relevant.

Limitations

- Low sensitivity and negative predictive value.
- Recommended only when clinical suspicion for PNS is very high.

Methodology

The assay employs recombinant amphiphysin protein as substrate in a standard immunoblot assay.

References

1. Graus F, Dalmau J. Paraneoplastic neurological syndromes: diagnosis and treatment. *Curr Opin Neurol* 2007;20(6):732-7.
2. Storstein A, Vedeler CA. Paraneoplastic neurological syndromes and onconeural antibodies: clinical and immunological aspects. *Adv Clin Chem* 2007;44:143-85.
3. Graus F, et al. Recommended diagnostic criteria for paraneoplastic neurological syndromes. *J Neurol Neurosurg Psychiatry* 2004;75:1135-40.
4. Sommer C, et al. Paraneoplastic stiff-person syndrome: passive transfer to rats by means of IgG antibodies to amphiphysin. *Lancet* 2005;365:1406-11.

Test Information

0051090

Neuronal Antibodies (Hu, Ri, Yo, Amphiphysin) IgG by Immunoblot

For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.

AUTHOR

Anne Tebo, PhD