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NEUROMYELITIS OPTICA PHENOTYPE ASSOCIATED WITH THERAPY-RESPONSIVE ACUTE PERIPHERAL NEUROPATHY

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Case report. A 51-year-old Hispanic woman with a history of Churg-Strauss syndrome (in remission for 20 years)—associated mesangial glomerulonephritis and end-stage renal disease with a recent renal transplant and previously cured cytomegalovirus (CMV) infection who was on a tapering dose of tacrolimus presented with sudden onset of lower extremity numbness. Symptoms progressed to complete paraplegia and sensory loss over 24 hours. The following day, ascending paresis extended to bilateral upper extremities, with high thoracic sensory level and complete blindness. Initial MRI revealed contrast enhancement of bilateral prechiasmatic optic nerve as well as T2 hyperintensities involving the central gray matter of the entire spinal cord with associated edema. CSF analysis documented neutrophilic pleocytosis (182 neutrophils per mm³) and increased total protein level (142 mg/dL) without oligoclonal banding. Bacterial, fungal, and mycobacterial cultures from the CSF were negative, as was PCR for CMV, Epstein-Barr virus, herpes simplex virus, human herpesvirus 6, and varicella-zoster virus. Serologic autoimmune assessment, including onconeural, anti-neutrophil cytoplasmic antibody, and other rheumatologic, Lyme, and aquaporin-4 (AQP4) antibody testing, was negative. Moreover, testing for sarcoidosis and HIV antibody was unrevealing. Nerve conduction studies (NCS) performed 2 weeks after symptom onset documented severe reduction in compound motor action potential amplitudes (worse in the lower extremities), <10% slowing of distal latencies but not conduction velocities, and mildly slowed upper extremity f-wave latencies. Sensory nerve action potentials were pathologically reduced in the lower extremities (table). Needle examination (EMG) showed active, severe denervation changes in lower extremity muscles and less severe changes in upper extremity muscles. Subsequent GM1, GM2, GD1a, GD1b, and GQ1b ganglioside antibody testing was negative. The patient was diagnosed with concurrent clinically definite neuromyelitis optica (NMO) phenotype¹ and acute axonal polyradiculoneuropathy with primarily axonal features.

The patient was treated initially with methylprednisolone followed by 5 cycles of plasma exchange, with minimal improvement in upper extremity muscle strength and sensation despite repeat MRI showing partial resolution of the previously seen lesions. Subsequently she received 4 weekly cycles of IV rituximab therapy. Follow-up at 7 and 14 months demonstrated normal strength in her upper extremities with decreased reflexes, and she was able to walk with use of a walker. Moreover, the patient regained complete right eye vision with improved left eye vision (20/400), clinically consistent with a monophasic process. Repeat NCS/EMG at 7 months revealed improvement, and at 14 months NCS were normal and EMG was significantly improved (table). Repeat AQP4 antibody testing was negative at 7 months posttreatment.

Discussion. Until recently, NMO was believed to be confined to the optic nerves and spinal cord, with no involvement of the peripheral nervous system (PNS). Routine EMG/NCS are not commonly indicated for patients with NMO, so the prevalence of PNS damage coexisting with this disorder is unknown. There have been 5 case reports of seropositive NMO with possible involvement of the PNS,²⁻⁴ speculated to result from AQP4 antibody-mediated astrocyte dysfunction or complement activation associated with peripheral AQP4 antibody targets.⁵ However, to the best of our knowledge, this association has not been described in the setting of seronegative NMO phenotype disease.

Recent studies have shown that some AQP4 antibody-seronegative patients have antibodies against myelin oligodendrocyte glycoprotein (MOG) and other proteins.⁶ Conceivably, although MOG is localized to the CNS, other targeted complement-activating antibodies might damage the PNS similarly to the mechanism hypothesized for AQP4 antibodies.^{1,6} Moreover, fulminant NMO spectrum disorders (NMOSDs) are characterized by the presence of severe inflammation, evidenced by neutrophilic pleocytosis and elevated protein in the CSF.⁷ Reduced local blood flow, hypoxia, and the blood-brain barrier destruction from severe inflammation may partly explain the involvement of the peripheral nerves. Coexistence of multiple autoimmune diseases with NMOSDs has been recently recognized.⁷ Similar to other immune-mediated diseases,

Table Compound motor and sensory nerve action potential amplitudes before and after immunomodulating therapies			
Site	Normal values	Pretreatment	Posttreatment
Left ulnar anti sensory (wrist)	>20 μ V	13.8 μ V	22.5 μ V
Right sural anti sensory	>6 μ V	0 μ V	4.6 μ V
Left ulnar motor (wrist)	>6 mV	2.6 mV	6.9 mV
Left median motor (wrist)	>6 mV	3.2 mV	8.1 mV
Right peroneal motor (ankle)	>2 mV	0.1 mV	2.5 mV
Right tibial motor (ankle)	>4 mV	0.1 mV	3.6 mV

We have included representative nerves that were highly affected by the disease and have shown robust improvement with treatment.

NMO may be a manifestation of a genetic predisposition to multiple autoimmune conditions.⁷ Immune reconstitution in the face of acute viral syndromes, medications, or other causes for immune activation has also been well-described in patients with HIV, as well as in transplant patients following tapering of immunomodulation. It is unknown whether simultaneous onset of the peripheral and CNS involvement in our patient results from an identical antigen targeting 2 different parts of the neuraxis. Lastly, peripheral B cell-mediated antibody activation of the complement system, inflammatory neuronal damage, and necrosis in NMOSDs may benefit from treatment agents like plasmapheresis and rituximab. It is possible that a common mechanism, likely autoimmune in nature, caused the concurrent damage to the central and peripheral neural elements seen in our patient.

This report highlights the association of NMOSDs with peripheral neuropathies and polyradiculopathies. It is essential that clinicians are aware of this unusual association and obtain NCS/EMG whenever there is a clinical suspicion for concomitant involvement of peripheral nerves with NMOSD.

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