Prognosis

MS is highly variable. It is occasionally "benign" in which case the disease has little impact on quality of life. It can also be severe with considerable disability or early death. Most patients fall in between these extremes. Poor prognostic indicators at onset of MS include primary progressive course, male gender, frequent attacks, prominent motor or cerebellar findings, and high initial MRI lesion burden. Expected lifespan of people with MS is reduced overall by 7 to 14 years. Suicide rate is 1.7 to 7.5 times that of the general population. Albeit controversial, the use of disease modifying therapies (BIFNs and GA) likely improves not only relapse rate but long-term disability and even mortality. In one non-randomized study, early initiation of disease modifying therapies within a year of symptom onset was associated with better long-term outcomes.

NEUROMYELITIS OPTICA (DEVIC'S DISEASE)

Definition/Epidemiology

Neuromyelitis optica (NMO), also called Devic's Disease, is an inflammatory CNS disorder causing both demyelination and necrosis. NMO can be monophasic, but is more often characterized by attacks of optic neuritis and longitudinally extensive TM that are not necessarily concurrent. NMO was once believed to be a subtype of MS, but now is known to be a different disorder associated in most cases with autoantibodies to the aquaporin 4 (AQP4) water channels, which are strongly expressed by astrocytes. Histopathological changes in NMO are mostly in the spinal cord and optic nerve; the brain is less involved. AQP4 is expressed outside of the CNS in the kidney, stomach, and other tissues, but curiously no pathology has been recognized in the non-CNS organs expressing AQP4.

NMO is much less common than MS, with estimates by the Guthy-Jackson Charitable Foundation of 4,000 patients in the United States, and a half million worldwide. It is even more female-preponderant than MS, with female to male ratio estimated from 4 : 1 to 8 : 1. Children and adults both develop NMO. Unlike MS, NMO is *not* associated with HLA-DRB1*15:01, and it affects those of Asian, African, and Hispanic ancestry disproportionately.

Clinical Presentation

NMO presents clinically as an acute attack of optic neuritis and/or TM; it often takes a relapsing course. Gradually progressive NMO has not been described (helping to distinguish it from progressive MS). Other autoimmune diseases often occur together with NMO including Sjögren's syndrome, systemic lupus erythematosis, Hashimoto's disease, and myasthenia gravis.

Diagnosis/Differential

In 2004, researchers first reported the presence of a serum IgG autoantibody to cerebral vessels in NMO; this was later found to target aquaporin 4. NMO-IgG/ AQP4-IgG is highly specific (>90%) and relatively sensitive (~75%) for NMO. Fulfilling two out of three of the following criteria is reported to be 99% sensitive and 90% specific for NMO in the setting of optic neuritis and TM: (1) longitudinally extensive spinal cord lesion, which is greater than or equal to 3 segments in length (Figure 120-3); (2) NMO-IgG positivity; and (3) brain MRI not typical or diagnostic for MS. NMO-IgG seropositive patients with isolated optic neuritis or longitudinally extensive TM are currently described as having "NMO spectrum disorder."

For a deeper discussion of these topics, please see Chapter 411, "Multiple Sclerosis and Demyelinating Conditions of the Central Nervous System," in Goldman-Cecil Medicine, *25th Edition.*

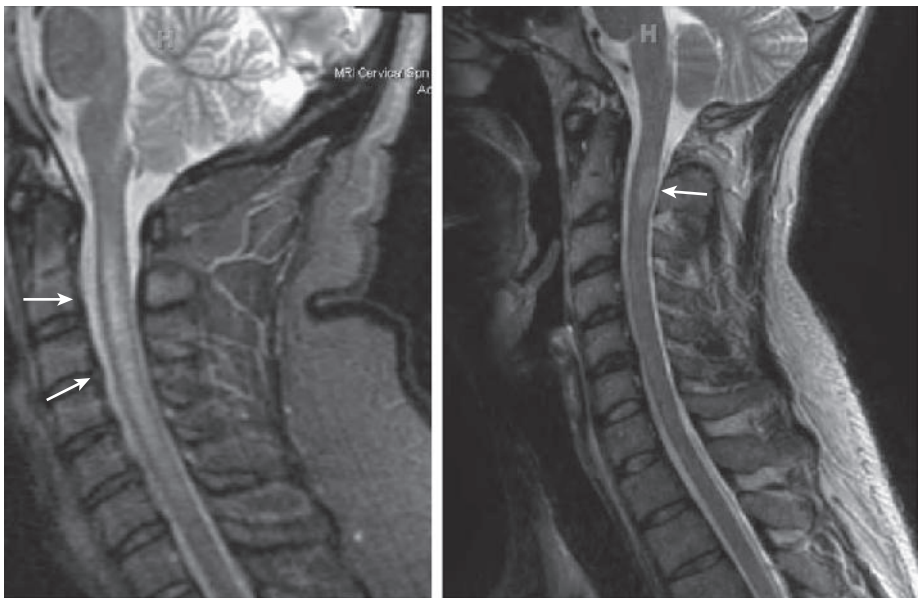

FIGURE 120-3 **A,** Sagittal T2w image of the upper spinal cord in a 37-year-old female with NMO. She developed quadriparesis over several days, and was AQP4-IgG seropositive. Two years later she had right eye optic neuritis, which left her with visual acuity of only 20/200. The spinal cord lesion *(arrows)* had mild mass effect and was contiguous over 6 vertebral segments. **B,** Sagittal T2w image of the upper spinal cord in a 24-year-old male with MS shows a lesion *(arrow)* in the posterior cord at C2. This patient had moderate vibration loss in the legs but was otherwise asymptomatic.