# NEWS IN NEUROMYELITIS OPTICA

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***Abstract:*** *Neuromyelitis optica (NMO) also known as Devic's disease or Devic's syndrome is an autoimmune disorder, in which the immune system of the body mistakenly attacks and destroys myelin cells in the optic nerves and the spinal cord. The damage of the optic nerve produces swelling and inflammation that cause ocular pain and inflammation bringing about pain and loss of vision. The damage of the spinal cord causes weakness or paralysis in the legs, loss of sensation, and problems with bladder and bowel function. In the past, NMO was considered to be a severe variant of multiple sclerosis. The recent discovery of an antibody in the blood of the individuals with NMO gives us a reliable biomarker to distinguish between them. There is no cure for NMO, but there are therapies to treat an attack, to reduce symptoms, and to prevent relapses.*

The first report of an association between myelitis and optic nerve damage was done by Sir Thomas Clifford Allbut in 1870. 24 years later, in 1894, Eugene Devic described 16 patients who had loss of vision in one or both eyes and who, within a few weeks, developed cerebral palsy. In 1984, Professor Gheorghe Benga from Cluj-Napoca first discovered the protein, which later was called aquaporin ("protein-water"). Much later, in 1992, Agre et al., as well, have studied this protein, for which they were given unfairly in our opinion, the Nobel Prize in 2004.

**Epidemiology**

The disease occurs sporadically. The age of onset is around 40 years old, but the disease can occur from childhood to old age. It seems that in children, the most common form is the NMO-IgG seronegative It appears quite rare, the frequency of occurrence representing less than 1% of all demyelinating diseases. Women account for over two thirds of the patients. The disease is more common in Asians than in Caucasians.(11)

**Physiopatology**

NMO is considered an autoimmune disease, in which the body's immune system produces antibodies (NMO-IgG) which act against the protein aquaporin 4, localized in the astrocytic cell membrane. Aquaporin 4 represents the waterborne channel and is located preferentially in the optic nerve and spinal cord. Blood-brain barrier is impaired, but until now, it is not known the manner in which demyelisation occurs, the NMO-IgG immune response.(3,4,7,8)

**Clinical picture**

The disease usually starts suddenly and rapidly evolving, producing a deficit of sight in one or both eyes. After a period of some days or weeks, a motor deficit of paraparesis / plegia type appears progressively.

There are described two main types of NMO:

- NMO that occurs in flares and relapses that succeed each other over a period of several years. Sometimes, the patient does not recover fully after flares, and the optic nerve damage and / or spinal cord becomes permanent, causing disability. This type of NMO is more common in women than in men,
- Monophasic NMO in which there is a single attack that takes place over a period of days or weeks, after which flares no longer appear in the evolution of the disease. This form of MNO affects both genders equally.

The clinical symptomatology of the NMO consists of:

a. Signs and symptoms of optic neuritis:
- loss or blurring of vision in one or both eyes, usually temporary,
- disorders of the visual field: central scotoma or paracentral, quadrantanopia, hemianopia;
- pain in the eyeball, which generally worsens through its mobilization. The pain intensifies gradually for about a week, then it disappears after a few days,
- impairment of colour vision.

b. Signs and symptoms of transverse myelitis:
- back pain and neck region,
- superficial and deep sensitivity disorders, motor deficit evolving from paraparesis / plegia to tetraparesis / plegia,
- incontinence of urine and / or feces.

c. Other signs, rarer, are represented by nausea, vomiting and incoercible hiccups.(6)

Diagnostic criteria have been proposed in 2006 by Wingerchuk and include:

a. Absolute criteria:
- Optic neuritis,
- Acute myelitis

b. Secondary criteria:
- NMO-IgG seropositive test,
- Brain Magnetic Resonance Imaging (MRI) that does not meet the criteria for multiple sclerosis,
- MRI at bone marrow level with an abnormal signal in T2, that expands into three or more spinal segments.

For the diagnosis of NMO, two absolute criteria and at least two of the three secondary criteria are required:(12)

**Paraclinical examinations:**

- ophthalmoscopic examination reveals an early papilledema with rare hemorrhages and exudates. In chronic forms, a pallor of the disc or even optic atrophy can be noticed.
- the examination of the cerebrospinal fluid (CSF) is most

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frequently abnormal with a slight increase of proteinorahia and pleocytosis (up to 3 000 cells / cc),
- highlighting NMO-IgG antibodies present in blood or CSF in approximately 70% of the patients with NMO,
- the spinal cord MRI revealed increased signal intensity on T2 images, as well as after the administration of gadolinium. The optic nerves can also capture gadolinium in T1 sequence. MRI brain is most often normal or with nonspecific changes.(5)

**Differential diagnosis**

It is made primarily with multiple sclerosis, taking into account that NMO was long time considered as a particular form of this disease. In NMO, symptoms are generally more severe after the first flare, the highlight of NMO-IgG antibodies, Magnetic Resonance Imaging (MRI) changes are the main elements which distinguish the two disorders.

**Prognosis**

Most patients with NMO have an unpredictable evolution, flares and remissions are succeeding for months or years. The disease is cumulative, each new flare affecting new myelin areas. Some individuals may be severe damaged, may lose vision in both eyes and severe deficits of para/or tetraparesis or plegia. In some severe cases, impaired muscle strength can cause some difficulties in breathing and may even require artificial respiration. Deaths occur most commonly by respiratory complications due to myelitis flares.

**Treatment**

There is no curative treatment for NMO, but there are some drugs that are used to relieve symptoms, to prevent the frequency and the intensity of flares.

Flares treatment is done according to the scheme used in multiple sclerosis with i.v. methylprednisolone 1 g/day for 3-5 days followed by the oral administration of 1 mg/kg body weight for 10 days. If flares progress or do not respond to corticosteroid therapy, plasmapheresis or gamma globulin i.v (9) can be used.

Disease-modifying treatment is to prevent the occurrence of the disease flares and to slow the evolution of the disease. The treatment consists of immunosuppressive therapy: azathioprine, methotrexate and mycophenolate. Other drugs which may be used are considered to be of second line, rituximab (monoclonal antibody), mitoxantrone, cyclophosphamide, glatiramer acetate.(2,10)

Symptomatic treatment:
- neuropathic pain: amitriptyline, gabapentin, pregabalin, carbamazepine,
- nociceptive pain: paracetamol, ibuprofen,
- painful tonic spasms: carbamazepine,
- increasing muscle tone in the lower limbs: baclofen, tizanidine, gabapentin,
- urinary incontinence: oxybutynin, tolterodine, personal catheterization.

Recovery treatment includes massage, active and passive kinesiotherapy, medical physical culture, balneophysiotherapy.

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