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Neuromyelitis Optica Spectrum Disorder: An Atypical Case of Rituximab-resistant Thoracoabdominal Paresthesia in Aquaporin-4 Seropositivity

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Introduction and Background

Neuromyelitis Optica Spectrum Disorder (NMOSD) represents a collection of immune-mediated inflammatory conditions of the central nervous system that result in demyelination and axonal damage of gray matter, most commonly the optic nerves and spinal cord. A key mediator of this autoimmune destruction is the aquaporin-4 autoantibody (AQP4-IgG) which facilitates the typical pathology of astrocytic damage via complement fixation and membrane attack complex (MAC) formation. AQP4 is the dominant water channel of the central nervous system which regulates fluid and electrolyte shifts, and it is found densely in areas including the hypothalamus, optic nerves, cerebral white matter, periaqueductal brainstem, cerebellum, and spinal cord.[1] Another crucial component of the pathogenesis is interleukin-6 (IL-6) which promotes the differentiation of B-lymphocytes into AQP4-IgG secreting plasmablasts. Limited epidemiologic studies demonstrate female gender predominance with onset of disease commonly in the 4th decade of life. In addition to optic neuritis and transverse myelitis, NMOSD may also present as brainstem syndromes including intractable nausea, vomiting, hiccupping, neurogenic respiratory failure, and possible death. Treatment focuses on managing exacerbations with intravenous (IV) corticosteroids and plasmapheresis, and preventing future relapses with immunosuppressant therapy.[2] Rehab medicine also serves to improve quality of life through neurorehabilitative therapy.[3]

Case Description

Here, our patient is a 49-year old, Afro-American female with past medical history of recently diagnosed AQP4-IgG positive NMOSD, vitamin D deficiency, and hypogammaglobulinemia (due to rituximab) who presented to acute care hospital with lower extremity (LE) weakness, gait difficulty, and paresthesia from mid-thorax through bilateral LEs. Exam findings were pertinent for decreased strength in the L2-L3-L4 myotomes, brisk LE reflexes, impaired sensation to light touch and pinprick in the LEs, dysmetria on heel-to-shin, and spastic gait due to foot drop. Initial diagnosis was acute C7-T8 transverse myelitis based on neuroimaging (Figure 1). Serum AQP4-IgG titer was elevated, confirming diagnosis of an acute NMOSD relapse despite active treatment with rituximab infusions. Medical management entailed 5-day course of IV methylprednisolone followed by 5 sessions of plasma exchange. Physiatry was consulted and evaluated patient as appropriate for acute inpatient rehabilitation. Over the course of acute rehab, she progressed well with mobility, transfers, strength, and activities of daily living to modified independence. However, she continued to be limited by impaired sensation, balance difficulty, and altered body mechanics. After discharge, she re-consulted with her neuroimmunologist who recommended to consider initiating a novel FDA-approved immunosuppressant, and she transitioned to satralizumab.

Case Description (continued)

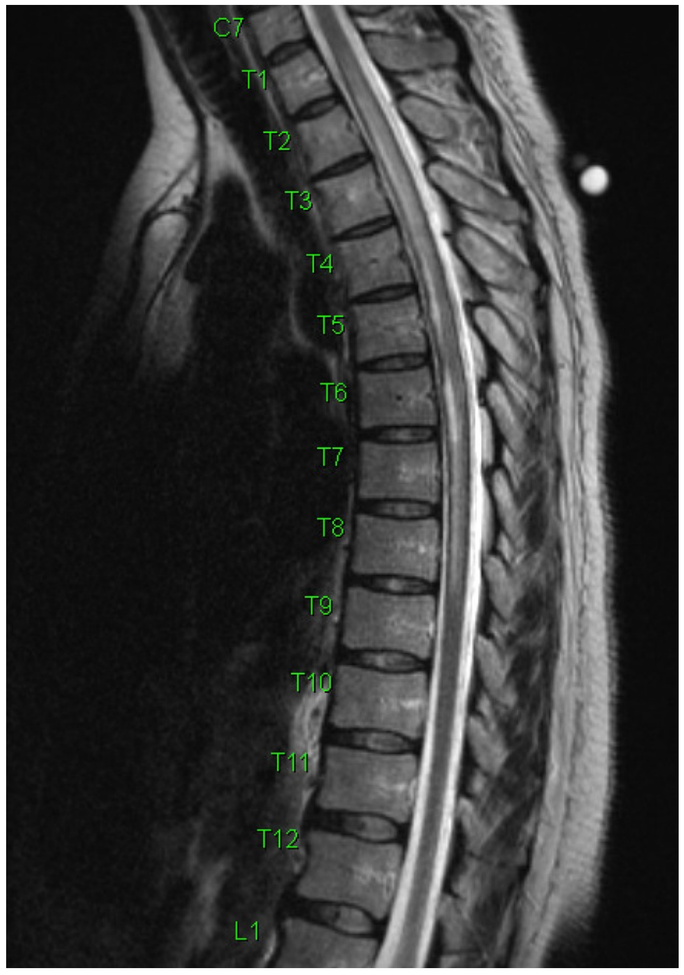

Figure 1: MRI Thoracic Spine Sagittal T2 – Findings include expansile cord signal abnormality extending from C7-T1 to proximal T8 levels with central cord enhancement extending from T3-T4 through T6-T8 levels which are compatible with active demyelination.

Discussion and Conclusion

Discussion: NMOSD varies greatly in presentation, clinical course, and intervention. Disability in NMOSD is usually more severe than multiple sclerosis, so prompt diagnosis is important in order to start the appropriate treatment as soon as possible.[1] AQP4-IgG seropositivity is particularly predictive of a relapsing course, and AQP4-IgG titers have been shown to correlate with length of longitudinally extensive spinal cord lesions. Treatment for NMOSD is multifaceted including medical, neurologic, physiatric, and rehabilitative models. Most patients with severe myelitis go through rehab and return to the community, and they benefit from the effects of medical rehabilitation on their recovery.[1] Rituximab, an anti-CD20 monoclonal antibody, has been used as prophylactic first-line immunotherapy as it can reduce the severity of disease recurrence.[4] However, in refractory cases as in this case study, there are now several newly FDA-approved immunosuppressants to consider including inebilizumab, tocilizumab, and satralizumab. Inebilizumab is an anti-CD19 monoclonal antibody so it functions similarly as rituximab and shown to reduce exacerbations by 27%, whereas tocilizumab and satralizumab are IL-6 receptor antagonists which reduced exacerbations by 23%.[4],[5]

Conclusion: A key prognostic factor for disability and mortality in NMOSD is accumulation of deficits from each exacerbation that result in stepwise deterioration. This case study reflects upon the significance of timely diagnosis and personalized treatment that includes effective long-term pharmacotherapy and rehabilitative medicine in order to effectively manage this patient population.

References

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