Clinical Reasoning: A man with rapidly ascending paralysis

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SECTION 1

A 38-year-old construction worker with no medical history presented with back pain, urinary retention, and flaccid lower extremity paralysis. Three weeks prior to presentation, he fell from a ladder with no immediate injury. Two weeks after the fall, he presented to another hospital for back pain

and urinary retention. MRI of the lumbar, cervical, and thoracic spine without contrast were reportedly normal, and his back pain improved with an oral methylprednisolone dose pack (figure). The urinary retention remained, and he was discharged with an indwelling catheter. Within a week of the initial urinary symptoms,

Figure MRI of the patient's brain and cervical and thoracic spine

Sagittal T2-weighted MRI cervical spine (A) and thoracic spine (B) show confluent cord signal abnormality from C6 to T9. Axial imaging (not shown) confirms central cord distribution. Coronal T1-weighted postcontrast MRI brain (C, D) shows left optic nerve enhancement (arrows).

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he developed ascending lower extremity numbness and paralysis, and was seen emergently at our hospital.

His examination was notable for intact cranial nerves with the exception of red desaturation in the left eye. He had full strength in the upper limbs without dysmetria, flaccid paralysis with decreased sensation below the T10

level, 2 + upper limb and patellar reflexes, absent ankle reflexes, and no Babinski response.

Questions for consideration:

1. How would you localize his deficits?
2. Does the red desaturation change your localization?
3. What further tests would you order?

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SECTION 2

Flaccid paralysis of the lower extremities localizes to the spinal cord, anterior horn cells, nerve roots, peripheral nerves, or muscle. The addition of sensory loss suggests a spinal cord, nerve root, or peripheral nerve injury. The combination of back pain with ascending motor and sensory loss raises concern for Guillain-Barré syndrome (GBS). However, the early urinary retention, sensory level, and preservation of patellar reflexes are more suggestive of a myelopathy. An acute myelopathy can present with lower motor signs, a syndrome known as spinal shock. Traumatic cord compression was considered unlikely given prior neuroimaging. However, normal imaging does not exclude a CNS process, as anterior horn cell injury

can occur without MRI findings in certain viral infections.¹ The patient's left eye red desaturation could indicate prior optic nerve injury, thus raising the possibility of both brain and spinal cord involvement. A lumbar puncture, performed to delineate the etiology of the patient's symptoms, revealed 118 mg/dL of protein, 78 mg/dL of glucose, 0 erythrocytes, and 298 leukocytes (93% lymphocytes).

Questions for consideration:

1. How do the CSF findings influence your differential diagnosis?
2. Would you begin empiric treatment? If so, for what?
3. What further investigations would you consider?

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SECTION 3

The CSF pleocytosis argues against GBS, though a lymphocytic pleocytosis can be seen with GBS in the setting of HIV infection.² The patient's presentation continued to raise concern for a spinal cord process, thus empiric acyclovir, vancomycin, and ceftriaxone were started to cover for an epidural abscess or an infectious myelitis. CSF culture, herpes simplex virus (HSV), Lyme, and varicella-zoster virus (VZV) PCRs were sent. Repeat MRI of the brain,

cervical, thoracic, and lumbar spine demonstrated enhancement of left optic nerve and extensive T2 signal prolongation in the central spinal cord from C6 to T9 without enhancement. The MRI brain was otherwise unremarkable.

Questions for consideration:

1. What is your differential diagnosis given the MRI findings?
2. What further investigations would you consider?

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SECTION 4

The differential diagnosis for longitudinal extensive myelitis (LEM) includes both infectious and noninfectious etiologies. Viruses, such as enterovirus D68, A71, D70, VZV, HSV 1 and 2, West Nile, HIV, and cytomegalovirus, should be considered. Enteroviruses and West Nile have been associated with an acute flaccid myelitis syndrome in both children and adults. These patients typically present with asymmetric weakness and endorse a prodromal respiratory or gastrointestinal illness. In this syndrome, the clinical pathology and its radiographic correlate are largely restricted to the gray matter and anterior horn cells.³ Bacterial infections, such as syphilis, Lyme disease, and *Mycobacterium tuberculosis*, can also be considered.

Noninfectious diseases, such as neurosarcoidosis, lupus, Sjögren syndrome, Behçet disease, and paraneoplastic syndromes, can also cause LEM. In neurosarcoidosis, spinal cord MRI classically shows subpial nodular enhancement, while the CSF may be remarkable for hypoglycorrhachia and elevated angiotensin-converting enzyme (ACE).⁴ A paraneoplastic myelitis has been associated with anti-HU, anti-CRMP5, and anti-amphiphysin antibodies (Abs), though it typically occurs concurrently with other nervous system insults, such as sensory and optic neuropathy.

Vascular etiologies, such as spinal cord infarction or arteriovenous malformations, should also be

considered. However, the ascending nature of the patient's paralysis, CSF pleocytosis, and absence of flow voids or serpiginous enhancement on MRI argue against these processes.

The combination of transverse myelitis and optic neuritis (ON) is suggestive of autoimmune demyelinating pathologies, chiefly neuromyelitis optica spectrum disorders (NMOSD) and multiple sclerosis (MS). The presence of LEM extending more than 3 vertebral segments with symmetric weakness is more suggestive of neuromyelitis optica than MS. Moreover, a CSF lymphocytic pleocytosis of the magnitude of our patient is more commonly seen in NMOSD.⁵

The patient's CSF analysis and serology were unremarkable, including negative CSF HSV and Lyme PCR, bacterial culture, oligoclonal bands, serum HIV, aquaporin-4 (AQP4), VZV, and Epstein-Barr virus serology, CMV PCR, QuantiFERON gold, serum protein electrophoresis, and rapid plasma reagin. His erythrocyte sedimentation rate, C-reactive protein, and ACE levels were normal.

Questions for consideration:

1. From the available data, how would you diagnose and manage this patient?
2. Are there additional tests that could clarify the diagnosis and guide therapy?

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SECTION 5

Despite the negative AQP4 serology, the patient met criteria for NMOSD in that he fulfilled 2 major clinical criteria: ON and LEM with characteristic MRI findings and exclusion of an alternative diagnosis. The lack of cord enhancement may be explained by the prior methylprednisolone treatment. Given the severity of his symptoms, he received IV methylprednisolone 1,000 mg daily for 5 days, followed by rituximab. At discharge, the patient's urinary retention had improved, and he had 2/5 and 3/5 strength in his proximal and distal leg muscles, respectively. Following the patient's discharge, a serum anti-MOG Ab assay returned positive.

DISCUSSION NMOSDs are a group of inflammatory disorders of the CNS characterized by demyelination and axonal damage predominately affecting the spinal cord and optic nerves. The diagnosis is made in part through serum autoantibodies against the water aquaporin-4 channel (AQP4). However, a smaller proportion of patients with NMOSD are found to have Ab against myelin oligodendrocyte glycoprotein (MOG), a protein expressed on myelin sheaths, and a marker of oligodendrocyte maturation.

There have been several studies comparing NMOSD phenotypes in people with autoantibodies to either MOG or AQP4. These studies have shown that compared with AQP4-Ab patients, MOG-Ab patients were typically male, had improved functional outcomes, and had similar CSF composition.^{6,7} Two studies showed that MOG-Ab patients were more likely to present with bilateral optic neuritis as their initial symptom.^{8,9} Unlike our patient, some studies found that people with MOG-Abs were more likely to have LEM involving the lumbar spine and conus.^{7,8} Similar to our patient, one of these studies found that MOG-Ab patients were more likely to present with urinary retention before weakness.⁷ A study examining a subgroup of patients with MS with NMOSD phenotypes, such as severe ON or transverse myelitis, found that some of these patients expressed Ab to MOG. These patients had a more aggressive disease course despite platform therapies, though they benefited from immunosuppressive agents such as rituximab.¹⁰

Management of NMOSD consists of treating the acute attack with glucocorticoids followed by plasma exchange for refractory symptoms. Chronic immunosuppression with rituximab, azathioprine, methotrexate, mitoxantrone, tocilizumab, or mycophenolate mofetil are recommended for long-term therapy. The rationale for these agents derives from their ability to suppress humoral immunity. Given the absence of randomized control trials, there is no consensus as

to which agent is preferred. Rituximab, a CD20 inhibitor, is a logical treatment for neuromyelitis optica given its efficacy and selective suppression of humoral immunity. In a recent retrospective review, rituximab was shown to have a greater reduction in relapse rate than azathioprine and mycophenolate mofetil.¹¹

Patients with MOG-Abs, similar to our patient, tend to be male and to have improved response to treatment compared to those with AQP4-Abs. Though not true of this patient, 2 studies found that MOG-Ab patients often have bilateral ON as their initial symptom, while other studies reported that they were more likely to have a LEM involving the lumbar spine. The literature comparing AQP4-Ab and MOG-Ab patients is limited by small sample size, thus may lack the power to detect further differences between these 2 populations.

This case illustrates 2 important diagnostic principles with therapeutic implications. Patients with NMOSD phenotypes should be tested for MOG in addition to AQP4-Ab to improve diagnosis and prognosis and to guide therapy. Spinal cord injury can present as ascending flaccid paralysis, though early urinary retention and preserved reflexes should make one suspect this diagnosis over GBS.

AUTHOR CONTRIBUTIONS

Jon Rosenberg: conception and drafting of the original manuscript, preparation of the images, and critical revisions to the manuscript. Stephen Aradi: drafting of the manuscript and critical revisions to the intellectual content. Amy Pruitt: drafting of the manuscript and critical revisions to the intellectual content.

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REFERENCES

1. Sejvar JJ, Leis AA, Stokic DS, Ven Gerpen JA, et al. Acute flaccid paralysis and west Nile virus infection. *Emerg Infect Dis* 2003;9:788–793.
2. Asbury A, Cornblath D. Assessment of current diagnostic criteria for Guillain-Barré syndrome. *Ann Neurol* 1990; 27:21–24.
3. Messacar K, Schreiner TL, Van Haren K, et al. Acute flaccid myelitis: a clinical review of US cases 2012–2015. *Ann Neurol* 2016;80:326–338.
4. Flanagan EP, Kaufman TJ, Kreckle KN, et al. Discriminating long myelitis of neuromyelitis optica from sarcoidosis. *Ann Neurol* 2016;79:437–447.
5. Wingerchuck D, Lennon V, Lucchinetti C, Pittock SJ, Weinshenker BG. The spectrum of neuromyelitis optica. *Lancet Neurol* 2007;6:805–815.
6. Sato DK, Callegaro D, Lana-Peixoto MA, Nakashima I, Fujihara K. Seronegative neuromyelitis optica spectrum: the challenges on disease definition and pathogenesis. *Arq Neuropsiquiatr* 2014;72:445–450.

7. Kitley J, Waters P, Woodhall M, et al. Neuromyelitis optica spectrum disorders with aquaporin-4 and myelin-oligodendrocyte glycoprotein antibodies: a comparative study. *JAMA* 2014;71:276–283.
8. Sato DK, Callegaro D, Lana-Peixoto MA, et al. Distinction between MOG antibody-positive and AQP4 antibody-positive NMO spectrum disorders. *Neurology* 2014;82:474–481.
9. Ramanathan S, Reddel SW, Henderson A, et al. Antibodies to myelin oligodendrocyte glycoprotein in bilateral and recurrent optic neuritis. *Neurol Neuroimmunol Neuroinflamm* 2014;1:e40.
10. Spadaro M, Gerdes LA, Krumbholz M, et al. Autoantibodies to MOG in a distinct subgroup of adults with multiple sclerosis. *Neurol Neuroimmunol Neuroinflamm* 2016;3:5e257.
11. Mealy MA, Wingerchuk DM, Palace J, Greenberg BM, Levy M. Comparison of relapse and treatment failure rates among patients with neuromyelitis optica: multicenter study of treatment and efficacy. *JAMA Neurol* 2014;71:324–330.

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