Dementia, Autoimmune Evaluation, Spinal Fluid

Useful For
Investigating new onset dementia or cognitive impairment with one or more of the following:

- Rapid onset and progression
- Fluctuating course
- Psychiatric accompaniments (psychosis, hallucinations)
- Movement disorder (myoclonus, tremor, dyskinesias)
- Headache
- Autoimmune stigmata (personal history or family history or signs of diabetes mellitus, thyroid disorder, vitiligo, poliosis [premature graying], myasthenia gravis, rheumatoid arthritis, systemic lupus erythematosus)
- Smoking history (20+ pack years) or other cancer risk factors.
- History of cancer
- Inflammatory cerebral spinal fluid
- Neuroimaging findings atypical for degenerative etiology

Clinical Information
The rapid identification of subacute cognitive decline as autoimmune dementia facilitates optimum treatment with immunotherapy and an expedited search for a limited stage of cancer in some patients. Traditionally, neurologists have been reluctant to consider a diagnosis of an autoimmune cognitive disorder in the absence of delirium. However, some recent case series and clinical-serologic observations have suggested a growing appreciation for autoimmune neurologic disorders presenting with features of a rapidly progressive dementia rather than delirium. These disorders can affect all age groups.

Unfortunately, these potentially reversible conditions may be misdiagnosed as being progressive neurodegenerative (currently irreversible) disorders, with devastating consequences for the patient. In the evaluation of a patient with cognitive decline, clinicians should consider the possibility of an autoimmune etiology on their list of differential diagnoses. The importance of not overlooking this possibility rests in the experience that these patients have a potentially immunotherapy-responsive, reversible disorder. The development and widespread availability of neural antibody marker testing has changed this perspective so that other presenting symptoms such as personality change, executive dysfunction and psychiatric symptoms are increasingly recognized in an autoimmune context.

Clues that are helpful in identifying patients with an autoimmune dementia can be summarized within a triad of: 1) suspicious clinical features (a subacute onset of symptoms, a rapidly progressive course, and fluctuating symptoms) and radiological findings, 2) the detection of cerebral spinal fluid (CSF) or serological biomarkers of autoimmunity and 3) a response to immunotherapy.

Detection of neural autoantibodies in serum or CSF serves 2 purposes; to inform the physician of a likely autoimmune etiology, and to raise suspicion for a paraneoplastic cause. The neurological associations of neural autoantibodies tend to be diverse and multifocal, although certain syndromic associations may apply. For example, neuronal voltage-gated potassium channel (VGKC) antibodies were initially considered to be specific for autoimmune limbic encephalitis or disorders of peripheral nervous hyperexcitability, but over time other presentations have been reported, including rapidly progressive course of cognitive decline mimicking frontotemporal dementia and Creutzfeldt-Jakob disease.

Since neurological presentations are often multifocal and diverse, comprehensive antibody testing is usually more informative than testing for one or two selected antibodies. Some of the antibodies are highly predictive of...
an unsuspected underlying cancer. For example; small-cell lung carcinoma (antineuronal nuclear antibody-type 1, ANNA-1; collapsin response-mediator protein-5 neuronal, CRMP-5-IgG) ovarian teratoma (N-methyl-D-aspartate receptor, NMDA-R), and thymoma (CRMP-5 IgG).

Also, a profile of seropositivity for multiple autoantibodies may be informative for cancer type. For example, in a patient presenting with a rapidly progressive dementia who has muscle acetylcholine receptor (AChR) binding, alpha 3 ganglionic AChR, and CRMP 5 IgG, the findings should raise a high suspicion for thymoma. If an associated tumor is found, its resection or ablation optimizes the neurological outcome.

Antibody testing on CSF is additionally helpful particularly when serum testing is negative. However, simultaneous testing on serum and CSF is recommended for some (such as NMDA-R antibody testing, since CSF is usually more informative).

**Interpretation**

Antibodies specific for neuronal, glial, or muscle proteins are valuable serological markers of autoimmune epilepsy and of a patient's immune response to cancer. These autoantibodies are not found in healthy subjects, and are usually accompanied by subacute neurological symptoms and signs. It is not uncommon for more than 1 of the following autoantibodies to be detected in patients with autoimmune dementia:

1. Plasma membrane antibodies (N-methyl-D-aspartate (NMDA) receptor; 2-amino-3-(5-methyl-3-oxo-1,2-oxazol-4-yl) propanoic acid (AMPA) receptor; gamma- amino butyric acid (GABA-B) receptor). These autoantibodies are all potential effectors of dysfunction.
2. Neuronal nuclear autoantibody type 1 (ANNA-1) or type 3 (ANNA-3).
3. Neuronal or muscle cytoplasmic antibodies (amphiphysin, Purkinje cell antibody-type 2 [PCA-2], collapsin response-mediator protein-5 neuronal [CRMP-5-IgG], or glutamic acid decarboxylase [GAD65] antibody).

**Cautions**

Negative results do not exclude autoimmune dementia or cancer.

The Dementia Autoimmune Evaluation does not detect Ma1 or Ma2 antibodies (alias: MaTa). Ma2 antibody has been described in patients with brainstem and limbic encephalitis in the context of testicular germ cell neoplasms. Scrotal ultrasound is advisable in men who present with unexplained subacute encephalitis.

**Reference Values**

To review all reference values go to [http://www.mayomedicallaboratories.com](http://www.mayomedicallaboratories.com)

**Analytic Time**

3 days if negative / 5 days if positive

**Clinical References**


For additional interpretation information and clinical references, please visit the following website: [http://www.mayomedicallaboratories.com/test-catalog/Overview/61507](http://www.mayomedicallaboratories.com/test-catalog/Overview/61507)