

Aquaporin-4 Autoantibody Testing

FOR CONFIRMATION AND MONITORING OF AUTOANTIBODIES IN PATIENTS WITH NEUROMYELITIS OPTICA

Clinical Background

Neuromyelitis optica (NMO)-specific IgG immunoglobulin (NMO_IgG) recognizes the water channel protein aquaporin-4 (AQP4). Both designations, NMO_IgG and AQP4, are used to refer to the autoantibody important in the differential diagnosis of NMO from other transverse myelitis diseases.

Disease Overview

- The spectrum of transverse myelitis (TM) disorders includes neuromyelitis optica (NMO), multiple sclerosis (MS), longitudinally extensive spinal cord lesions/transverse myelitis (LESCL/LETM), optic spinal MS (OSMS), acute disseminated encephalomyelitis (ADEM), acute complete TM (ACTM), and acute partial TM (APTM).
- These disorders are differentiated by clinical course (monophasic or relapsing), the presence and extent of lesions evident in the spinal cord and/or brain on magnetic resonance imaging (MRI), the accompanying presence of optic nerve inflammation (optic neuritis), and the presence of aquaporin-4 autoantibodies.
- Definitive differentiation among these diseases is problematic since all present with similar symptoms of pain, visual-field deficits, muscle weakness, and bladder or bowel dysfunction.
- NMO is often mistaken for MS; however, it is particularly important to distinguish between these two diseases since patients with NMO have a worse prognosis and the recommended treatments for these two disorders are different. Treatment of NMO usually consists of immunosuppressive therapy or plasmapheresis, whereas treatment for MS consists of immunomodulation therapy, with corticosteroids being administered only during periods of worsening inflammation.
- Criteria required for diagnosis of NMO includes optic neuritis and acute myelitis, as well as important supportive criteria of negative brain MRI and longitudinally extensive spinal cord lesion extending over three or more vertebral segments with the presence of leukocytosis (50 WBC/mm³ or more) in the CSF.^{1,2}

Epidemiology

- Insufficient data is available regarding the incidence and prevalence of NMO.

- The incidence of acute transverse myelitis is reported to be 1–4:100,000, of which less than 1 percent is represented by NMO.^{1,3}
- Monophasic NMO affects both genders equally; however, a female to male ratio of 5:1 is reported for relapsing NMO.⁴

Indications for Ordering

- Confirmation of neuromyelitis optica diagnosis.
- Assessment and prognosis of disease progression.

Interpretation

The presence of AQP4 antibodies should be used in conjunction with proposed diagnostic criteria for neuromyelitis optica. Positive AQP4 antibody results should not be used as the sole criteria for diagnosis of NMO.

Limitations

- A sensitivity of 71 percent and specificity of 98 percent have been reported for AQP4 antibody detection by enzyme-linked immunosorbant assay (ELISA).⁵
- Sensitivity and specificity for detection of NMO-IgG by indirect fluorescent antibody (IFA) assay have been reported as 73 percent and 91 percent, respectively.⁶
- Relatively poor agreement of 62 percent has been observed between ELISA and IFA detection methods for patients with NMO.⁵

References

1. Wingerchuk DM. Neuromyelitis optica. *Int MS J* 2006;13:42–50.
2. Wingerchuk DM, et al. The clinical course of neuromyelitis optica (Devic's syndrome). *Neurology* 1999;53:1107–14.
3. Pandit L. Transverse myelitis spectrum disorders. *Neurol India* 2009;57:126–33.
4. Jacob A, et al. Neuromyelitis optica: changing concepts. *J Neuroimmunol* 2007;187:126–38.
5. Hayakawa S, et al. Neuromyelitis optica and anti-aquaporin-4 antibodies measured by an enzyme-linked immunosorbant assay. *J Neuroimmunol* 2008;196:181–7.
6. Lennon VA, et al. A serum autoantibody marker of neuromyelitis optica: distinction from multiple sclerosis. *Lancet* 2004;64:2106–12.

Test Information

2003036

Aquaporin-4 Receptor Antibody

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.