Anti-NMDA Receptor (NR1) IgG Antibodies

Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is an autoimmune disease caused by antibodies against the brain protein NMDA. Affected individuals display distinctive symptoms, including significant psychiatric disturbances, seizures, confusion, memory loss, and agitation. Women are affected more often than men. Testing is used to confirm a diagnosis of NMDAR encephalitis and to monitor disease progression and treatment response.

For more information, refer to the ARUP Consult N-methyl-D-Aspartate (NMDA)-Type Glutamate Receptor Autoantibody Disorders - Anti-NMDA Receptor Encephalitis topic.

Disease Overview

Incidence
Unknown

Age of Onset
Affects all age groups, with a low prevalence in individuals >50 years.

Symptoms
- Prodromal symptoms similar to a nonspecific viral-like illness:
  - Low-grade fever
  - Headache
- Rapid progression to other neurological symptoms (psychotic and catatonic phases):
  - Autonomic dysfunction (hyperventilation, tachycardia, hypertension, hyperthermia)
  - Cardiac dysrhythmias
  - Delusions, psychoses
  - Dyskinesia, movement disorders
  - Hallucinations
  - Memory loss
  - Paranoia
  - Seizures
  - Unresponsiveness
- Significant portion of patients are nonparaneoplastic:
  - Ovarian teratoma is the most common tumor-related cause.
  - Men, women, and children without tumors have also been diagnosed with anti-NMDAR encephalitis.

Diagnostic Issues
- Neurological symptoms of anti-NMDAR encephalitis are clinically indistinguishable from encephalitis associated with etiologies of:
  - Infection
  - Toxin/metabolic
  - Autoimmune
- Diagnosis is based on the exclusion of other causes.
- Anti-NMDAR IgG antibody detected in serum confirms the diagnosis of anti-NMDAR encephalitis.
  - Abdominal imaging (ultrasound or MRI) should also be performed due to strong association with ovarian neoplasms.
  - Testicular ultrasound should replace abdominal ultrasound in men.

Physiology
- NMDA receptors are ligand-gated cation channels necessary for synaptic transmission.
  - Highly expressed in the forebrain, limbic system, and hypothalamus
- NMDA receptors are composed of two subunits: NR1 and NR2.
Anti-NMDA IgG binds to NMDA receptors (usually NR1):
- Decreases the number of receptors on postsynaptic neuronal dendrites, causing synaptic dysfunction
- Presumed cause of psychotic symptoms characteristic of anti-NMDAR encephalitis

**Typical Testing Strategy**

Initial testing to rule out infectious process may include:

- Complete blood count with platelet count and differential
- Electrolyte panel
- Cerebrospinal fluid (CSF) testing:
  - Protein, glucose, cell count with differential
  - Viral polymerase chain reaction testing:
    - Herpes simplex virus
    - Human herpes virus-6
    - Varicella-zoster virus
    - Enterovirus
  - Oligoclonal band profile
  - Bacterial culture and Gram stain
  - Fungal culture
  - CSF antigen testing
- Computed tomography/magnetic resonance imaging
- Other testing based on symptoms/history (e.g., metabolic disorders, multiple sclerosis)

Consider the following tests based on clinical presentation, age, sex, and/or risk for cancer:

- Autoimmune serologies for:
  - Antinuclear antibodies (ANA)
  - Antineutrophil cytoplasmic antibodies (ANCA)
  - Antiphospholipid syndrome (APS)
  - Thyroiditis
- Autoimmune encephalitis evaluation
- Paraneoplastic antibody evaluation
- N-methyl-D-aspartate receptor antibody, serum or CSF

**Test Interpretation**

**Sensitivity/Specificity**

- Analytical sensitivity: unknown
- Analytical specificity: ~100%

**Results**

- Positive: NMDAR IgG antibody identified in serum strongly supports a diagnosis of anti-NMDAR encephalitis.
- Negative: absence of NMDAR IgG antibody does not rule out a diagnosis of other forms of autoimmune encephalitis.

**Related Information**

Antinuclear Antibody (ANA) With HEp-2 Substrate
N-methyl-D-Aspartate (NMDA)-Type Glutamate Receptor Autoantibody Disorders - Anti-NMDA Receptor Encephalitis

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