USEFUL FOR

Aids in the diagnosis of paraneoplastic neurological autoimmune disorders related to carcinoma of lung, breast, ovary, thymoma, or Hodgkin lymphoma.

CLINICAL INFORMATION

Several antineuronal and glial autoantibodies are recognized clinically as markers of a patient’s immune response to specific cancers (paraneoplastic autoantibodies). Seropositive patients present with neurologic symptoms and signs in >90% of cases. The cancers are most commonly small-cell lung carcinoma, ovarian (or related mullerian) carcinoma, breast carcinoma, thymoma, or Hodgkin lymphoma. The cancers may be new or recurrent, are usually limited in metastatic volume, and are often occult by standard imaging procedures. Detection of the informative marker autoantibodies allows early diagnosis and treatment of the cancer, which may lessen neurological morbidity and improve survival.

Serum is the preferred specimen for paraneoplastic autoantibodies. However, cerebrospinal fluid (CSF) results are sometimes positive when serum results are negative (especially for CRMP-5 and other inflammatory central nervous system autoimmunity). Additionally, CSF is more readily interpretable because it generally lacks the interfering nonorgan-specific antibodies that are common in serum of patients with cancer. Because neurologists typically perform spinal taps in these patients, we recommend that CSF be submitted with serum, either for simultaneous testing or to be held for testing only if serum is negative.

CRMP-5-IgG Western blot is also performed by specific request for more sensitive detection of CRMP-5-IgG. Testing should be requested in cases of subacute basal ganglionic disorders (chorea, Parkinsonism), cranial neuropathies (especially loss of vision, taste, or smell), and myelopathies.

INTERPRETATION

Antibodies directed at onconeural proteins shared by neurons, glia, muscle, and certain cancers are valuable serological markers of a patient’s immune response to cancer. They are not found in healthy subjects, and are usually accompanied by subacute neurological symptoms and signs. Several autoantibodies have a syndromic association, but no autoantibody predicts a specific neurological syndrome. Conversely, a positive autoantibody profile has 80% to 90% predictive value for a specific cancer. It is not uncommon for more than 1 paraneoplastic autoantibody to be detected, each predictive of the same cancer.
REFERENCE VALUES

**Neuronal Nuclear Antibodies**
- Antineuronal Nuclear Antibody-Type 1 (ANNA-1): Negative at <1:2
- Antineuronal Nuclear Antibody-Type 2 (ANNA-2): Negative at <1:2
- Antineuronal Nuclear Antibody-Type 3 (ANNA-3): Negative at <1:2
- Anti-Glial/Neuronal Nuclear Antibody-Type 1 (AGNA-1): Negative at <1:2

**Neuronal and Muscle Cytoplasmic Antibodies**
- Purkinje Cell Cytoplasmic Antibody, Type 1 (PCA-1): Negative at <1:2
- Purkinje Cell Cytoplasmic Antibody, Type 2 (PCA-2): Negative at <1:2
- Purkinje Cell Cytoplasmic Antibody, Type TR (PCA-TR): Negative at <1:2
- Amphiphysin Antibody: Negative at <1:2
- Collapsin Response-Mediator Protein-5 Neuronal (CRMP-5-IGG): Negative at <1:2

**Islet Cell Antibodies**
- Glutamic Acid Decarboxylase (GAD65) Antibody Assay: ≤ 0.02 nmol/L

**Western Blot**
- Paraneoplastic Western Blot: Negative
- CRMP-5-IgG Western Blot: Negative
- Amphiphysin Western Blot: Negative
- N-Methyl-D-aspartate receptor (NMDA-R)
  - CBA: Negative
  - IFA <1:2
- 2-amino-3-(5-methyl-3-oxo-1,2- oxazol-4-yl) propanoic acid receptor (AMPA-R)
  - CBA: Negative
  - IFA <1:2
- Gamma-Amino Butyric acid-type B receptor (GABA-B-R)
  - CBA: Negative
  - IFA <1:2
- NMO/AQP4-IgG: Negative
- VGKC-Complex Antibody IPA: ≤ 0.02 nmol/L