Mimickers of Cervical Spondyloïtic Myelopathy

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Abstract

» Many disorders present similar to cervical spondyloïtic myelopathy.

» Mimickers can be differentiated from cervical spondyloïtic myelopathy through a detailed history and physical examination.

» Differentiating between etiologies is aided by electrodiagnostic studies and adjunctive studies using radiographs and magnetic resonance images.

Cervical spondyloïtic myelopathy is a condition of neurologic impairment resulting from the spinal canal narrowing secondary to the degeneration of cervical structures. This causes spinal cord compression gradually. Severity varies across individuals. Progression is typically slow and generates changes in both the cord and the periphery. Cervical spondyloïtic myelopathy is the most common disorder causing dysfunction of the spinal cord. However, patients may present with similar symptoms caused by various other conditions. Pathologic conditions that affect the spinal cord, or neighboring structures, should not be overlooked when evaluating patients with myelopathy. Table I provides other conditions that must be considered.

Cervical Spondyloïtic Myelopathy

Cervical spondyloïtic myelopathy typically presents insidiously and comprises a broad spectrum of signs and symptoms. Patients may initially present with axial neck pain or limitations in the neck range of motion. Subtle signs such as decreased hand dexterity or mild balance impairment may go unnoticed in early disease. Difficulty opening jars, buttoning shirts, or writing may be clinical indicators of cervical spondyloïtic myelopathy. Ono et al. used the term myelopathy hand when describing upper-extremity findings. This includes the inability to grip and release the hand rapidly and the presence of the finger escape sign, in which the ulnar 2 digits drift into flexion and abduction during extension of the metacarpophalangeal and interphalangeal joints. Severe sequelae include loss of bowel and bladder function, spasticity, and gait instability. Positive Hoffman or Babinski signs are clinical indicators of myelopathy.

Table I demonstrates the common signs and symptoms of cervical spondyloïtic myelopathy.

Patients may experience stable periods with slow, stepwise decline in function or rapid decline. Persistent symptoms, without transience or fluctuation, distinguish cervical spondyloïtic myelopathy from other disorders. Sequelae such as sensory loss, motor weakness, or gait instability may not be present in every patient.

Diagnosing cervical spondyloïtic myelopathy is largely reliant on history and physical examination. However, other modalities are critical in making the diagnosis. Rhee et al. performed a prospective case-control study on the prevalence of physical signs in cervical spondyloïtic myelopathy. Thirty-nine patients with cervical spondyloïtic myelopathy and 37 controls were included. Twenty-one percent of patients with cervical spondyloïtic myelopathy did not have any myelopathic signs on examination.

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<th>Mimicker</th>
<th>History and Physical Examination</th>
<th>Diagnosis</th>
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<tr>
<td>Multiple sclerosis</td>
<td>Fatigue, diplopia, bladder disturbances, difficulty with gait, unilateral leg numbness</td>
<td>2 lesions in the white matter, 2 episodes in the disease course, oligoclonal bands in cerebrospinal fluid, raised IgG</td>
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<tr>
<td>Amyotrophic lateral sclerosis</td>
<td>Muscle atrophy, weakness, fasciculations, Hoffman sign, clonus, Babinski sign, foot drop, loss of dexterity, difficulty with gait</td>
<td>Widespread lower motor neuron disease on EMG, bilateral changes within corticospinal tracts on brain MRI</td>
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<tr>
<td>Parkinson disease</td>
<td>Slowness of initiation, movement, and thought; postural and resting tremors; and extrapyramidal rigidity; symptoms will start in 1 limb and, over 2 to 5 years, will involve both limbs</td>
<td>On brain MRI, striatum and pallidum will appear normal; on high-field T2-weighted sequences, an altered nigral signal will be demonstrated; surface EMG can be helpful in determining the frequency and amplitude of a tremor</td>
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<tr>
<td>Carpal tunnel syndrome</td>
<td>Pain in hand, decreased sensation in median nerve distribution, reduced grip strength, night symptoms, thenar atrophy in late stages</td>
<td>Based on history and physical examination, in equivocal cases, electrodiagnostic studies are helpful</td>
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<tr>
<td>Cubital tunnel syndrome</td>
<td>Decreased sensation in the ulnar nerve distribution, intrinsic weakness and weakness of the small and ring finger flexor digitorum profundus, Wartenberg sign</td>
<td>Based on history and physical examination, in equivocal cases, electrodiagnostic studies are helpful; on electrodiagnostic studies, ulnar nerve velocity must be &lt;50 m/s at elbow level</td>
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<td>HIV</td>
<td>Lower-extremity weakness, vague discomfort in legs, gait ataxia, erectile dysfunction (men), bowel or bladder disturbance</td>
<td>Spinal MRI shows extensive central high-signal areas on T2, mainly cervicodorsal</td>
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<td>HTLV-1</td>
<td>Slowly progressive chronic spastic paraparesis, spastic bladder</td>
<td>HTLV-1 antibodies in serum and cerebrospinal fluid</td>
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<td>Syphilis</td>
<td>Incoordination, pain, absent ankle jerks, impaired vibratory sensation, Romberg sign, Argyll-Robertson pupils, autonomic dysfunction</td>
<td>High signal on T2 MRI with enhancement of the spinal surface that disappears</td>
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<td>Guillain-Barré syndrome</td>
<td>Rapidly progressive distal weakness that spreads proximally, severe weakness in shoulder abduction and elbow extension, urinary retention, ileus, sinus tachycardia, hyperreflexia, and areflexia</td>
<td>Illness 7 to 10 days prior; clinical diagnosis, but EMG and nerve conduction study demonstrate severe neuropathy; cerebrospinal fluid may have raised protein content</td>
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<tr>
<td>Acute transverse myelitis</td>
<td>Flaccid paraparesis of lower extremities that can also involve the arms, well-defined sensory level</td>
<td>Focal and central high-signal areas in T2 sequences, occupying more than two-thirds of the spinal cord axially, and extending over 3 to 4 segments</td>
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<td>Vitamin B12 deficiency</td>
<td>Diminished proprioception, decreased vibration sensation, motor weakness, hyperreflexia, gait disturbance, intellectual impairment, impaired vision</td>
<td>Vitamin B12 serum levels; MRI shows T2 hyperintense signal alterations usually confined to posterior columns, but may involve lateral columns or brain stem</td>
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<td>Syringomyelia</td>
<td>Intrinsic weakness, cape-like sensory loss, loss of pain and temperature sensation, hyperreflexia, gait disturbance, diplopia, dizziness</td>
<td>MRI demonstrating syrinx</td>
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<tr>
<td>Radiation damage</td>
<td>Lhermitte sign, Brown-Sequard-type symptoms, ascending sensorimotor disturbance, tetraplegia and paraplegia, local myelopathy</td>
<td>Spinal cord segment in irradiated zone, &gt;6-month latency period, normal cerebrospinal fluid analysis, local spinal edema, and contrast enhancement on T2 for at least 8 months after latency period</td>
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<td>Paraneoplastic etiology</td>
<td>Insidiously progressive myelopathy; may occur prior to cancer diagnosis</td>
<td>Increased protein concentration in cerebrospinal fluid; longitudinally extensive, symmetric, tract-specific signal changes on MRI</td>
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<td>Vascular etiology</td>
<td>Asymmetric leg weakness, worse with walking or standing for long periods</td>
<td>Flow voids on MRI, engorged draining medullary veins and feeding arteries within cerebrospinal fluid</td>
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<td>Hepatic etiology</td>
<td>Progressive pure motor spastic paraparesis, minimal sensory deficit</td>
<td>Diagnosis of exclusion; decompensated liver disease, post-liver transplant, post-shunt surgery</td>
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<td>Alcoholic etiology</td>
<td>Paresthesias of feet with progressive spastic paraparesis, sometimes bladder dysfunction</td>
<td>Alcoholism without substantial liver disease</td>
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Magnetic resonance imaging (MRI) is the imaging standard for cervical spondylotic myelopathy because it evaluates the spinal soft tissues. It is imperative to match the clinical findings with the MRI because it has been reported that up to 57% of patients >65 years of age have degenerative disc disease and herniation with no symptoms.

In diagnosing cervical spondylotic myelopathy, electrodiagnostic studies are not typically useful. However, they can help to rule out other diagnoses. Evidence suggests that somatosensory-evoked potentials (in 61.9% of cases) and motor-evoked potentials (in 71.4% of cases) demonstrate changes in the presence of cervical spondylotic myelopathy findings on MRI.

Neuromuscular Mimickers

Multiple sclerosis is a chronic autoimmune central nervous system disease. It destroys myelin and axons to varying degrees by attacking central nervous system myelinated axons. The disease course is highly varied, but typically presents as episodes of reversible deficits, followed by progressive neurologic deterioration.

Initial findings are sensory disturbances, most commonly paresthesias, dysesthesias, diplopia, incontinence, and vertigo. Unilateral leg numbness that ascends the pelvis, abdomen, or thorax and spreads to the other leg is a common finding.

Amyotrophic lateral sclerosis is a term that encompasses several adult-onset conditions characterized by progressive motor neuron degeneration. Amyotrophic lateral sclerosis is also a term for one specific disease. Amyotrophic refers to the lower motor neuron disease signs and symptoms. These include the muscle atrophy, weakness, and fasciculations seen with this disease. Lateral sclerosis refers to corticospinal tract hardening from gliosis causing upper motor neuron signs, including overactive tendon reflexes, the Hoffman sign, clonus, and the Babinski sign. Lower motor neuron loss causes substantial weakness. Often, the weakness from lower motor neuron loss is more disabling than the upper motor neuron symptoms.

Initially, patients with amyotrophic lateral sclerosis have unilateral and focal symptoms. This begins in the arms in two-thirds of patients, but can be seen in the legs as well. Early findings include foot drop, difficulty walking, and loss of hand dexterity. As the disease progresses, patients increasingly require the help of caregivers. Many patients with amyotrophic lateral sclerosis lose the ability to ambulate.

The diagnosis is 95% accurate when made by experienced clinicians. Electrodiagnostic studies confirm widespread lower motor neuron disease and exclude other diseases. To rule out upper motor neuron conditions, advanced imaging is necessary, and brain and spinal MRI scans are best. Findings consistent with amyotrophic lateral sclerosis demonstrated on a brain MRI scan include bilateral signal changes within the corticospinal tracts.

Parkinson disease, along with parkinsonian syndromes, has symptoms that are often confused with cervical spondylotic myelopathy. Progressive supranuclear palsy, multiple system atrophy, and corticobasal degeneration are parkinsonian syndromes. The underlying pathology of Parkinson disease is apoptosis in the basal ganglia, specifically the substantia nigra’s dopamine-secreting neurons. Also

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<td>Common symptoms</td>
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<td>Clumsy or weak hands</td>
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<td>Leg weakness or stiffness</td>
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<td>Neck stiffness</td>
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<td>Pain in shoulders or arms</td>
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<td>Unsteady gait</td>
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<td>Common signs</td>
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<td>Weakness of the hand musculature</td>
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<td>Hyperreflexia</td>
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<td>Lhermitte sign (electric shock-like sensation down the center of the back following flexion of the neck)</td>
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<td>Sensory loss</td>
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In >33% of patients with multiple sclerosis, moderate to severe lower-extremity spasticity is seen. The symptom most routinely seen is fatigue, which affects 80% of patients. The patients with multiple sclerosis who are most affected by fatigue are those with progressive disease and those who have difficulty with ambulation. Fatigue causes substantial morbidity, even in those patients who are nonambulatory.

Chronic neuropathic pain can evolve from sensory disturbances, although this is uncommon. Trigeminal neuralgia also occurs. Optic neuritis is another common symptom and presents with complete or partial vision loss.

No single diagnostic test exists for multiple sclerosis. To make the diagnosis of multiple sclerosis, there must be 2 separate central nervous system white matter lesions along with chronic central nervous system inflammation. Central nervous system inflammation is determined by analyzing the cerebrospinal fluid. In addition to these findings, the patient must have had 2 different symptomatic episodes.

On cerebrospinal fluid analysis of patients with multiple sclerosis, oligoclonal bands are present in >90% of patients and a raised immunoglobulin G index is present in >60% of patients. One additional study that may prove helpful is visually evoked response testing. Subclinical optic nerve involvement may be evident in some patients.

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Peripheral Nerve Entrapment

Carpal tunnel syndrome is the most common entrapment neuropathy. It is caused by median nerve compression at the level of the carpal tunnel. Clinically, patients report pain in the hand, decreased sensation in the thumb and the index, long, and radial ring fingers, and weakened grip strength. Night symptoms are typically present. Clumsiness while performing tasks is reported. In late stages, thenar atrophy appears.18

Diagnosis can often be made on history and examination. Patients may have positive provocative signs, which can help differentiate carpal tunnel syndrome from cervical spondylotic myelopathy. If examination is equivocal, electrodiagnostic studies can be helpful in establishing the site of compression.19

Ulnar nerve entrapment at the elbow, called cubital tunnel syndrome, can mimic myelopathic hand, and is the second most common entrapment neuropathy. With cubital tunnel syndrome, patients experience decreased sensation in the ulnar nerve distribution. As compression worsens, motor dysfunction begins. Intrinsic weakness and weakness of the small and ring finger flexor digitorum profundus cause catching when reaching into pockets.20 This is from overpowering of the small finger extensor without intrinsic opposition, causing abduction, or the Wartenberg sign. In cervical spondylotic myelopathy, insufficiency of finger adduction and/or extension starts and is greatest in the ulnar digits.21

Radiographs should be obtained to evaluate cervical spine degeneration. Electrodiagnostic studies are helpful in establishing the site of compression. For a finding to be positive for cubital tunnel syndrome, the ulnar nerve velocity should be <50 m/s at the level of the elbow.20

Peripheral nerve disorders, either peripheral nerve entrapment or polyneuropathy, can mask signs of myelopathy such as sensory loss, intrinsic muscle atrophy, and clumsiness.22 This combination of peripheral and central nerve disorders has been referred to as double-crush syndrome or multifocal neuropathy, in which the nerve is compressed at multiple sites.23 This can lead to symptoms of radiculopathy or myelopathy. A centrally located lesion may make the distal site more vulnerable to compression. Patients with double-crush syndrome who undergo peripheral nerve decompression have poorer results.24,25

It is important to continually question whether the working diagnosis of a peripheral nerve disorder explains the clinical findings, if a neurologic decline is observed, or whether a superimposed worsening myelopathy may coexist. Early diagnosis is aided by assessing spinohalamic and posterior column sensation and assessing these sensory modalities for proximal and distal portions of the limbs. Hyperreflexia of muscles distal and proximal should also be assessed. Electrodagnostic studies and MRI are helpful in making the diagnosis.22,25

Infectious and Immune-Mediated Mimickers

Timely diagnosis is imperative in infectious myelopathies. In para infectious myelopathy, infection and an associated immune reaction cause neurologic damage. In the context of infectious myelopathies, many different organisms may be the source. These include Treponema pallidum, Mycobacterium tuberculosis, herpes viruses, human immunodeficiency virus (HIV), human T-cell lymphotropic virus type I (HTLV-I), enteroviruses, fungi, and parasites. Some of the more common organisms are discussed below.

HIV-associated vacuolar myelopathy is the most common form of HIV myelopathy. Patients report lower-extremity weakness, difficulty with balance and gait, and bladder dysfunction.26 Some have indistinct discomfort in the lower extremities as well as parasthesias. A hallmark of HIV-associated vacuolar myelopathy is erectile dysfunction in men.27

On examination, spastic paraparesis is present, with weakness that exceeds spasticity. Other symptoms that may been seen are greater weakness in 1 leg, monoparesis, quadriparesis, gait ataxia, or dysmetria. On examination,
weakness may be present or absent. However, hyperreflexia of the lower extremities and a Babinski sign are typically present.28

Spinal MRI may be helpful in making a diagnosis. Diffuse central high-signal areas in T2 sequences in the cervicodorsal region are seen. Brain MRI is often not helpful; however, some abnormalities may be seen and include white matter changes similar to the findings in acute demyelinating encephalopathy.28

The incidence of HTLV-I has increased in recent years because the disease has been found in many intravenous drug abusers. In addition to chronic progressive myelopathy, HTLV-I has been associated with adult T-cell leukemia and lymphoma.29

Tropical spastic paraparesis (TSP) or HTLV-I–associated myelopathy (HAM) are terms that describe HTLV-I myelopathy. Often in HAM/TSP, patients will have chronic spastic paraparesis that is gradually progressive and spastic bladder.29,31 Patients may also experience areflexia, decreased sensation, and pain. Chronic pyramidal tract involvement is present.

The HAM/TSP diagnosis is based on laboratory and clinical evidence, including HTLV-1 antibodies in serum and cerebrospinal fluid. A very effective method of diagnosing HAM/TSP is by combining cerebrospinal fluid HTLV-I DNA and the intrathecal synthesis of antibodies to HTLV-I.32

Within the first year, the infectious agent of syphilis, *Treponema pallidum*, can occupy the central nervous system. Spinal syphilis has variable manifestations. *Tabes dorsalis* is the most common form, followed by meningomyelitis, and finally spinal vascular syphilis. Historically, syphilis was the most common cause of spinal cord disease. However, it has become much rarer since the advent of antibiotics.33

*Tabes dorsalis* presents with pain, sensory disturbances, incoordination, and visceral trophic abnormalities.33 Findings commonly observed are absent ankle reflexes and decreased vibratory sensation. The course of disease comprises 3 phases. The first stage is called the pre-ataxic phase, or period of lightning pain. Early findings include impotence and sphincter disturbances. Examination demonstrates muscle stretch reflex absence, sensory disturbance, Argyll-Robertson pupils, and a positive Romberg sign. The second phase is the ataxic phase, characterized by worsening tabetic pain and severe lower-extremity ataxia. The third stage is called the terminal or paralytic stage. Spastic paraparesis, cachexia, and autonomic dysfunction are typical characteristics. This includes severe constipation and bladder incontinence.33

Syphilitic myelopathy appears as a high signal on a T2-sequence MRI, with spinal surface enhancement that disappears, signifying that it is reversible.33

Guillain-Barré syndrome is an acute autoimmune disorder, in which the immune system attacks the peripheral nervous system, resulting in neuropathy. It is the leading cause of flaccid paralyzis in the world today. Guillain-Barré syndrome expresses in several different ways. It presents as a spectrum involving varying peripheral-nerve disorders and is characterized by the distribution of weakness of the limbs or cranial-nerve-innervated muscles, pathologic abnormalities, and findings of autoantibodies on testing.34,35

The onset of disease presents with sensory changes in the legs, followed by rapidly progressive weakness distally that spreads proximally. Another common finding is lumbar pain, which may represent nerve root inflammation. The weakness is typically pyramidal, with knee and hip flexion and ankle dorsiflexion being severely affected. The weakness in the upper extremities is worse in shoulder abduction and elbow extension. Sensation loss is typically minimal; however, vibratory sensation and proprioception may be affected.35

In Guillain-Barré syndrome, autonomic involvement is common. This can cause hypertension, ileus, postural hypotension, urinary retention, sinus tachycardia, and cardiac arrhythmia.37 Although most patients with Guillain-Barré syndrome have findings of hyporeflexia or areflexia, normal or brisk reflexes are present in a small subset of patients.37

Seventy-five percent of patients have a preceding illness, which may be mild or asymptomatic. Often, the illness is respiratory or gastrointestinal in nature. Typically, the neuropathy begins 7 to 10 days after infection.37 In most cases, the patient has an acute neuropathy, which peaks within 4 weeks. These patients typically have weakness, diminished reflexes, and raised cerebrospinal fluid protein concentrations.

Because of the rapid onset of the neuropathy, and associated weakness in someone recovering from illness, patients may be incorrectly diagnosed with a psychological disorder. Patients typically reach a plateau phase, which can vary in length of time. Following the plateau, recovery begins with return of proximal, then distal, strength over weeks or months. Despite modern advances, this remains a dangerous disease, with 4% to 15% of patients dying, and up to 20% remaining disabled after a year.36,37 There is a large differential diagnosis and the correct diagnosis is reliant upon the clinician recognizing that the problem is an acute peripheral neuropathy, not central.

Electrodiagnostic studies can be helpful in characterizing the neuropathy. A lumbar puncture is used to rule out infection or malignancy, such as lymphoma.37 However, raised cerebrospinal fluid protein content may be seen with Guillain-Barré syndrome.

Acute transverse myelitis is an inflammatory disorder of the spinal cord. The term acute transverse myelitis is occasionally used synonymously with non-compressive myelopathy. However, the term non-compressive myelopathy covers a diverse group. At the level of the spinal cord, the entire cross-sectional area at 1 level is involved, including pyramidal tracts, spinothalamic tracts, and posterior columns.

There are multiple different non-compressive causes of acute transverse myelitis. These include but are not
limited to paraneoplastic causes, anterior spinal artery thrombosis, and vasculitis in autoimmune diseases. Autoimmune diseases with associated vasculitis include systemic lupus erythematosus, mixed connective tissue disease, and scleroderma. Other causes are infections such as herpes zoster, rubella, HIV, Epstein-Barr virus, Mycoplasma pneumoniae, Echo-25 virus, and mumps. It may follow cholera vaccination, typhoid, and poliomyelitis and has been reported with penicillin injections, heroin abuse, sulfasalazine chemotherapy, B-cell lymphoma, myelomonocytic leukemia, and general anesthesia or acupuncture.

A typical presentation of acute transverse myelitis includes leg weakness that appears suddenly, diminished sensation with loss of sphincter control, and pain with no obvious spinal cord compression. The weakness is typically a progressive flaccid paraparesis, and it can involve the upper extremities. Generally, by the second week of illness, pyramidal signs appear. Within 10 days of onset, most patients, about 80%, reach their clinical low-point. During the acute phase, patients’ neurologic function usually deteriorates progressively. This typically occurs over a period of 4 to 21 days.

The defined sensory level is between T5 and T10 in 70% of cases. There is a cervical sensory level in about 20% of cases. Adults with acute transverse myelitis note paresthesias at the outset of the disorder. In a large percentage of children (approximately 40%), an illness occurs within 3 weeks of the onset of acute transverse myelitis.

The diagnosis of transverse myelitis is one of exclusion, and the time course lasts from 4 hours to 4 weeks. Transverse myelitis criteria includes spinal cord dysfunction bilaterally with a defined sensory level and no compressive history. On MRI, there are findings specific to acute transverse myelitis, which makes it helpful for diagnosis. On T2 axial cuts, central high-signal areas occupy more than two-thirds of the spinal cord and extend over 3 to 4 segments. In 40% of cases, no MRI findings are present.

**Vitamin B12 Deficiency**

Vitamin B12 deficiency can cause several different disorders. Typical causes of vitamin B12 deficiency include pancreatic insufficiency, medications, and malabsorption. A rare, but notable, cause of acute vitamin B12 inactivation is nitrous oxide exposure.

The neurologic symptoms present in vitamin B12 deficiency include autonomic dysfunction, gait disturbance, paraesthesia, diminished proprioception and vibratory sensation, weakness, hyperreflexia, areflexia, intellectual or behavioral impairment, and impaired vision.

Vitamin B12 deficiency primarily causes deficiency of the posterior columns, but also affects the anterolateral and anterior portions of the spinal cord as well. This is known as subacute combined degeneration. It is most commonly seen in the cervical and thoracic cord, and includes a diffuse, multifocal pattern of demyelination and axonal loss. Furthermore, myelin sheath swelling and a patchy myelopathic spongiform vacuolation of affected regions of the cord are typically seen.

On MRI, subacute combined degeneration presents as a T2 hyperintense signal that is usually confined to the posterior columns, but may include the lateral columns and brainstem.

**Syringomyelia**

Syringomyelia is a rare condition, in which fluid-filled areas along the spinal cord develop slowly. This is also known as a syrinx. Causes may be congenital or acquired. These include trauma, tuberculosis-associated chronic arachnoiditis, and tumors. Chiari malformation causes most nontraumatic forms. Chiari malformation is a congenital abnormality in which the cerebellar arachnoid阙 herniates through the foramen magnum. This causes altered cerebrospinal fluid flow, which can lead to syrinx formation.

Patients may experience diplopia, headaches, dizziness, and arm weakness.

The classic symptoms associated with Chiari malformation include upper-limb weakness and cape-like suspended sensory loss. The hand weakness begins in the intrinsic musculature and spreads proximally. Although classic findings, these are rare since the advent of MRI.

In the early stages, there may be progressively worsening neurologic deficits. In some cases, there is an acute loss of spinal cord function. The earliest symptoms are often gait disturbance or radiculopathy with associated numbness or weakness in one arm. The hands may be especially affected. The sensory symptoms of capelike sensory loss appear late, typically once spinal cord dysfunction becomes obvious. On examination, leg weakness may be present, as well as spasticity, hyperreflexia, and upper-limb weakness and wasting. Patients may experience sensory loss in dissociated patterns, with preservation of touch and position sense, but loss of pain and temperature sensation.

**Radiation Damage**

A rare but devastating complication of radiation therapy is radiation-induced myelopathy. It is seen with previous exposure to head and neck irradiation. Radiation therapy can cause central nervous system injury at 3 different points in time. During radiation therapy, patients can experience a transient increase in cerebral edema from blood-brain-barrier disruption. This is an acute radiation injury. Weeks to months after the administration of radiation therapy, early-delayed radiation injury can occur. Finally, transient demyelination can occur following cervical spine irradiation. This primarily affects the posterior columns, causing Lhermitte syndrome. This final stage presents like chronic progressive Brown-Séquard syndrome and lasts 3 months to 5 years.

The presentation is slowly progressive ascending sensorimotor disturbance including tetraplegia or paraplegia, with bowel and bladder disturbances. The sensory loss often resolves within 2 to 36 weeks.
To make the diagnosis of radiation-induced myelopathy, the affected spinal cord segment must be in the irradiated zone, the symptoms must correspond to the involved spinal cord segment, and there must be a latency period of >6 months. Cerebrospinal fluid analysis is typically normal. MRI shows a local spinal high T2-sequence signal at least 8 months after the end of the latency period. Subsequently, signal intensity is normal but severe atrophy remains.

**Paraneoplastic Etiology**

Paraneoplastic syndromes are symptoms that occur in conjunction with a tumor or metastases. They are rare, but essential considerations when evaluating myelopathy. Symptoms may occur before any cancer is suspected. The myelopathy due to paraneoplastic etiology is normally insidiously progressive. Rarely, patients undergo a relapsing-remitting course.

Paraneoplastic syndromes are caused by several factors, including antibodies and neurochemical factors. Subacute myelopathy can be associated with antibodies present with lung, breast, prostate, ovarian, and thyroid cancers and Hodgkin lymphoma. For instance, patients with small-cell lung carcinoma can develop autoimmunity to collapsing response mediator protein 5 (CRMP5). Autoimmunity to this antibody leads to myelopathy and optic neuropathy, which mimics neuromyelitis optica. Other paraneoplastic conditions mimic myelopathy, but are due to neurochemical mediators. One such neurochemical mediator is glutamate decarboxylase 65 (GAD65). Autoimmunity to GAD65 causes stiff person syndrome. The associated spasms with this condition may mimic spasticity. Additionally, anti-amphiphysin antibodies, occasionally present in stiff person syndrome, cause rigidity and myoclonus, which may mimic the spasticity seen in cervical spondylotic myelopathy.

The pathognomonic finding on MRI is longitudinal and symmetric signal changes specific to tracts within the spinal cord that enhance with administration of gadolinium. Often, increased cerebrospinal fluid protein concentration is present.

**Vascular Etiology**

Spinal cord vascular malformations may cause myelopathy. This presents with nonspecific symptoms, often distal to the malformation. Early treatment offers the best chance for recovery.

Spinal vascular malformations are categorized on the basis of anatomy and location. The most common are dural arteriovenous fistula malformations. An arteriovenous fistula malformation is dural, or extraspinal, in 75% of cases. In 10% of cases, intraspinal arteriovenous fistula malformations are present. Twelve percent of spinal malformations are cavernous malformations.

Initial symptoms include gait disorders, paresthesias, numbness, radiculopathy, asymmetric lower-extremity weakness, and bleeding in 25% of cases. The symptoms of myelopathy from spinal cord arteriovenous fistula malformations are exacerbated with walking or standing for long periods.

Another cause of vascular myelopathy is acute vascular occlusion, which causes an infarct. The initial symptoms include severe motor and sphincter dysfunction, pain, and temperature changes, with no loss of proprioception or vibratory sensation. These symptoms present within 4 hours.

In the acute stage, diagnosing myelopathy due to cord ischemia is challenging because of a lack of diagnostic criteria. It is generally found in patients >50 years of age. To define the spinal arteriovenous fistula malformation nidus on MRI, flow voids must be visible in the form of decreased signals on T1 and T2-weighted images. On T2 images, engorged draining medullary veins and feeding arteries are demonstrated. In patients suspected of having spinal arteriovenous fistula malformations, spinal angiography must be included in the evaluation. This is the gold standard.

**Hepatic Etiology**

Hepatic myelopathy is a neurologic condition that is seen in those with chronic liver disease. In patients with evident liver failure or patients who have a surgical or spontaneous systemic portocaval shunt, a progressive pure motor spastic paraparesis may develop.

These patients typically have minimal sensory deficit or bowel and bladder involvement. Many of these patients experience episodes of hepatic encephalopathy. Occasionally, following the creation of surgical shunts, myelopathy can develop.

It is imperative to recognize the circumstances under which hepatic myelopathy occurs. Early recognition is important because patient liver transplantation can reverse the myelopathy. Most cases of hepatic myelopathy are in patients who have decompensated liver disease. Hepatic myelopathy is a diagnosis of exclusion and has also been associated with congenital hepatic fibrosis, acute hepatitis E, and childhood portal vein thrombosis.

The neuropathology of hepatic myelopathy demonstrates demyelination in the lateral corticospinal tracts. Evidence suggests that motor-evoked potentials may be used to make an early diagnosis of hepatic myelopathy.

**Alcoholic Etiology**

Myelopathy associated with alcoholism occurs in patients who heavily consume alcohol and have cirrhosis with portosystemic shunting. However, Sage et al. proposed another syndrome of progressive posterior and lateral column dysfunction in alcoholics without substantial liver disease. Symptoms typically begin with paresthesias of the feet and progress to a spastic paraparesis. Patients may also present with bladder dysfunction. Abstinence from alcohol usually prevents further progression, but is not usually followed by improvement.
Differential Workup

While evaluating a patient with myelopathic symptoms, one must rule out mimickers, especially in unusual or equivocal cases. A comprehensive workup should include an MRI of the brain and spinal cord, spinal angiography in those with suspected vascular causes, electrodiagnostic studies, cerebrospinal fluid analysis, and laboratory analysis. However, a thorough history and physical examination remain the most critical components in the myelopathy workup. Table III lists the similarities and differences between mimickers and cervical spondylotic myelopathy.

Summary

The most common cause of non-traumatic spastic paraparesis and quadriplegia in the United States is cervical spondylotic myelopathy. This is due to degenerative changes of the cervical spinal column. Although this is the most common cause of myelopathy, several mimickers can cause similar symptoms, and a thorough workup is necessary to rule them out.

<table>
<thead>
<tr>
<th>Mimicker</th>
<th>Similarities to Cervical Spondylotic Myelopathy</th>
<th>Differences from Cervical Spondylotic Myelopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple sclerosis</td>
<td>Bladder disturbances, difficulty with gait, hyperreflexia, arm numbness and pain</td>
<td>Fatigue, diplopia, unilateral leg numbness, reversible deficits, vertigo, optic neuritis with loss of vision</td>
</tr>
<tr>
<td>Amyotrophic lateral sclerosis</td>
<td>Muscle atrophy, weakness, Hoffman sign, clonus, Babinski sign, loss of dexterity, difficulty with gait</td>
<td>Foot drop, fasciculations, difficulty speaking or impaired voice, difficulty swallowing, severe unintentional weight loss</td>
</tr>
<tr>
<td>Parkinson disease</td>
<td>Gait slowing, poor balance, neck tightness, reduced arm swing</td>
<td>Asymmetric tremor at rest, shuffling gait, extrapyramidal rigidity, impaired voice, soft speech, difficulty swallowing, reduced facial expression, small handwriting, involuntary movements</td>
</tr>
<tr>
<td>Carpal tunnel syndrome</td>
<td>Hand numbness or paresthesias in median distribution, reduced grip strength, thenar atrophy, clumsiness</td>
<td>Absence of upper motor neuron signs, symptoms isolated to median hand, positive provocative signs on examination</td>
</tr>
<tr>
<td>Cubital tunnel syndrome</td>
<td>Hand numbness or paresthesias in ulnar distribution, reduced grip strength, intrinsic muscle atrophy, Wartenberg sign</td>
<td>Absence of upper motor neuron signs, symptoms isolated to ulnar hand or forearm, positive provocative signs on examination</td>
</tr>
<tr>
<td>HIV</td>
<td>Gait ataxia, bowel and bladder disturbance, hyperreflexia</td>
<td>Lower-extremity weakness, erectile dysfunction (men), distal limb pain and numbness, slowly progressive spastic paraparesis</td>
</tr>
<tr>
<td>HTLV-1</td>
<td>Paresthesias, difficulty walking, sensory disturbances, spastic bladder, hyperreflexia</td>
<td>Slowly progressive chronic spastic paraparesis; painful stiffness and weakness of legs</td>
</tr>
<tr>
<td>Treponema pallidum</td>
<td>Incoordination, muscle weakness, paresthesias</td>
<td>Absent ankle jerks, impaired vibratory sensation, impotence, Romberg sign, vision change, Argyll-Robertson pupils, autonomic dysfunction</td>
</tr>
<tr>
<td>Guillain-Barré syndrome</td>
<td>Difficulty with coordination, neck pain, severe weakness in upper extremity, urinary retention</td>
<td>Rapidly progressive distal weakness that spreads proximally, ileus, sinus tachycardia, hyporeflexia and areflexia, weakness of facial muscles</td>
</tr>
<tr>
<td>Acute transverse myelitis</td>
<td>Well-defined sensory level, extremity weakness and paresthesias, hyperreflexia</td>
<td>Flaccid paraparesis of upper and lower extremities, autonomic dysfunction, lower-extremity paresthesias, difficulty flexing legs and extending arms</td>
</tr>
<tr>
<td>Vitamin B12 deficiency</td>
<td>Diminished proprioception, motor weakness, hyperreflexia, gait disturbance</td>
<td>Decreased vibration sensation, intellectual impairment, impaired vision</td>
</tr>
<tr>
<td>Syringomyelia</td>
<td>Intrinsic weakness, hyperreflexia, gait disturbance, loss of sensation in hands</td>
<td>Cape-like sensory loss, loss of pain and temperature sensation, diplopia, trigeminal nerve sensory loss, dizziness, neuropathic arthropathy</td>
</tr>
<tr>
<td>Post-radiation damage</td>
<td>Lhermitte sign, weakness of extremities, muscle atrophy</td>
<td>Brown-Sequard syndrome, ascending sensorimotor disturbance</td>
</tr>
<tr>
<td>Paraneoplastic etiology</td>
<td>Rigidity or myoclonus, bladder dysfunction, weakness, difficulty with ambulation</td>
<td>Optic neuropathy, rarely relapsing remitting course</td>
</tr>
<tr>
<td>Vascular etiology</td>
<td>Gait disturbance, paresthesias, radiculopathy</td>
<td>Asymmetric leg weakness worse with walking or standing for long periods</td>
</tr>
<tr>
<td>Hepatic etiology</td>
<td>Minimal sensory deficit, no bowel or bladder dysfunction</td>
<td>Progressive pure motor spastic paraparesis</td>
</tr>
<tr>
<td>Alcoholic etiology</td>
<td>Muscle weakness, muscle, atrophy, hyperreflexia, bladder dysfunction</td>
<td>Paresthesias of feet with spastic paraparesis of lower extremities, numbness of lower extremities</td>
</tr>
</tbody>
</table>

TABLE III  Similarities and Differences Between Mimickers and Cervical Spondylotic Myelopathy
differential etiologies exist, including neuromuscular, infectious, vascular, and neoplastic processes. For this reason, a thorough history and physical examination must be performed. Examinations may show limitations in cervical spine range of motion, spasticity, and an unsteady gait. MRI, electrodiagnostic studies, and cerebrospinal fluid analysis aid in making the diagnosis.

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