

DEVIC'S NEUROMYELITIS OPTICA (NMO) IS A SEPARATE ENTITY FROM MS AND SHOULD BE TREATED BY PLASMAPHERESIS (PRO)

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Neuromyelitis optica (NMO) is an inflammatory demyelinating disease, as is MS¹. It has a monophasic form, which constitutes a minority of cases, and the relationship of this subtype to its vastly more common relapsing form remains uncertain^{2, 3}. It is characterized primarily by optic neuritis and transverse myelitis, both of which are symptoms that can occur in MS. However, it is clinically, radiologically, and pathologically distinct from MS⁴. The relapsing form of NMO predominates in women (80-90% of cases), and typically begins in late-middle age, although there is a childhood-onset form that may have some unique features⁵. Attacks are generally more severe than in MS, and accompanied by long lesions in spinal cord and optic nerve. Although the brain was previously thought to be spared, it is now well accepted that brain lesions occur, and often are distinct from those seen in MS⁶. Characteristic syndromes associated with brain involvement include intractable vomiting or hiccoughs⁷ associated with lesions in the dorsal medulla and encephalopathy associated with hypothalamic or brainstem/corpus callosum lesions, which are rarely seen in MS. Brain involvement is particularly prominent in children with NMO⁵. Pathologically, features that distinguish NMO from MS include prominent eosinophil/neutrophil infiltrate, prominent necrosis and cavitation in the cord, prominent perivascular deposition of immunoglobulin and activated complement components accompanied by hyalinization of blood vessels⁸.

A serum autoantibody directed to aquaporin-4, when detected (in approximately 70% of patients with this condition in contemporary series that use appropriately stringent clinical criteria), is able to distinguish NMO from MS and other conditions with which it might be confused⁹. When contemporary diagnostic criteria that incorporate clinical, radiological and serological studies are applied, MS can be distinguished from NMO in 90% of cases¹⁰. The presence of aquaporin-4 specific autoantibodies predicts conversion to NMO and not MS in patients with incomplete forms of the disease, such as transverse myelitis or optic neuritis^{11, 12}. Although passive transfer of this disease with immunoglobulin has not yet been successfully reported, a number of compelling pieces of evidence argue for the pathogenicity of the autoantibody, including the absence of AQP4 immunostaining in lesions of NMO despite the preservation of other markers of astrocytes which are the cells that express AQP4¹³.

The distinction between NMO and MS is more than academic as immunomodulatory treatments for MS are ineffective for NMO as documented by extensive clinical experience and published case series¹⁴. Treatment choices in NMO are limited by a lack of randomized controlled clinical trials. However, treatment of acute attacks of NMO is informed by a randomized, sham-controlled clinical trial that convincingly established the benefits of plasmapheresis when corticosteroids fail¹⁵. This observation has been supported by other uncontrolled clinical series that document benefit in approximately half of NMO patients treated with plasmapheresis^{16, 17}.

Effective long term treatment with a variety of immunosuppressive agents (typically azathioprine, mycophenolate mofetil and more recently, rituximab) is often accompanied by decrease in titer or elimination of detectable autoantibody to aquaporin-4^{18, 19}, which lends support to the hypothesis that antibodies to aquaporin-4 are pathogenic.

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