Atypical Fulminant Seronegative Neuromyelitis Optica in a Post-renal Transplant Patient

Anteneh M. Feyissa, MD, MSc, Rahul Shah, MD, Elena Shanina, MD, Robert G. Smith, MD, PhD
Department of Neurology, The University of Texas Medical Branch, Galveston, Texas, USA

Introduction
Neuromyelitis Optica (NMO) has generated significant interest in recent years as a severely disabling antibody-mediated autoimmune disease of the central nervous system (CNS). It preferentially targets optic nerves and the spinal cord, and in many cases is associated with autoantibodies to aquaporin-4 (AQP4 Ab) water channels. Few case reports have highlighted NMO involving the entire cerebrospinal cord. Moreover, until recently NMO has been thought to exclusively affect the CNS, sparing the peripheral nervous system (PNS). Here in, we report a renal transplant patient who developed severe, rapidly progressive AQP4 Ab negative, clinically definite NMO, resulting in quadriparesis and blindness. In our patient, neurophysiologic studies were suggestive of concomitant involvement of the PNS in the context of NMO.

Case report
A 51 year old Hispanic female, status post renal transplant one year ago, on tapering dose of tacrolimus, with post transplant course complicated by cytomegalovirus infection, presented with sudden onset lower extremity numbness. Presenting symptoms progressed to complete paraplegia and sensory loss over 24 hours. The following day, she developed weakness and numbness in bilateral upper extremities, T3-T4 sensory level, and complete vision loss. MRI at presentation revealed prechiasmatic optic nerve enhancement and deep white matter lesions that met multiple sclerosis imaging criteria. Cerebrospinal fluid analysis documented elevated protein with neutrophilic pleocytosis. Nerve conduction studies (NCS) showed severe reduction in compound motor action potential amplitudes (CMAP), most pronounced in lower extremities (Figure 3-A,B). Slowing motor conduction velocities and slowing of distal latencies and F- wave latencies were also seen. Needle examination (EMG) showed active denervation without reinnervation in sciatic/peroneal nerve innervated muscles. Serum AQP4 Ab was negative. At presentation, high dose intravenous (IV) methylprednisolone closely followed by five sessions of plasmapheresis (PLEX) were administered. Subsequently, weekly cycles of IV rituximab therapy (X4) were given. Despite the resolution of spinal cord lesions could suggest concomitant involvement of PNS. Maintenance of NMO case is possible. In our patient, the persistence of sensory and motor symptoms despite the resolution of spinal cord lesions could suggest concomitant involvement of PNS at disease onset. Moreover, NCS/EMG demonstrating a reduction in CMAP and acute denervation with no signs of myopathy whereas MRI showing grey matter involvement suggests an involvement of the second motor neuron (PNS) in the context of NMO. To our knowledge only three cases of seropositive NMO with neurophysiologically documented lower motor neuron involvement have been described. In our patient, the persistence of sensory and motor symptoms despite the resolution of spinal cord lesions could suggest concomitant involvement of PNS at disease onset. Moreover, NCS/EMG demonstrating a reduction in CMAP and acute denervation with no signs of myopathy whereas MRI showing grey matter involvement suggests an involvement of the second motor neuron (PNS) in the context of NMO.

Results
Recently Wingerchuk et al. has proposed revised diagnostic criteria for NMO. Our case described here meet the new criteria, although she lacked AQP4 Ab. AQP4 antibodies are undetectable in ~40% of patients with the disease and AQP4 Ab seronegativity does not necessarily preclude a diagnosis of NMO. Interestingly, recent studies show that AQP4 Ab positive NMO differs clinically and epidemiologically from seronegative disease: strong predominance in women, more severe clinical attacks, higher spinal cord lesion load, and frequent association with coexisting autoimmunity.

Conclusions
NMO has been previously described as an inflammatory condition restricted to the CNS with no documentation of PNS involvement. In addition to lesions in the CNS, in our patient, NCS/EMG studies are suggestive of concomitant involvement of the PNS. To our knowledge only three cases of seropositive NMO with neurophysiologically documented lower motor neuron involvement have been described. In our patient, the persistence of sensory and motor symptoms despite the resolution of spinal cord lesions could suggest concomitant involvement of PNS at disease onset. Moreover, NCS/EMG demonstrating a reduction in CMAP and acute denervation with no signs of myopathy whereas MRI showing grey matter involvement suggests an involvement of the second motor neuron (PNS) in the context of NMO. On a pathophysiological level, it has been hypothesized that involvement of the PNS may be due to reduced local blood flow in consequence of severe inflammation, hypoxia, local blood–brain barrier break down and tissue swelling.

Immunosuppressive agents such as azathioprine, rituximab, cyclophosphamide, and mycophenolate are the mainstay of NMO maintenance treatment. In our patient maintenance therapy with rituximab significantly improved neurologic deficits, radiologic disease burden as well as nerve conduction parameters.

References