Mystery Case:

A 61-year-old woman with lower extremity paralysis and sensory loss

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SECTION 1

A 61-year-old woman presented to the hospital with acute onset of numbness and weakness in the lower extremities. Her symptoms rapidly progressed, reaching maximal intensity within hours. She developed acute urinary retention but without bulbar or upper extremity involvement. There was no constitutional symptom or preceding trauma. Prior medical conditions included hypertension, hyperlipidemia, left-sided sciatica, and low back pain. Family history was unremarkable.

Initial examination uncovered sensory loss to all modalities below the T11 level, weakness in both lower extremities (right: 0/5 throughout; left: 1/5

iliopsoas, 2/5 gluteals, 2/5 hamstrings, 3/5 quadriceps, 2/5 tibialis anterior, and 2/5 gastrocnemius) and absent patellar and ankle deep tendon reflexes bilaterally. Vital signs, mental status, cranial nerve, and upper extremity strength and sensation were otherwise normal.

Questions for consideration:

1. What category of neurologic disorder is described in this case?
2. What is the differential diagnosis for this type of spinal cord lesion?
3. Which testing should be ordered at this time?

[GO TO SECTION 2](#)

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From the Department of Neurology, University of Pittsburgh, PA.

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SECTION 2

The presentation is consistent with transverse myelopathy localizing to the thoracic spinal cord (table e-1 at Neurology.org). Transverse myelopathy has a wide range of differential diagnoses, including trauma, inflammatory (i.e., transverse myelitis), malignant, metabolic, and vascular etiologies.¹

Inflammatory conditions include neuromyelitis optica (NMO), multiple sclerosis, vasculitis, postradiation demyelination, or postinfectious demyelination. Other systemic inflammatory diseases include sarcoidosis, Sjögren syndrome, and systemic lupus erythematosus. Infectious etiologies include HIV, herpesvirus, human T-cell lymphotropic virus, enterovirus, flavivirus, *Treponema*, or parasitic infection. Bacterial infections typically cause epidural abscess and can progress to direct spinal cord infection. Primary malignancies such as lymphoma, ependymoma, or astrocytoma, or a paraneoplastic syndrome can involve the spinal cord but tend to have a subacute presentation and are often associated with constitutional symptoms. Metabolic derangements including vitamin B₁₂ or copper deficiency can cause transverse myelopathy, though they primarily involve the posterior columns. Vascular etiologies include vascular compression (vascular malformation or

iatrogenic causes due to, for example, endovascular procedure), hypoperfusion (due to systemic hypotension or local atherosclerosis), embolism (thromboembolic disorder, iatrogenic, fibrocartilaginous emboli), or hypercoagulable state causing spinal cord infarction. Spinal cord infarction due to embolism typically affects the anterior spinal cord. Spinal dural arteriovenous fistula (DAVF) tend to have a subacute onset, typically occur in a thoracic or lumbar location, and may sometimes manifest as flow voids on MRI.²

Serologic testing including metabolic panel, complete blood count, and liver function panel were within normal limits. Additional studies to evaluate metabolic, infectious, and inflammatory markers were unrevealing except that vitamin B₁₂ level was borderline low at 281 pg/mL (normal 211–911 pg/mL). CSF was notable for pleocytosis (133 white blood cells, 92% neutrophils, 136 red blood cells), elevated protein (376 mg/dL), and elevated immunoglobulin G (IgG) index (0.78), but without any oligoclonal bands. MRI of the entire spine showed longitudinal T2-weighted hyperintense lesions from T6/T7 to conus, with patchy enhancement on postgadolinium sequences. Given the acute onset of symptoms, a vascular etiology was initially suspected; however, spine MRI did not show evidence of restricted diffusion or abnormal flow voids.

GO TO SECTION 3

SECTION 3

In this patient, initial evaluation led to a working diagnosis of NMO given the longitudinally extensive spinal cord lesion on MRI and nonspecific evidence of inflammation in CSF with an otherwise negative infectious, metabolic, and systemic inflammatory evaluation. While awaiting the results of serum and CSF NMO antibodies to return, the patient began empiric treatment with high-dose methylprednisolone, followed by 5 sessions of plasmapheresis over 10 days. By the time of discharge to inpatient rehabilitation 1 week after initial onset, strength in her legs had modestly improved, but the abdominal sensory level persisted. During outpatient follow-up 6 weeks after initial presentation, the patient continued to have pronounced left leg weakness. NMO antibody tests returned negative. A diagnosis of NMO was not made in this case as aquaporin-4 IgG antibody was negative and only 1 of 2 necessary core clinical

criteria was present (i.e., acute myelitis without optic neuritis, area postrema syndrome, acute brainstem or diencephalic syndrome, or symptomatic cerebral syndrome), thus the working diagnosis remained idiopathic transverse myelitis.²

Two months later, the patient was readmitted after developing intense pain in the abdomen and groin and increasing weakness in the left leg. Neurologic examination was notable for worsened left lower extremity weakness, now 1/5 throughout, with diffusely brisk reflexes in upper and lower extremities but without other upper motor neuron signs. Exacerbation was attributed initially to a urinary tract infection, but urine culture turned out to be negative.

Question for consideration:

1. What further investigation should be considered at this time and why?

GO TO SECTION 4

SECTION 4

Further evaluation included a brain MRI to look for evidence of prior or occult inflammatory lesions in the brain that may aid diagnosis. In this case, the brain MRI was normal. Repeat MRI of the spine showed an increase in the extent of the T2-weighted hyperintense lesion in the thoracic spinal cord, by then extending from T3 to the conus (figure, A), with greater involvement of the gray matter and diffuse contrast enhancement (figure, B). Marked edema in the thoracic spinal cord suggested venous hypertension, prompting vascular imaging.

A diagnostic catheter-based spinal angiogram identified a dural arteriovenous fistula at the L2 level as well as a draining vein extending to T10 with extensive engorgement (figure, C). During the spinal angiogram, the feeding arterial medullary branch at right L1 level was embolized, and a coil was placed to guide operative management (figure, D).

Questions for consideration:

1. What further treatment can be offered at this time?
2. What is the prognosis of this lesion?

(A) T2-weighted image (fast relaxation fast spin echo) with sagittal view of the MRI thoracic spine shows central hyperintensities extending from T3 to conus. (B) T1-weighted postgadolinium image of the same MRI study shows diffuse, patchy contrast enhancement of the central cord. (C) During diagnostic spinal angiogram, selective injection of contrast at the right L1 level reveals a spinal dural fistula (*) with enlarged early draining vein (arrows). (D) Coil was placed at the level of right L1 segmental artery (*) to guide subsequent operative treatment, which included right T12 and L1 semihemilaminectomy for intradural exploration and microscopic ligation of dural arteriovenous fistula.

[GO TO SECTION 5](#)

SECTION 5

For definitive treatment, the patient underwent a right T12/L1 hemilaminectomy and decompression with ligation of the dural arteriovenous fistula. The extent of the spinal cord lesion slightly diminished on repeat MRI spine several days after the surgery. One month later, the patient completed inpatient rehabilitation, and reported gradual improvement in lower extremity strength and bladder sensation. Six months later, she regained antigravity movement in her lower extremities, though the sensory level remained.

DISCUSSION Although spinal DAVF is the most common vascular malformation of the spinal cord, affecting predominantly elderly men, it remains a rare etiology of longitudinally extensive myelopathy.³ The abnormal connection of arterial to venous vasculature results in an increase in venous pressure and congestion in the spinal cord, which produces intramedullary edema that interrupts descending and ascending fiber tracts.

Prognosis of spinal DAVF depends on the time to definitive treatment. Early embolization or ligation soon after symptom onset has the best outcome. Time to treatment is often delayed as spinal DAVF can remain undiagnosed for an average of 15 months.⁴ Definitive treatment typically stops disease progression, but symptomatic recovery is often variable, with sensory symptoms being the most refractory to improvement. Following definitive treatment, symptomatic exacerbation warrants repeat angiography to evaluate for possible recurrence of venous hypertension through recanalization.⁵

This case highlights an important diagnostic challenge in evaluating myelopathy. The initial CSF findings (elevated IgG Index and protein as well as pleocytosis), while suggestive of an inflammatory process causing transverse myelitis, are not specific, and can also be consistent with venous hypertension. The typical flow voids suggestive of venous hypertension were not present on the initial or the repeat MRI spine, though the diffuse intramedullary signal change and edema were consistent with spinal DAVF. The progression of symptoms prompted additional evaluation in this case. In retrospect, several features in this case suggested spinal DAVF: sudden onset of symptoms, reaching maximal intensity over hours, thoracolumbar localization with paraplegia, and a T11 sensory level. Another potential clue to diagnosis in cases of spinal DAVF is that of transient worsening of symptoms within a few days after administration of steroids in part due to reduction in retrograde venous perfusion through changes in capillary permeability.⁶

Without careful evaluation of recurrent symptoms and evaluation of other potential etiologies of

myelopathy in this case, it is possible that the underlying etiology would remain undiagnosed and untreated. This case highlights the importance of close follow-up in patients with longitudinally extensive myelopathy.

AUTHOR CONTRIBUTIONS

J.M., A.P.J., and Z.X. contributed to the concept and study design. J.M., A.P.J., and Z.X. contributed to the data acquisition and analysis. J.M. and Z.X. contributed to the drafting of the manuscript. J.M., A.P.J., and Z.X. contributed to the drafting of the figure.

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DISCLOSURE

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MYSTERY CASE RESPONSES

The Mystery Case series was initiated by the *Neurology*[®] Resident & Fellow Section to develop the clinical reasoning skills of trainees. Residency programs, medical student preceptors, and individuals were invited to use this Mystery Case as an educational tool. Responses were solicited through a group e-mail sent to the American Academy of Neurology Consortium of Neurology Residents and Fellows and through social media.

Sixty-one people responded to this case about a 61-year-old woman who acutely developed numbness and weakness in the lower extremities and was found to have evidence of a thoracic longitudinally extensive transverse myelopathy on MRI. A reasonable initial differential diagnosis—with the percentage of respondents who agreed in parentheses—included NMO (60.9%), sarcoidosis (35.0%), Sjögren

syndrome (24.1%), multiple sclerosis (28.5%), systemic lupus erythematosus (28.5%), B₁₂ myelopathy (11.3%), intramedullary infection (34.7%), and spinal cord infarction (61.7%). Given serum and CSF studies listed in the case, a working diagnosis of NMO was made and the patient received high-dose methylprednisolone and plasmapheresis. Two months later, however, the patient presented with worsening lower extremity weakness. The most popular choice for an immediate next step in additional diagnostic workup was to repeat whole spine MRI, chosen by 65.7% of respondents. The next 2 most popular answers were to repeat an inflammatory workup including NMO antibody and CSF oligoclonal band testing (53.6%) and to obtain a paraneoplastic antibody panel of CSF and serum (52.6%). These choices were not, however, preferred ones. An isolated longitudinally extensive transverse myelitis would be unusual for a paraneoplastic syndrome and prior negative NMO and oligoclonal band testing combined with poor response to immunotherapy make a missed diagnosis of a demyelinating process less likely, albeit not impossible. Instead, recommended next steps would be to get brain MRI (49.3%) to evaluate for occult inflammatory lesions, add magnetic resonance angiography of the spine (16.4%), and also consider a diagnostic catheter angiogram (26.6%). By this point, it was obvious that this case was moving towards a vascular cause. The T2-weighted sagittal spinal MRI showed longitudinally extensive hyperintense lesions from the high thoracic cord to the conus and patchy contrast enhancement of the central cord was seen on T1-weighted postgadolinium imaging. The spinal angiogram shows a dural

arteriovenous fistula at the level of L2 with a draining vein extending to T10. All those hanging on to thoughts of immune-mediated causes were swayed, and 100% of respondents correctly chose spinal DAVF as the final diagnosis—a Mystery Case record. This patient was treated with endovascular embolization and eventually underwent a right T2/L1 hemilaminectomy and decompression with ligation of the DAVF.

A spinal DAVF is the most common vascular malformation of the spinal cord, classically occurring in men aged 55 years or older, and is a rare etiology of longitudinally extensive myelopathy. The arterial to venous connection results in increased venous pressure and congestion of the spinal cord that can lead to intramedullary edema that disrupts spinal tracts. Symptoms can be nonspecific, slowly progressive, and ascending with time. Acute onset of neurologic deficits, as occurred in this patient, with fluctuations of remission and exacerbation of symptoms have also been described.¹ This case highlights the importance of reevaluating the differential diagnosis in longitudinally extensive spinal cord lesions when initial workup fails to yield a specific etiology.

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