62-Year-Old Man With Back Pain and Lower Extremity Weakness

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A 62-year-old man presented to the emergency department with progressive lower back pain and bilateral lower extremity weakness and numbness. His medical history was notable for poliomyelitis characterized by residual weakness of the proximal right lower extremity and chronic back pain. He also had a history of multilevel compressive radiculopathy in the lumbar spine. His symptoms had begun 6 weeks previously with both weakness and numbness in the lower extremities, which progressed to difficulty ambulating. He felt that his weakness was worse proximally than distally. The numbness was described as a “pins and needles” feeling rather than an actual loss of sensation. The back pain was located in the lumbar area midline and radiated to the abdomen with no radiation to his legs. Also of note, he had had a diarrheal illness 2 weeks before symptoms started. He worked at a desk job and reported no tobacco, alcohol, or illicit or prescription drug use. He stated that he had approximately 50 different male sexual partners dating back over 20 years. He used protection only intermittently and had been treated previously for genital herpes. He did not have fever, chills, night sweats, or weight loss.

On initial presentation, he reported that his pain and weakness had worsened and the numbness had spread proximally up his legs and also involved his hands and forearms bilaterally. Physical examination revealed bilateral lower extremity weakness. His strength was graded as 3 (on a scale of 0-5) in the proximal right lower extremity, 4/5 in the distal right lower extremity, and 4/5 both proximally and distally in the left lower extremity. Left triceps weakness was also noted and graded as 3/5. Muscle wasting was noted over the medial and lateral quadriceps, right worse than left with intermittent fasciculations. He was areflexic in the lower extremities and left triceps and had flexor plantar response bilaterally. Decreased superficial pain sensation was also noted in the lateral aspect of the left leg and foot without a clear sensory level. There was no loss of proprioception or vibratory sensation. He was able to stand with some assistance and walk with the aid of a walker. At his baseline, he could stand without assistance and only occasionally needed a walker.

Laboratory studies including a complete blood cell count, electrolyte panel, measurement of hemoglobin A1c, thyrotropin, creatine kinase, aldolase, vitamin B12, thiamine, and monoclonal protein levels, tests for cyclic citrullinated peptide antibodies, antinuclear antibodies, extractible nuclear antigen, and human immunodeficiency virus (HIV), and a tick-borne disease panel yielded no abnormalities. The patient’s C-reactive protein level was elevated at 26.7 mg/L (reference range, €8.0 mg/L). Electromyography was complicated because of his history of poliomyelitis and compressive polyradiculopathy. Results suggested an acute-on-chronic process, likely a polyradiculoneuropathy with mixed axonal and demyelinating features. Lumbar puncture revealed the following (reference ranges provided parenthetically): protein, 111 mg/dL (0-35 mg/dL); total nucleated cells, 27/μL (0-5/μL) with 93% lymphocytes (40%-80%); and glucose, 71 mg/dL (60% of blood value; the patient’s blood glucose level was 143 mg/dL [70-140 mg/dL]). Results of cytologic examination were negative for malignancy. All viral studies performed on the cerebrospinal fluid (CSF) yielded negative results.

Inflammatory demyelinating polyradiculoneuropathy was initially suspected because of the patient’s history of recent diarrheal illness, areflexia, and lower extremity—predominant symptoms. The elevated CSF protein level was noted, although he did not have classic albuminocytologic dissociation because his total nucleated cell level was 27/μL. Classic
albuminocytologic dissociation would include an elevated CSF protein level without an elevated CSF white blood cell count. Treatment with plasma exchange was initiated, and 5 treatments were administered with no notable change in the patient’s symptoms.

1. Which one of the following is the most likely diagnosis at this point?
   a. Motor neuron disease
   b. Multiple sclerosis
   c. Neurosyphilis
   d. Ischemic stroke
   e. Poliomyelitis

   Motor neuron disease can present with primarily upper or lower motor neuron signs or with both upper and lower signs simultaneously. Symptoms typically do not progress as quickly as those experienced by our patient and are initially unilateral in most cases. This patient’s sensory symptoms also make motor neuron disease unlikely. Multiple sclerosis typically presents with intermittent attacks of symptoms followed by periods of recovery or stability. Symptoms are caused by demyelinating disease of the central nervous system, leading to primarily upper motor neuron signs. Our patient had primarily lower motor neuron signs, as well as a progressive course over weeks to months without periods of remission. Neurosyphilis should be strongly considered because of the patient’s history of multiple sexual partners and only intermittent use of protection. Neurosyphilis can present in a wide variety of ways through a variety of mechanisms and should be considered in all patients with neurologic symptoms. Progressive symptoms over a period of weeks to months are not typical of ischemic stroke. Our patient’s symptoms could be localized to an arterial distribution and did not have sudden onset. Poliomyelitis would not explain the clinical worsening or the new sensory symptoms. The patient’s weakness progressed too quickly and was outside the distribution of his previous baseline, which was due to poliomyelitis.

   At this point, syphilis testing returned positive results, and neurosyphilis was diagnosed.

2. Which one of the following is the most specific test for evaluation of the patient’s condition?
   a. CSF-Venereal Disease Research Laboratory (CSF-VDRL) test
   b. Serum rapid plasma reagin (RPR) test
   c. CSF fluorescent treponemal antibody absorption (CSF-FTA-ABS) test
   d. Magnetic resonance imaging (MRI) of the brain
   e. C-reactive protein measurement

   Examination of the cerebrospinal fluid is essential during evaluation for neurosyphilis. The CSF-VDRL test is the most specific of the listed tests for neurosyphilis; however, results may be falsely negative in up to 50% of patients. It is widely available and inexpensive. A reactive CSF-VDRL test establishes a diagnosis of neurosyphilis even if the patient is asymptomatic, although a negative test result does not rule it out. The serum RPR test is a sensitive test for syphilis and has been used as a marker of disease activity. It is not specific for syphilis. The CSF-FTA-ABS test is a sensitive test for neurosyphilis. In the presence of a negative result on CSF-VDRL testing, a negative result on the CSF-FTA-ABS test can effectively rule out the diagnosis of neurosyphilis. Tests for syphilis can be divided into nontreponemal, treponemal, and direct tests. Nontreponemal tests (RPR, CSF-VDRL) are semiquantitative in that the results wax and wane over time, especially with treatment. They are not specific studies. Treponemal tests (FTA-ABS) are qualitative only and are based on the detection of antibodies against Treponema pallidum. They have historically been used as confirmatory studies after positive results on nontreponemal tests because they are generally more specific and are more expensive and difficult to perform. Direct tests include dark-field microscopy and direct fluorescent antibody testing. They are not commonly used and involve direct visualization of spirochetes. No single test is both highly sensitive and specific for neurosyphilis, and these tests may not rule out the diagnosis when clinical suspicion is high. Although it can be used to visualize gummas, MRI in patients with neurosyphilis can reveal swelling of the optic nerves and edematous changes mimicking viral encephalitis. It is generally nonspecific. C-reactive protein is an acute-phase reactant and is elevated in a wide variety of infectious and noninfectious inflammatory diseases.
Results of the CSF-VDRL, serum RPR, and syphilis IgG antibody tests were positive in our patient. A retinal photograph revealed some mild optic disc edema, and MRI of the head and orbits showed left optic disc edema.

3. Which one of the following is not a known presentation of infection with this organism?
   a. Tabes dorsalis
   b. Meningitis
   c. Vasculitis
   d. Progressive demyelinating disease
   e. General paresis

   Tabes dorsalis is primarily a disease of the dorsal roots and posterior columns of the spinal cord that occurs anywhere from 3 to 20 years after primary infection with *T. pallidum*. It is associated with bladder dysfunction, shooting pains, sensory ataxia, pupillary abnormalities, and loss of vibratory and position sensation. Symptomatic meningitis caused by infection with *T. pallidum* typically occurs within the first year of infection and can coexist with other findings of early syphilis. Symptoms can include headache, nausea, and vomiting, mental status change, polyradiculopathy, back or neck pain, sensory changes, muscle atrophy, weakness, or cranial neuropathies. It can also present with gummas causing symptoms of mass effect including seizures. *Treponema pallidum* can also lead to arteritis resulting in infarction or ischemia, often associated with the aforementioned meningeal symptoms. Infection with *T. pallidum* causes disease through a wide variety of mechanisms but has not been associated with a progressive demyelinating condition. General paresis typically develops 10 to 25 years after primary infection and is a progressive dementing illness. Symptoms include forgetfulness, mood changes, and personality changes. Affected patients may have generally normal results on neurologic examination, and this is an important diagnosis to consider when treating a patient with dementia.1,2

   Our patient presented with progressive polyradicular symptoms, including weakness, pain, muscle atrophy, and sensory changes. These symptoms are most typical of somewhat early neurosyphilis associated with infection and inflammation of the meninges and nerve roots of the spinal cord.

4. Which one of the following is the most appropriate treatment for the patient’s condition?
   a. Penicillin G
   b. Doxycycline
   c. Plasma exchange
   d. Intravenous corticosteroids
   e. Azithromycin

   Penicillin G is the treatment of choice for neurosyphilis. It can be administered in an aqueous crystalline intravenous form at 18 to 24 million U/d divided into doses given every 4 hours for 10 to 14 days.3 A loading dose of 5 million U is sometimes used in addition. Desensitization is recommended in patients who are allergic to penicillin. Doxycycline can be used to treat early syphilis as well as latent syphilis in penicillin-allergic patients. It is not recommended by any guidelines for patients with neurosyphilis. Plasma exchange has no role in the treatment of neurosyphilis. It is used in a variety of conditions including inflammatory demyelinating polyneuropathy, myasthenia gravis, and hematologic and immunologic conditions. Intravenous corticosteroids are not a part of the current treatment regimen for neurosyphilis. Corticosteroids have been used to attempt to reduce the severity of Jarisch-Herxheimer reaction, but their effectiveness remains unproven. Azithromycin is a macrolide antibiotic used to treat a wide variety of diseases. It is one of the most commonly prescribed antibiotics in the United States and has been used to treat early-stage syphilis in patients with penicillin allergies who also have a contraindication to doxycycline. Its use is not currently recommended in treatment guidelines for neurosyphilis.

   Treatment with intravenous penicillin G at 5 million U was initiated, followed by continuous infusion of 24 million U/d for 14 days.

5. Which one of the following is the most important follow-up step in a patient treated for this condition?
   a. Lifelong antibiotics
   b. Repeated CSF testing
   c. Repeated serum IgG testing for *T. pallidum*
   d. MRI of the brain
   e. Antiepileptic medication

   Lifelong antibiotics are not a part of current neurosyphilis treatment regimens. Treatment...
typically lasts a total of 10 to 14 days with possible retreatment based on follow-up testing results. Repeated cerebrospinal fluid testing is an important part of treatment in patients with neurosyphilis. It should be performed every 6 months until normalization of the CSF white blood cell count and the CSF-VDRL test is nonreactive. Failure to meet these criteria by 1 year after therapy should prompt retreatment. All CSF abnormalities should be completely resolved by 2 years after initial therapy. Normalization of the CSF may take longer in patients who are also infected with HIV. Serum IgG test results for T. pallidum antibodies can remain positive for years to life after infection and are not a good measure of response to treatment or current disease activity. Imaging studies, including MRI, are not typically used to monitor treatment response or disease activity in patients with neurosyphilis and are not typically included in follow-up testing. Antiepileptic medication is not a standard part of follow-up in patients with neurosyphilis and there was no other indication for it in our patient.

Our patient was discharged to a skilled nursing facility with plans to recheck the CSF every 6 months until the VDRL test result, white blood cell count, and protein level returned to normal. Follow-up neurology and ophthalmology appointments were scheduled.

DISCUSSION

Syphilis is an infection with T. pallidum and can affect many systems including the integumentary, musculoskeletal, cardiovascular, and central nervous systems. Infection begins with invasion of the CSF and spreads to the meninges, blood vessels, spinal cord, brain, or nerve roots.

In our patient, the primary risk factor was unprotected sexual intercourse with multiple partners. Currently, neurosyphilis is most frequently seen in HIV-infected patients, although it is not known if this prevalence is due to a difference in patient-to-patient susceptibility or if it simply reflects patient lifestyle and common risk factors. Presentations vary by site of infection and can range from asymptomatic to potentially fatal disease. Patients with lower CD4 counts are more likely to be symptomatic than those with higher counts.

Other risk factors for syphilis among HIV-infected patients include sildenafil and methamphetamine use, as well as having recent partners found on the Internet. Compared with HIV-negative patients, HIV-positive patients may have a higher risk of treatment failure or early progression to neurologic disease. Neurosyphilis is diagnosed with lumbar puncture and treponemal, nontreponemal, and direct testing. Lumbar puncture should be considered in patients with unexplained neurologic signs or with known risk factors for syphilis, particularly HIV-infected individuals. This cohort of patients should undergo lumbar puncture with VDRL testing if they experience any unexplained neurologic symptoms or have any reactive serum serologic test result with accompanying neurologic deficit. Lumbar puncture should also be considered in any patient with RPR titers of 1:32 or higher.

Our patient’s situation was complicated by his history of poliomyelitis as well as spinal disease. He presented with symptoms of polyradiculopathy including back pain, weakness, sensory deficits, and muscle wasting. By not focusing on a diagnosis of inflammatory demyelinating polyradiculoneuropathy, we were able to determine the true cause of our patient’s symptoms. In his classic syphilis text Modern Clinical Syphilology, Dr John Stokes wrote, “The frequency of neurosyphilis in general medical practice depends to a large extent on the thoroughness of the search for signs of neuraxis involvement and the frequency with which the spinal fluid examination is employed.” This case is a good reminder that Stokes’ statement remains true today, and testing for “the great imitator” should be considered when investigating neurologic disease.

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REFERENCES


CORRECT ANSWERS: 1. c. 2. a. 3. d. 4. a. 5. b