Neuromyelitis Optica

What is Neuromyelitis Optica (NMO)?

Neuromyelitis Optica is also called NMO, Devic’s disease or Devic disease. NMO was first described by Eugene Devic, a French neurologist, in 1894. It is often mistaken for multiple sclerosis (MS). Though it resembles MS in some aspects, it differs in several important ways. The cause of the disease and pathology of the disease differ from that of MS. The treatment is also different.

What is the pathology of NMO?

In NMO, there are areas of damage in the central nervous system. These areas of damage affect the spinal cord and the optic nerves the most. The spinal cord tends to be affected along several levels, usually extending for the length of 3 or more levels of the bones in the spine. The optic nerves carry the signal for vision from the eye to the brain. Though these areas are most affected by NMO, other areas of the brain may also be involved. These brain lesions may be large, involving a major portion of the cerebral hemisphere in contrast to MS where the lesions tend to be smaller. Alternatively, they may be clustered around the 3rd or 4th ventricle of the brain and brainstem.

In NMO, the pathology is centered around the blood vessels. This leads to inflammation around the blood vessels, and also necrosis. Necrosis means that the part of the brain served by a particular artery dies because the blood supply is blocked. This differs from MS where the pathology does not involve necrosis but rather consists primarily of inflammation centered around the small veins.

What are the symptoms of NMO?

Like MS, NMO patients have attacks of their disease. During these attacks, damage is done to the nervous system with the symptoms depending on the location of the damage. The number of attacks that a person might have and the severity of these attacks is not predictable. Rarely, patients may slowly worsen over months or years rather than having acute attacks.

Spinal cord symptoms include weakness and numbness below the level of injury to the spinal cord. In addition, there can be altered sensation (paresthesias). This altered sensation could include tingling, pins and needles, burning, coldness, pain or other odd sensations. There is often the feeling of a tight band around the torso at the level of the spinal cord injury. The nerves to the bladder may be affected causing urinary urgency, difficulty starting to void or inability to empty the bladder adequately. If the nerves to the bowels are affected, constipation results. Sexual function may be affected by numbness, erectile dysfunction or decreased lubrication.
Optic nerve involvement results in decreased vision. This may be one eye, but more commonly affects both eyes. There is a decrease in light perception. This differs from MS because NMO patients tend to have more severe vision loss.

Hiccoughs may occur for prolonged periods of time and may be difficult to control. Nausea and vomiting may also occur without other explanation.

Rarely, the endocrine system can be affected through involvement of the hypothalamus at the base of the brain. This could cause a number of symptoms including irregular periods, breast engorgement and milk production, decrease sexual drive or performance, or low thyroid.

If large lesions develop in the brain, then confusion, sleepiness or decreased consciousness could result.

**How is NMO diagnosed?**

Originally, NMO was diagnosed when patients had severe sudden loss of spinal cord function combined with blindness. This severe form of the disease was sometimes fatal, and early reports suggested that as many as 2/3 of patients would die from the disease. In recent years, there has been a recognition that milder forms also exist and in fact that the majority of cases are more mild and have a much better prognosis and much lower change of dying. This change in recognition of the disease has come about because of two factors.

First, it was discovered that many people with NMO have an antibody in their blood directed against a protein named aquaporin-4. This protein is located on astrocytes, which are supporting cells of the brain that are located around blood vessels. The aquaporin-4 serves as a channel to move and regulate water flow from the blood into the brain. The aquaporin-4 tends to be located in the spinal cord, optic nerves and areas of the brain typically affected by NMO. Antibodies against aquaporin-4 are called NMO-IgG. These antibodies are commonly found in patients with classic (severe) NMO. It is now recognized that NMO-IgG is found in patients with less severe disease as well.

The second discovery was that patients with NMO and NMO-IgG tend to have spinal cord lesions that extend along the length of the spinal cord for 3 or more levels. These levels are defined as the distance of one spine bone.

Using these new findings, criteria have now been developed to diagnose NMO.

The diagnosis requires all three of the following major criteria

- Optic Neuritis
- Acute Myelitis \( \geq 3 \) segments during acute episode
- No other explanation
In addition, one of the two minor criteria is required

- Most recent brain MRI normal or not meeting MS criteria
  - Nonspecific T2 lesions
  - Dorsal medulla lesions
  - Hypothalamic/brainstem lesions
  - “Linear” periventricular or corpus callosum not extending into parenchyma of hemisphere
- NMO-IgG positive

**Can the spinal cord MRI be normal?**

It is unusual for the spinal cord MRI to be normal. However, it is important to note that the requirement that the spine MRI be abnormal over 3 or more segments applies to the acute episode of spinal cord dysfunction. This abnormality can shrink over time and be much smaller than 3 segments if a long time has passed since the spinal cord event.

**Can the NMO-IgG be normal?**

If the NMO-IgG is positive, then there is a very high likelihood that the disease is NMO. If the NMO-IgG is negative, then the disease can still be NMO because this test is normal in approximately 30-50% of NMO patients.

**Are other tests abnormal?**

Blood tests for lupus (ANA) are positive in 40-45% of patients with NMO. Blood tests for Sjogren’s syndrome (SSA/SSB) are positive in 15-20% of patients with NMO. Spinal fluid may show elevated white blood cells in up to 79% of cases. About 1/3 have white blood counts above 50/mm$^3$ in the spinal fluid. Oligoclonal bands, which are frequently positive in the spinal fluid of patients with MS, is occasionally positive in patients with NMO.

**How are acute attacks of NMO treated?**

Acute attacks of NMO are treated with corticosteroids. The most commonly used steroid is methylprednisolone. If this fails and the symptoms are severe enough to warrant it, then plasma exchange can be used to treat acute attacks.

**What treatment is used to prevent recurrence of NMO?**

Without treatment to prevent attacks, virtually all NMO patients will have future attacks. Medications are generally recommended for life to prevent these future attacks.
The medications used for MS do not work well for NMO. NMO responds best to immunosuppressants. The most common treatment used for first line treatment is azathioprine (Imuran). If this fails, a number of other immunosuppressants have been used including mycophenolate (CellCept), rituximab (Rituxan), mitoxantrone (Novantrone), cyclophosphamide (Cytoxan), intravenous immunoglobulin (IVIG) or bone marrow transplant (stem cell transplant).

**Treating the symptoms of NMO**

The symptoms of NMO are treated the same as the symptoms of other demyelinating disease. These are covered on the pages devoted to symptom management.

**NMO Spectrum Disorders**

There are several disorders that may represent partial forms of NMO.

**Longitudinally Extensive Transverse Myelitis** includes the spinal cord changes of NMO, but no other parts of the disease. The rate of recurrence of this form of transverse myelitis is extremely high. It is treated the same as NMO.

**Chronic Relapsing Inflammatory Optic Neuropathy** includes the optic nerve changes of NMO, but no other parts of the disease. Many of these patients have recurrent inflammation and these require immunosuppressive treatments.

**NMO associated with autoimmune disease** includes NMO is the presence of other autoimmune diseases such as lupus or Sjogren’s syndrome. These generally require treatment of the underlying autoimmune disease first.

**Optico-spinal MS** is actually a form of MS rather than NMO. The spinal lesions tend to be less than 3 segments in length. The optic nerve involvement is usually not as severe as seen in NMO. This is treated like MS.