An expanding transverse myelitis leading to the diagnosis of AQP4-IgG positive Neuromyelitis Spectrum Disorder: A case report

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INTRODUCTION

Neuromyelitis Optica Spectrum Disorder (NMOSD) is an inflammatory neurologic disease characterized by immune-mediated demyelination and axonal damage, primarily affecting the central nervous system and optic nerves. The majority of cases of NMOSD are due to serum IgG autoantibody to aquaporin 4 (AQP4-IgG), which binds to astrocytes and activates the classical complement cascade. This initially injures astrocytes, then progresses into damaging oligodendrocytes causing demyelination and neuronal loss. Disease prevalence is .37 to 10 per 100,000 with females' incidence being up to 10 times higher than males[4]. Acute attacks of optic neuritis or transverse myelitis occurring over days with a relapsing course are highly characteristic of the disease[4]. Here we describe a case of NMOSD in a 56-year-old female who presented to the Emergency Department after a fall.

CASE PRESENTATION

A 56-year old female with a past medical history of seizures and obesity presented to the emergency department due to progressive worsening lower extremity numbness and weakness for one month. She also had difficulty ambulating secondary to weakness and one week of left hand weakness with decreased grip strength. Physical exam was remarkable for 4/5 left hand grip, 5/5 lower extremities, diminished sensation in bilateral lower extremities, lower back and abdomen. Initial workup included CBC and CMP, which were unremarkable.

CLINICAL COURSE

- MRI lumbar spine was unremarkable. MRI C-spine showed expansile intramedullary cord abnormality extending from C3 to at least the level of T3.
- Lumbar puncture was performed and showed: opening pressure of 14cm H20, no organism growth, increase protein at 127 mg/dL (normal 15-45mg/dL), increase WBC at 25 (normal <5/mcL), predominantly lymphocytic, no oligoclonal bands present.
- Lyme disease, Meningitis/Encephalitis Panel, EBV, West Nile, CMV, Hep B and C, HSV 1 and 2, Polio, Syphilis, TB and HIV testing were all negative.
- Autoimmune testing including ANA, ANCA, anti-ds DNA, Sjogren SS A/B antibody, CCP, Rheumatoid Factor, Scleroderma SCL 70 antibody, were all negative.
- Patient completed a 5-day course of IV Solumedrol (IVSM) 500mg for possible acute transverse myelitis, without much improvement.
- Laminectomy with biopsy of thoracic tumor was performed which showed a possible dural AV malformation. A follow-up spinal angiogram was performed which ruled out a spinal dural fistula and AV shunting.
- Over the course of a few weeks, the patient's symptoms progressed to gait instability along with urinary and bowel incontinence.
- Patient had a follow-up T-spine MRI which showed interval progression of abnormal hyperintense T2 intramedullary signal now to the level of T7.
- A NMO/AQP4 Facs Titer was ordered to evaluate for Neuromyelitis Optica Spectrum Disorder and the results came back positive.
- A second 5-day course of IVSM was started, followed by prednisone daily, and a 5-day course of IVIG.
- Plasmapheresis was started every other day for 5 sessions, followed by recommendation for Rituximab as outpatient with patient discretion.
- Patient was discharged to inpatient rehabilitation center due to continued gait instability and urinary incontinence.

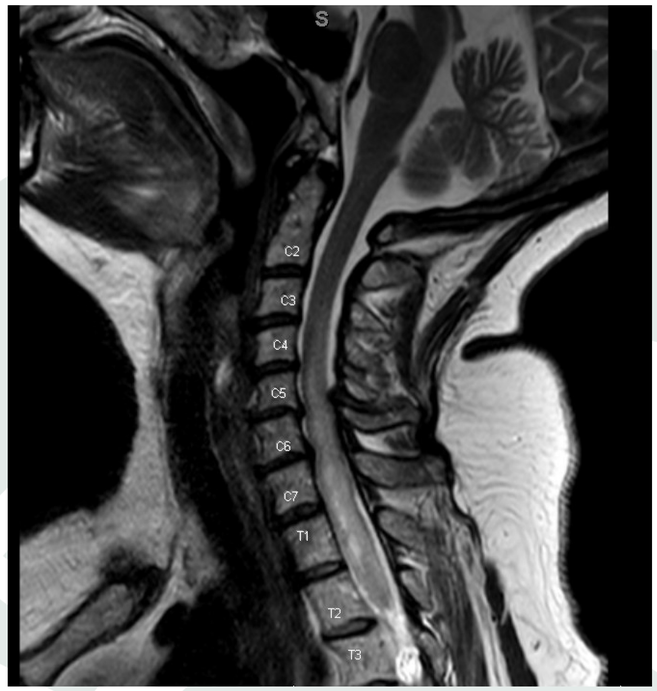

Figure 1. MRI of cervical spine showed expansile intramedullary cord abnormality extending from C3 to at least the level of T3.

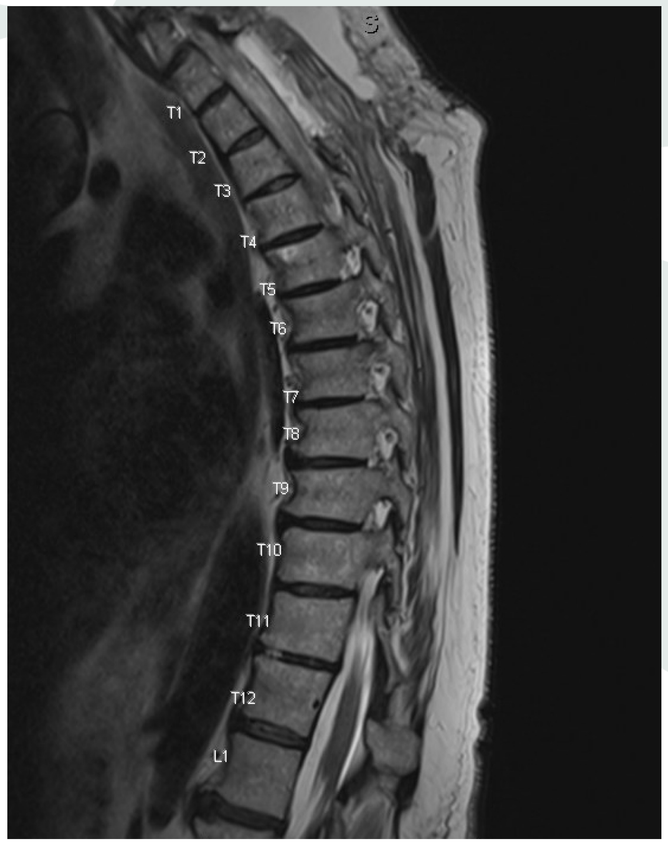

Figure 2. MRI of thoracic spine showed progression of abnormal hyperintense T2 intramedullary signal now extending to the level of T7.

DISCUSSION

- Longitudinal extensive transverse myelitis (LETM) is defined as a lesion extending over three or more vertebral segments on spinal MRI, as seen in our patient[6]. Although LETM is a common presentation for NMOSD, it is not pathognomonic and other pathologies need to be ruled out. This includes a workup for infections, other neuroimmune disorders such as multiple sclerosis, and dural arteriovenous fistula.
- NMOSD is often a clinical challenge because its initial presentation often mimics multiple sclerosis. In recent research, glial fibrillary acidic protein (GFAP) in CSF and blood has shown to be a useful biomarker in determining if astrocytic destruction is occurring, and it is often more elevated in NMOSD in comparison to MS. Another distinction between the two in CSF is oligoclonal bands, which are only present in 10-30% of NMOSD patients while it is present in 90% of MS patients[2].
- Our patient met the diagnostic criteria for NMOSD because she had one core clinical characteristic, which was LETM, in addition to a positive AQP4-IgG antibody test and exclusion of all other possible diagnoses[7]. Determining seropositivity is important as it has been found that AQP4+ patients often have more severe attacks with worse prognosis and higher relapse rates[5].
- In acute attacks, high dose steroids are administered with the goal of reducing edema and inflammation. Only a third of patients who receive high dose steroids return to their neurologic baseline, and further intervention is often required[1]. Plasmapheresis is often necessary, as seen in our patient. The goal is to remove inflammatory cytokines and AQ4+ antibodies.
- NMOSD follows a relapsing course in 90% of people[3]. Because of this, long term treatment of seropositive patients is often done with a monoclonal antibody, such as rituximab. This depletes CD20+ B-cells, thereby suppressing the production of AQP4 antibodies.

CONCLUSION

NMOSD is a rare disorder that can often be a diagnostic challenge. Presentation typically involves acute attacks of optic neuritis or, as seen in our patient, transverse myelitis. Longitudinal expanding transverse myelitis is a classic sign and should raise the index of suspicion in doing a work up for NMOSD, as early treatment and diagnosis is critical in decreasing morbidity.

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