Pelvic Pain as an Unusual First Presentation of a Demyelinating Disease

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Pelvic pain as the presenting symptom of demyelinating disease is rare. We report on a 49-year-old female patient that initially had symptoms of pain and anesthesia in the perineum. Symptoms later evolved to include both lower and upper extremity weakness and were associated with enhancing spinal cord lesions on MRI. Recognizing that the patient's disease was localized only to the spinal cord led to an eventual serological diagnosis of neuromyelitis optica (Devic's disease), a demyelinating syndrome that is now considered distinct from multiple sclerosis and that primarily affects the spinal cord and optic nerves. Pelvic pain is an unusual first presentation of this illness. Additionally, this case illustrates the challenges of establishing a diagnosis of neuromyelitis optica. Recognizing the distinct clinical features of this rare illness, referring specifically from a spinal cord or ophthalmological etiology, is essential for its rapid diagnosis, and hence for initiation of appropriate therapy.

KEY WORDS: demyelinating disease; pelvic pain; neuromyelitis optica (Devic's disease).

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INTRODUCTION

Pelvic pain is a common complaint of female patients in primary care practices,¹ and the differential diagnosis for this symptom is broad. Pain often refers from pathology of the pelvic viscera or the surrounding muscles and soft tissues, but it may also be of neurological origin, such as from the pelvic or spinal nerves. Neurological pain may be characterized by the patient by using typical neuropathic descriptors, such as numbness or tingling. It is important to recognize objective physical examination signs such as perineal anesthesia as reflecting spinal cord or spinal nerve pathology, since rapid identification and treatment of disease processes such as malignancy or demyelinating disorders such as multiple sclerosis and neuromyelitis optica is crucial.

CASE REPORT

A 49-year-old African American female presented to our hospital's emergency department with a one-week history of new-onset, intermittent episodes of sharp perineal pain, predominantly occurring at night, with anesthesia in the area. The patient denied having incontinence or retention of stool or urine, or having other genitourinary complaints. Examination by the emergency department physicians at that time was notable only for anesthesia of the right buttock, perianal, and vulvar areas. She was discharged to home with a referral to gynecology.

Over the ensuing three weeks, symptoms progressed to become constant and of greater intensity. One week prior to hospitalization, the perineal pain began to radiate to the bilateral lower extremities and the patient developed dysesthesia and paresthesia of the plantar surfaces of both feet. Shortly thereafter, she also developed gait instability and required assistance with ambulation, which prompted her to again seek medical attention in the emergency department. The general internal medicine teaching service was consulted to admit her and further evaluate her symptoms. On review of systems, the patient admitted to having a 20-pound weight loss over the preceding three months, which she attributed to having had a poor appetite. She denied lower extremity weakness, incontinence, visual changes, or other complaints at this time. The patient had no contributory past medical, family, or social history to report besides a 10-pack-year history of smoking, and she took no home medications. Her physical examination was notable solely for several neurological abnormalities. These included the presence of an ataxic gait, a positive Romberg sign, and anesthesia of the perineum and bilateral plantar surfaces. Cranial nerves, the motor and remaining sensory exam, and deep tendon reflexes were all intact.

A gadolinium-enhanced MRI was obtained of the lumbosacral spine (Fig. 1), which revealed an enhancing lesion of the conus medullaris, extending over a 3 cm length of the spinal cord at the T12 level, and measuring 10–12 mm in diameter. A subsequent MRI of the brain and remaining spine was negative. Lumbar puncture was performed, and CSF examination was normal and specifically negative for pleocytosis or oligoclonal bands. The differential diagnosis at this time included transverse myelitis, demyelinating disease, neurosarcoidosis, and mass lesion of the spinal cord. Shortly thereafter, the patient developed new-onset urinary and stool incontinence. It was decided at this point to transfer her to the neurosurgical service of a tertiary care center for possible diagnostic biopsy of the spinal cord lesion. The neurosurgical team first attempted a five-day trial course of intravenous dexamethasone (4 mg every 6 hours), and the patient regained

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Figure 1. Post-gadolinium T2 weighted image of lumbar spine showing a diffuse swelling of the distal conus medullaris, with abnormally-enhancing central cord signal (white arrow). The enhancing central component measures 0.7x0.6x2.7 cm.

some sensation in the feet and had improvement in her gait. Hence, the planned biopsy was cancelled. The patient's pain was controlled using gabapentin, amitriptyline, and NSAIDs. The patient was discharged with an in-dwelling Foley catheter, recommendations for physical therapy, and close follow-up on an outpatient basis with neurology, neurosurgery, and urology physicians.

Approximately five months later, the patient presented again to our hospital after developing profound new-onset right upper extremity weakness, without associated paresthesias. Her neurological exam demonstrated grade 0/5 right upper extremity strength, with normal upper and lower extremity deep tendon reflexes, and no other focal changes from her prior examinations. Gadolinium enhanced MR imaging of the cervical spine (Fig. 2) demonstrated the presence of signal abnormality with cord expansion extending from the foramen magnum to the C7 level. Again the patient was admitted. A second lumbar puncture was performed and the CSF was once more unremarkable. Due to her symptom progression and development of a second spinal cord lesion, an expanded diagnostic approach was taken and a serum neuromyelitis optica (NMO) IgG antibody assay was sent out to a referral laboratory. Once again corticosteroids were administered, and the patient was transferred to the tertiary care center for evaluation. A trial of plasmapheresis was initiated at that hospital, and six sessions of adjunctive therapy with cyclophosphamide were administered. Despite this treatment, the patient regained only limited function in the affected extremity. The patient was discharged to an inpatient rehabilitation facility on daily prednisone and planned monthly cyclophosphamide. Subsequently, the diagnosis of neuromyelitis optica (or Devic's disease) was highly suggested by the return of a positive NMO IgG antibody assay.

Currently, the patient remains with persistent neurological deficits, including right upper extremity weakness (grade 3 out of 5 strength), bilateral lower extremity weakness (grade 4 out of 5 strength), and urinary incontinence. During an outpatient follow-up visit, four months after her last hospital presentation, the patient complained of intermittent right eye pain without visual loss or changes. Her neurological examination remained unchanged and she had a normal fundoscopic exam and intact visual acuity. A subsequent repeat gadolinium-enhanced MRI of the brain was normal.

DISCUSSION

Pelvic pain is a common problem among women of reproductive age seeking care in primary care practices, with one study estimating its prevalence at 39%.¹ Pelvic pain may rarely be a symptom reflecting pathology in the peripheral and central nervous systems, and this case illustrates how demyelinating disease of the spinal cord can result in such a chief complaint. Although acute pain is an increasingly recognized symptom in demyelinating diseases, such as multiple sclerosis (MS), this most commonly occurs in the form of trigeminal neuralgia or L'hermitte's syndrome. Other painful disease manifestations such as complex regional pain syndrome are rare in MS patients.² In fact, a literature search for case reports where pelvic pain was the presenting sign of MS produced only one result.³ No case reports of pelvic pain as the presenting complaint in NMO were identified. When applying a diagnostic approach to a patient with pelvic pain, and in particular to a patient with perineal anesthesia, the general internist should pay mind to a possible spinal cord or spinal nerve etiology of the symptoms. This is particularly relevant in those patients with an unremarkable pelvic examination.

Figure 2. Gadolinium-enhanced MR imaging of the cervical spine demonstrates the presence of signal abnormality with cord expansion extending from the foramen magnum to the C7 level (between the white arrows).

As the presented patient's symptoms progressed to include the lower extremities, the anatomical source of the pain became more obvious. However, lesions of the spinal cord are not easy to diagnose as MRI findings can be non-specific and there are limited serological assays to further assist with the diagnosis. As NMO is a demyelinating disease specifically of the optic nerves and spinal cord, NMO should be considered in patients whose symptoms refer to lesions only in these areas and who have a non-diagnostic brain MRI.⁴ The syndrome should therefore also be entertained in patients with a recurrent episode of transverse myelitis. The diagnostic criteria for NMO (listed in Text Box 1) remain debated by experts, and proposed revisions to those criteria have been made (listed in Text Box 2) in the medical literature.⁴ Current knowledge is supportive of NMO being a distinct disease entity.⁴⁻⁶ With the discovery of the serum NMO IgG antibody, discriminating NMO from other demyelinating syndromes such as variant multiple sclerosis has become possible.⁷ The antigenic target for the NMO IgG appears to be the astrocyte-specific aquaporin-4 (AQP-4) water channel.⁵⁻⁶ Research suggests that NMO-IgG has a sensitivity of 58–73% and specificity of 90–99% for the diagnosis.⁷ As this serum assay is not 100% specific, and the patient presented had ophthalmic symptoms without confirmatory evidence for optic neuritis, a definitive diagnosis for NMO cannot strictly be made by the current diagnostic criteria. Nonetheless, with the patient meeting two absolute criteria, two major criteria, and one minor criterion, and with a positive NMO-IgG assay, an underlying diagnosis of NMO remains extremely likely. Additionally, other diagnostic models for NMO have been previously assessed,¹⁶ and it was suggested that the combined criteria of myelitis (≥ 3 spinal cord segments) and a positive NMO-IgG assay, such as is present in this patient, reaches 100% specificity for the NMO diagnosis.

Text Box 1. Proposed diagnostic criteria for neuromyelitis optica (Devic's disease). Diagnosis requires all absolute diagnostic criteria and additionally either one major supportive criterion or two minor supportive criteria. Additional factors may assist in the diagnosis.

<i>Absolute diagnostic criteria (patient must have all three)</i>
• Acute myelitis
• Optic neuritis
• Absence of clinical disease beyond the spinal cord and optic nerves
<i>Major supportive diagnostic criteria</i>
• Brain MRI at disease onset either normal or not meeting radiological diagnostic criteria for multiple sclerosis
• Spinal cord MRI with T2-weighted signal abnormality extending over more than three vertebral segments
• CSF pleocytosis of $>50 \times 10^6$ WBC/L (or $>5 \times 10^6$ neutrophils/L)
<i>Minor supportive diagnostic criteria</i>
• Bilateral optic neuritis
• Severe optic neuritis with fixed visual acuity worse than 20/200 in at least one eye
• Severe, fixed, attack-related weakness (grade 2 or less strength) in one or more limbs

Legend: MRI, magnetic resonance imaging; CSF, cerebrospinal fluid; WBC, white blood cells; L, liter. Modified after: Wingerchuk, DM. Diagnosis and Treatment of Neuromyelitis Optica. *The Neurologist*. 13(1):2–11, January 2007

Text Box 2. Proposed additional diagnostic criteria for neuromyelitis optica (Devic's disease) to assist in the diagnosis.⁴

• Allowance for clinical symptoms and signs outside spinal cord and optic nerves, or presence of brain MRI lesions, if other diagnostic criteria are satisfied
• Absolute requirement for greater than three vertebral segment spinal cord lesion on T2-weighted MRI
• Positive NMO-IgG antibody; how to incorporate serologic status into the diagnostic scheme remains debated ¹⁴

Legend: MRI, magnetic resonance imaging; NMO, Neuromyelitis Optica. Modified after: Wingerchuk, DM. Diagnosis and Treatment of Neuromyelitis Optica. *The Neurologist*. 13(1):2–11, January 2007

Table 1. Clinical and Other Features That Assist in Differentiating a Diagnosis of NMO from That of MS.^{4,9,17}

	Neuromyelitis optica	Multiple sclerosis
Epidemiology	<ul style="list-style-type: none"> • 90% of patients are female • Patients are usually 40–60 years old at disease onset • Non-white ancestry is common • Other autoimmune diseases may be present 	<ul style="list-style-type: none"> • 70% of patients are female • Patients are usually 20–40 years old at disease onset • Non-white ancestry is very uncommon • Other autoimmune diseases are usually not present
Clinical features	<ul style="list-style-type: none"> • Symptoms from involvement of the brain are uncommon except in late disease • Optic neuritis and myelitis attacks are generally severe • Attacks are often followed by a significant residual neurological deficit • Death from respiratory failure is common • Disease is usually characterized by relapsing flares, and is rarely monophasic 	<ul style="list-style-type: none"> • Symptoms from involvement of the brain are common in early disease • Optic neuritis and myelitis attacks are generally less severe than in NMO • Attacks are often followed by a less significant residual neurological deficit than in NMO • Death from respiratory failure is not common except in patients with long-term disabilities from MS • Disease is usually characterized by relapsing flares, but often eventually has a progressive course
Radiological findings	<ul style="list-style-type: none"> • MRI of the spinal cord shows extensive involvement of disease, longitudinally across ≥ 3 vertebral segments • MRI of the brain is either normal or has non-specific findings 	<ul style="list-style-type: none"> • MRI of the spinal cord shows disease lesions in asymmetrical, peripheral locations, spanning across <2 vertebral segments • MRI of the brain demonstrates periventricular and subcortical demyelinating lesions
Laboratory testing	<ul style="list-style-type: none"> • Oligoclonal bands are usually not present in the CSF • The NMO-IgG antibody assay is most often positive 	<ul style="list-style-type: none"> • Oligoclonal bands are usually present in the CSF • The NMO-IgG antibody assay is usually negative

Legend: NMO, Neuromyelitis Optica; MRI, magnetic resonance imaging; CSF, cerebrospinal fluid. Modified after: Weinshenker BG. Neuromyelitis Optica Is Distinct From Multiple Sclerosis. *Archives of Neurology*. 2007; 64:899–901

The epidemiology of NMO is not well understood, largely since it may be an underdiagnosed syndrome, confused clinically with MS.⁸ Nonetheless, certain clinical features can assist in differentiating NMO from MS (see Table 1). Both diseases predominantly affect women. However, the median age of onset in NMO is about a decade later than in MS, usually late into the patient's 3rd decade.⁴ NMO also has a greater predilection to affect non-Caucasians.⁴ In general, NMO flares are more severe and result in a greater residual neurological deficit than those in MS.^{4,9} NMO is also predominantly a disease of flare and relapse, with only 10% of patients having monophasic disease.⁴

Although significant advances have been made in the diagnosis of NMO, guidelines for treatment are not well established.^{4,10} Accurately confirming a diagnosis of a demyelinating syndrome in a timely fashion is essential, so as to initiate appropriate immunosuppressive therapy promptly. In general, chronic immunosuppressive therapy is instrumental in both suppressing attack recurrence and in limiting disease severity during an acute attack in NMO.⁴ Whether or not to initiate therapy after the first attack remains controversial.⁹ Promising approaches include using azathioprine,⁴ mitoxantrone,¹¹ and the monoclonal antibody rituximab,¹² with greater relapse-free periods observed. The use of methylprednisolone⁴ and plasmapheresis¹⁰ during acute flares has been documented with variable success, with the latter generally recommended when symptoms do not recede with steroids.⁴ However, given the low disease prevalence, there are no large randomized studies of any great significance to support a standard approach to acute or chronic therapy for the disease.¹² To date, treatment has been guided mostly by sparse case reports and clinical experience.⁴ Overall, patients with NMO have a poor prognosis. Optic nerve disease may cause permanent blindness and spinal cord involvement may lead to loss of limb use or death from respiratory failure.¹³ Acute mortality at the time of diagnosis is 20%, and five-year mortality is estimated between 35 and 50%.¹³

CONCLUSION

Although rare, pelvic pain may be referred from demyelinating lesions in the spinal cord. Furthermore, NMO is a distinct illness that may go unrecognized due to clinical overlap with other demyelinating diseases and spinal cord disorders such as transverse myelitis and neurosarcoidosis. Differentiating NMO from MS is of substantial importance given the difference in outcomes and the treatment modalities used in NMO. When encountered with an atypical presentation of a demyelinating disease, NMO should be included in the differential diagnosis, and testing for presence of serum NMO-IgG antibody should be strongly considered as it can supplement evidence from non-specific MRI findings.

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REFERENCES

1. Jamieson DJ, Steege JF. The prevalence of dysmenorrhea, dyspareunia, pelvic pain, and irritable bowel syndrome in primary care practices. *Obstet Gynecol*. 1996;87(1):55-8. Jan.
2. Kassirer M. Multiple sclerosis and pain: a medical focus. *Int J MS Care*. 2000;2(3):40-7. [Serial online]. Oct.
3. Solaro C, Uccelli MM, Mancardi GL. A patient with multiple sclerosis and Down's syndrome with a rare paroxysmal symptom at onset. *Eur J Neurol*. 1999;6(4):505-7. Jul.
4. Wingerchuk DM. Diagnosis and Treatment of Neuromyelitis Optica. *Neurologist*. 2007;13(1):2-11. January.
5. Misu T, Fujihara K, Kakita A, et al. Loss of aquaporin 4 in lesions of neuromyelitis optica: distinction from multiple sclerosis. *Brain*. 2007;130(5):1224-34. May.
6. Roemer SF, Parisi JE, Lennon VA, et al. Pattern-specific loss of aquaporin-4 immunoreactivity distinguishes neuromyelitis optica from multiple sclerosis. *Brain*. 2007;130(5):1194-205. May.
7. Jarius S, Franciotta D, Bergamaschi R, et al. NMO-IgG in the diagnosis of neuromyelitis optica. *Neurology*. 2007;68(13):1076-77. 27 March.
8. Wingerchuk DM. Neuromyelitis optica. *Int MS J*. 2006;13:42-50.
9. Matiello MA, Jacob AA, Wingerchuk DM, Weinshenker BG. Neuromyelitis optica. *Curr Opin Neurol*. 2007;20(3):255-60. June.
10. Weinshenker BG, O'Brien PC, Petterson TM, et al. A randomized trial of plasma exchange in acute central nervous system inflammatory demyelinating disease. *Ann Neurol*. 1999;46:878-86.
11. Weinstock-Guttman B, Ramanathan M, Lincoff N, et al. Study of Mitoxantrone for the Treatment of Recurrent Neuromyelitis Optica (Devic Disease). *Arch Neurol*. 2006;63:957-63.
12. Cree BA, Lamb S, Morgan K, Chen A, Waubant E, Genain C. An open label study of the effects of rituximab in Neuromyelitis optica. *Neurology*. 2005;64:1270-72.
13. Wingerchuk DM, Hogancamp WF, O'Brien PC, Weinshenker BG. The clinical course of neuromyelitis optica (Devic's syndrome). *Neurology*. 1999;53(5):1107-14. 22 September.
14. Hemmer B, Stüve O. Revised criteria for neuromyelitis optica—a new diagnostic standard? *Nat Clin Pract Neurol*. 2007;3:132-3.
15. Jantos M. Understanding Chronic Pelvic Pain. *Pelvipainology*. 2007;26:66-9.
16. Wingerchuk DM, Lennon VA, Pittock SJ, Lucchinetti CF, Weinshenker BG. Revised diagnostic criteria for neuromyelitis optica. *Neurology*. 2006;66:1485-9.
17. Weinshenker BG. Neuromyelitis Optica Is Distinct From Multiple Sclerosis. *Arch Neurol*. 2007;64:899-901.