NMO (Neuromyelitis Optica) Autoantibody

What is Neuromyelitis Optica?

Neuromyelitis optica (NMO or Devic syndrome) is a rare disease in which the immune system destroys the myelin (fatty material that insulates nerve fibers so that the body and the brain can communicate using electrical messages) in the optic nerve and spinal cord

The age of onset in NMO ranges from childhood to late adulthood with the incidence tapering off after the fifth decade, the median onset age is in the late 30s. In the recurrent disease course (80–90%), women (ratio 5–10:1) are overrepresented

Myelin destruction (demyelination) in these parts of the central nervous system (CNS) causes pain and swelling (inflammation) of the optic nerve (optic neuritis) and spinal cord (myelitis)

The resultant disruption of communication along these nerves means that patients with NMO experience temporary or permanent blindness in one or both eyes that is preceded or followed by limb weakness or paralysis and loss of bladder and bowel control

What is Neuromyelitis Optica?

There is no cure for NMO, but corticosteroids or plasmapheresis reduce inflammation during acute attacks and, because NMO is an autoimmune disease (one in which the immune system attacks the body's own tissues instead of foreign organisms), long-term immunosuppression may prevent further attacks

Early differentiation of NMO from MS and other inflammatory and demyelinating diseases of the CNS—such as vasculitis, paraneoplastic neurological syndromes, or vitamin B12 deficiency—is highly desirable, as treatment options and prognoses differ widely. However, such differentiation may be difficult or even impossible owing to overlap in clinical presentation and cerebrospinal fluid (CSF) and magnetic resonance imaging (MRI) findings

What is the clinical similarity with Multiple Sclerosis?

- There are many inflammatory/demyelinating diseases of the CNS with clinical symptoms similar to those of NMO
- It is particularly hard to distinguish between NMO and multiple sclerosis, an autoimmune disease that involves widespread demyelination
- **Multiple sclerosis** (**MS**), also known as "disseminated sclerosis" or is an inflammatory disease in which the fatty myelin sheaths around the axons of the brain and spinal cord are damaged, leading to demyelination and scarring as well as a broad spectrum of signs and symptoms.
- Disease onset usually occurs in young adults, and it is more common in women

Differentiating NMO and MS

Clinical differentiation

The predominant course of NMO is characterized by recurrent severe attacks of myelitis and/or uni- or bilateral ON with incomplete recovery and is up to 10 times more prevalent in women than in men. Age of onset, the late 30s, is approximately 10 years later than age of onset in MS

Investigations

MRI appearance of spinal cord lesions plays a central role in the diagnosis of NMO (Brain MRI mostly normal in NMO)

The frequency of OCB (in CSF) in NMO ranges from 0% to 37% and are present in over 90% in established MS. CSF findings with a lymphomononuclear pleocytosis>50 cells/ll, occasional presence of neutrophils/eosinophils, and lack of OCB may be indicative of, but not specific for, NMO

AQP4 a transmembrane protein important for CNS function

- Aquaporin 4 is a type III transmembrane protein that regulates water entry into and out of specific cells in the brain
- In humans, expression of AQP4 in the brain, spinal cord, and optic nerves is associated with astrocyte membranes that closely appose endothelial cell basal membranes
- Aquaporin 4 exists as two major isoforms (M1 and M23)
- A recent study evaluated the plasma cell population taken from an early patient with
- NMO at the molecular level and reported that AQP4- specific IgG is synthesized intrathecally at disease onset and contributes directly to CNS pathology

NMO-IgG Diagnostic Utility

- NMO-IgG is highly specific for NMO, differentiating it from MS presenting with Optic Neuritis or myelitis
- NMO-IgG alone

  75% sensitive

  90% specific

  …when trying to differentiate NMO from MS with optic nerve/spinal cord involvement
- Normal brain MRI plus NMO-IgG +ive
  - >94% sensitive
  - >90% specific

  …for clinical diagnosis of NMO

Recommendations for NMO Ab testing

- Testing for NMO-IgG/AQP4 antibodies is an important element in the work-up of NMO and NMO spectrum disorders
- Standard specimen is serum
- It may be helpful to use different detection methods and determine AQP4 antibodies in CSF in highly suspicious AQP4 seronegative NMO and NMO spectrum disorders
- There are different assays, and the ideal detection method remains to be elucidated.

METHOD: IMMUNOFLOUROSCENCE

(IF)

SAMPLE REQUIREMENT: 3ml serum

COST: Rs. 2980

SCHEDULE: Wednesday 9.00 am

COMPLETION: next day 10.00 am

Maternal Screening