

Anti-NMDA Receptor (NR1) IgG Antibodies

FOR DIAGNOSIS OF LIMBIC ENCEPHALITIS

Test Highlights

Anti-NMDA receptor autoantibodies are specific markers for anti-NMDA receptor encephalitis.

Clinical Background

- The N-methyl-D-aspartate receptor (NMDAR) is an ion channel located in the post-synaptic membrane that plays a key role in synaptic transmission and plasticity. The receptor is made up of two subunits, NR1 and NR2, that contain extracellular epitopes. Anti-NMDAR antibodies are directed against the extracellular epitope of the NR1 subunit.
- This test is a cell-based indirect immunofluorescence antibody (IFA) assay for anti-NR1, which is strongly associated with treatment-responsive limbic encephalitis.
- Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is an inflammatory encephalopathic autoimmune disease frequently affecting young women with teratomas of the ovary. It is also observed in men, children, and females without tumors.
- Teratomas of the ovary are usually benign. Also called dermoid cysts, teratomas of the ovary characteristically contain a diversity of tissues such as hair, teeth, bone, thyroid, and neural tissue.
- Prodromal symptoms of anti-NMDAR encephalitis include low-grade fever, headache, and non-specific viral-like illness. Once the disease reaches the psychotic stage, symptoms include:
 - Visual or auditory hallucinations
 - Delusions
 - Severe behavioral and personality changes (memory problems)
 - Paranoid thoughts
 - Unresponsiveness (decreased consciousness)
 - Seizures (epileptic attacks)
 - Dyskinesia, movement disorders
 - Autonomous instability
 - Cardiac dysrhythmias
 - Central hypoventilation
- The symptoms of this form of encephalitis are very similar to those of other conditions; it is therefore difficult to determine the prevalence of this disorder.

Indications for Ordering

This test is indicated for patients with suspected anti-NMDAR encephalitis.

Interpretation

- Diagnosis of anti-NMDAR encephalitis depends on the presence of the characteristic clinical picture, supporting results from brain magnetic resonance imaging (MRI), electroencephalogram (EEG), and cerebrospinal fluid (CSF), and the detection of anti-NMDA receptor antibodies in serum or CSF.

- A positive result showing the presence of anti-NMDAR antibodies in serum is strongly supportive of a diagnosis of anti-NMDAR encephalitis.
- In a positive serological event in a female, a full teratoma investigation should be carried out.
- A negative result indicates the absence of NMDAR encephalitis, but neuropilic coloring of rat hippocampus and cerebellum can also point to the presence of other autoantibodies associated with limbic encephalitis (e.g., anti-VGKC antibodies and anti-AMPA receptor antibodies).
- There is a reduction and possible disappearance of antibody titer with clinical improvement.
- Other forms of limbic encephalitis, vasculitis, and infectious encephalomyelitis need to be included in the differential diagnosis.

Methodology

The presence of anti-NMDAR antibodies in serum is detected by IFA using a human cell line (Hek293) transfected with the NR1 receptor subunit.

Related Tests

In addition to testing serum, an analogous investigation of CSF can also be of great importance, as intrathecal synthesis of anti-NMDAR antibodies is frequent and may only be detected in CSF. Brain MRI and EEG analysis can also support diagnosis if necessary. Other autoantibodies associated with limbic encephalitis, such as Hu and amphiphysin, may also be of additional diagnostic value.

References

1. Dalmau J, et al. Anti-NMDA-receptor encephalitis: case series and analysis of the effects of antibodies. *Lancet Neurol* 2008;7(12):1091–8.
2. Vincent A, Bien CG. Anti-NMDA-receptor encephalitis: a cause of psychiatric, seizure, and movement disorders in young adults. *Lancet Neurol* 2008;7:1074–5.
3. Prüss H, et al. Anti-NMDA-receptor encephalitis. An interdisciplinary clinical picture. *Nervenarzt* 2010;81(4):396, 398, 400.
4. Tüzün E, Dalmau J. Limbic encephalitis and variants: classification, diagnosis and treatment. *Neurologist* 2007;13(5):261–71.

Test Information

2004221 **N-methyl-D-Aspartate Receptor Antibody, IgG**

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.