Mimickers of Cervical Spondylotic Myelopathy

Anthony Kouri, MD

Mina Tanios, MD

Joseph S. Herron, MD

Maxwell Cooper, MD

Mustafa Khan, MD

Investigation performed at the University of Toledo Medical Center, Toledo, Ohio

Abstract

» Many disorders present similar to cervical spondylotic myelopathy.

» Mimickers can be differentiated from cervical spondylotic 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 spondylotic 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 spondylotic 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 Spondylotic Myelopathy

Cervical spondylotic 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[1]. 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 spondylotic myelopathy[2]. Ono et al. used the term myelopathy hand when describing upper-extremity findings[3]. 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[4]. Table II demonstrates the common signs and symptoms of cervical spondylotic myelopathy.

Patients may experience stable periods with slow, stepwise decline in function or rapid decline[4]. Persistent symptoms, without transience or fluctuation, distinguish cervical spondylotic myelopathy from other disorders. Sequelae such as sensory loss, motor weakness, or gait instability may not be present in every patient.

Diagnosing cervical spondylotic 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 spondylotic myelopathy. Thirty-nine patients with cervical spondylotic myelopathy and 37 controls were included. Twenty-one percent of patients with cervical spondylotic myelopathy did not have any myelopathic signs on examination[2].

Disclosure: There was no source of external funding for this study. The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (http://links.lww.com/JBJSREV/A386).

TABLE I Differential Diagnosis in Cervical Spondylotic Myelopathy

Mimicker	History and Physical Examination	Diagnosis
Multiple sclerosis	Fatigue, diplopia, bladder disturbances, difficulty with gait, unilateral leg numbness	2 lesions in the white matter, 2 episodes in the disease course, oligoclonal bands in cerebrospinal fluid, raised IgG
Amyotrophic lateral sclerosis	Muscle atrophy, weakness, fasciculations, Hoffman sign, clonus, Babinski sign, foot drop, loss of dexterity, difficulty with gait	Widespread lower motor neuron disease on EMG, bilateral changes within corticospinal tracts on brain MRI
Parkinson disease	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	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
Carpal tunnel syndrome	Pain in hand, decreased sensation in median nerve distribution, reduced grip strength, night symptoms, clumsiness, thenar atrophy in late stages	Based on history and physical examination, in equivocal cases, electrodiagnostic studies are helpful
Cubital tunnel syndrome	Decreased sensation in the ulnar nerve distribution, intrinsic weakness and weakness of the small and ring finger flexor digitorum profundus, Wartenberg sign	Based on history and physical examination, in equivocal cases, electrodiagnostic studies are helpful; on electrodiagnostic studies, ulnar nerve velocity must be $<$50 m/s at elbow level
HIV	Lower-extremity weakness, vague discomfort in legs, gait ataxia, erectile dysfunction (men), bowel or bladder disturbance	Spinal MRI shows extensive central high-signal areas on T2, mainly cervicodorsal
HTLV-1	Slowly progressive chronic spastic paraparesis, spastic bladder	HTLV-1 antibodies in serum and cerebrospinal fluid
Syphilis	Incoordination, pain, absent ankle jerks, impaired vibratory sensation, impotence, Romberg sign, Argyll-Robertson pupils, autonomic dysfunction	High signal on T2 MRI with enhancement of the spinal surface that disappears
Guillain-Barré syndrome	Rapidly progressive distal weakness that spreads proximally, severe weakness in shoulder abduction and elbow extension, urinary retention, ileus, sinus tachycardia, hyporeflexia, and areflexia	Illness 7 to 10 days prior; clinical diagnosis, but EMG and nerve conduction study demonstrate severe neuropathy; cerebrospinal fluid may have raised protein content
Acute transverse myelitis	Flaccid paraparesis of lower extremities that can also involve the arms, well-defined sensory level	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
Vitamin B12 deficiency	Diminished proprioception, decreased vibration sensation, motor weakness, hyperreflexia, gait disturbance, intellectual impairment, impaired vision	Vitamin B12 serum levels; MRI shows T2 hyperintense signal alterations usually confined to posterior columns, but may involve lateral columns or brain stem
Syringomyelia	Intrinsic weakness, cape-like sensory loss, loss of pain and temperature sensation, hyperreflexia, gait disturbance, diplopia, dizziness	MRI demonstrating syrinx
Radiation damage	Lhermitte sign, Brown-Sequard-type symptoms, ascending sensorimotor disturbance, tetraplegia and paraplegia, local amyotrophy	Spinal cord segment in irradiated zone, $>$6-month latency period, normal cerebrospinal fluid analysis, local spinal edema, and contrast enhancement on T2 for at least 8 months after latency period
Paraneoplastic etiology	Insidiously progressive myelopathy; may occur prior to cancer diagnosis	Increased protein concentration in cerebrospinal fluid; longitudinally extensive, symmetric, tract-specific signal changes on MRI
Vascular etiology	Asymmetric leg weakness, worse with walking or standing for long periods	Flow voids on MRI, engorged draining medullary veins and feeding arteries within cerebrospinal fluid
Hepatic etiology	Progressive pure motor spastic paraparesis, minimal sensory deficit	Diagnosis of exclusion; decompensated liver disease, post-liver transplant, post-shunt surgery
Alcoholic etiology	Paresthesias of feet with progressive spastic paraparesis, sometimes bladder dysfunction	Alcoholism without substantial liver disease

TABLE II Clinical Presentation of Cervical Spondylotic Myelopathy

Common symptoms
Clumsy or weak hands
Leg weakness or stiffness
Neck stiffness
Pain in shoulders or arms
Unsteady gait
Common signs
Weakness of the hand musculature
Hyperreflexia
Lhermitte sign (electric shock-like sensation down the center of the back following flexion of the neck)
Sensory loss

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[5].

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[6].

Neuromuscular Mimickers

Multiple sclerosis is a chronic autoinflammatory central nervous system disease[7,8]. It destroys myelin and axons to varying degrees by attacking central nervous system myelinated axons[8]. The disease course is highly varied, but typically presents as episodes of reversible deficits, followed by progressive neurologic deterioration[8].

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.

In >33% of patients with multiple sclerosis, moderate to severe lower-extremity spasticity is seen[8]. 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[9].

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[8]. 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[8-10].

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[11]. 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[12]. Lower motor neuron loss causes substantial weakness. Often, the weakness from lower motor neuron loss is more disabling than the upper motor neuron symptoms[12].

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[13].

The diagnosis is 95% accurate when made by experienced clinicians[13]. 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[14].

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[15]. The underlying pathology of Parkinson disease is apoptosis in the basal ganglia, specifically the substantia nigra's dopamine-secreting neurons. Also

contributing is the presence of Lewy bodies in the remaining neurons[16].

Parkinson disease has variable characteristics. Common symptoms include resting and postural tremors, extrapyramidal rigidity, and slowness of initiation, movement, and thought. Idiopathic Parkinson disease presents later in life. Often, symptoms will start in 1 limb and, over the course of 2 to 5 years, will involve both limbs[16].The asymmetry seen in the early stages of idiopathic Parkinson disease persists as the disease progresses.

Early in the disease course, postural reflexes remain intact; however, patients ultimately have difficulty with balance. A tremor is typically present in 40% of patients initially, and many of those patients demonstrate an asymmetric rest tremor. The rigidity seen in Parkinson disease is described as a lead pipe, meaning constant throughout full motion. When a postural tremor is overlaid on the rigidity, it becomes ratchet-like, and is known as cogwheel rigidity. Approximately half of all patients with Parkinson disease report slowing in their maneuvering. Additionally, writing becomes smaller and patients develop difficulty with activities of daily living in the later stages of the disease. As Parkinson disease progresses, patients begin to have a nonspecific feeling taking longer to get around. This eventually leads to a slowed gait. While ambulating, a 1-sided decreased arm swing is often present. Later in the disease course, shuffling develops. This is followed by difficulty initiating gait and spontaneous acceleration[15].

In Parkinson disease, laboratory results are normal. On a brain MRI scan, the striatum and pallidum will appear normal. However, on T2-weighted sequences, an altered nigral signal will be demonstrated. Typically, electromyograms are not helpful for Parkinson disease. However, a surface electromyogram can be helpful if there is doubt concerning the frequency and amplitude of a tremor[17].

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 to 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 spinothalamic 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. Electrodiagnostic studies and MRI are helpful in making the diagnosis[22,25].

Infectious and Immune-Mediated Mimickers

Timely diagnosis is imperative in infectious myelopathies. In parainfectious 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 paresthesias. 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-1 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[30,31]. Patients may also experience paresthesias, 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 paralysis 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[36]. 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[38]. 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[38].

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[39].

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[40].

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[40]. 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[41].

Vitamin B12 Deficiency

Vitamin B12 deficiency can cause several different disorders[42]. Typical causes of vitamin B12 deficiency include pancreatic insufficiency, medications, and malabsorption[42-44]. A rare, but notable, cause of acute vitamin B12 inactivation is nitrous oxide exposure[45].

The neurologic symptoms present in vitamin B12 deficiency include autonomic dysfunction, gait disturbance, paresthesias, diminished proprioception and vibratory sensation, weakness, hyperreflexia, areflexia, intellectual or behavioral impairment, and impaired vision[44].

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[44]. Furthermore, myelin sheath swelling and a patchy myelopathic spongy vacuolation of affected regions of the cord are typically seen[46,47].

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[46].

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[48,49]. Chiari malformation is a congenital abnormality in which the cerebellar amygdalae herniates through the foramen magnum. This causes altered cerebrospinal fluid flow, which can lead to syrinx formation[50,51]. Patients may experience diplopia, headaches, dizziness, and arm weakness[52].

The classic symptoms associated with Chiari malformation include upper-limb weakness and cape-like suspended sensory loss[50]. 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[50,51,53]. 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 cape-like 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[49].

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[54]. 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[55]. This final stage presents like chronic progressive Brown-Séquard syndrome and lasts 3 months to 5 years[54].

The presentation is slowly progressive ascending sensorimotor disturbance including tetraplegia or paraplegia, with bowel and bladder disturbances[55]. 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[55]. Cerebrospinal fluid analysis is typically normal[54]. 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[54].

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[56].

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[55,56].

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[56].

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[57].

Spinal vascular malformations are categorized on the basis of anatomy and location. The most common are dural arteriovenous fistula malformations[58]. An arteriovenous fistula malformation is dural, or extraspinal, in 75% of cases[57]. In 10% of cases, intraspinal arteriovenous fistula malformations are present. Twelve percent of spinal malformations are cavernous malformations[58].

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[59].

Another cause of vascular myelopathy is acute vascular occlusion, which causes an infarct[57]. 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[59,60]. 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[57].

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[61].

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[61-64].

It is imperative to recognize the circumstances under which hepatic myelopathy occurs. Early recognition is important because patient liver transplantation can reverse the myelopathy[65]. Most cases of hepatic myelopathy are in patients who have decompensated liver disease[66]. Hepatic myelopathy is a diagnosis of exclusion and has also been associated with congenital hepatic fibrosis[67], acute hepatitis E, and childhood portal vein thrombosis[68].

The neuropathology of hepatic myelopathy demonstrates demyelination in the lateral corticospinal tracts[70]. Evidence suggests that motor-evoked potentials may be used to make an early diagnosis of hepatic myelopathy[61,65].

Alcoholic Etiology

Myelopathy associated with alcoholism occurs in patients who heavily consume alcohol and have cirrhosis with portosystemic shunting[69,70]. However, Sage et al. proposed another syndrome of progressive posterior and lateral column dysfunction in alcoholics without substantial liver disease[71,72]. Symptoms typically begin with paresthesias of the feet and progress to a spastic paraparesis. Patients may also present with bladder dysfunction[69]. Abstention from alcohol usually prevents further progression, but is not usually followed by improvement[73].

TABLE III Similarities and Differences Between Mimickers and Cervical Spondylotic Myelopathy

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

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 nontraumatic spastic paraparesis and quadriparesis 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

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.

Anthony Kouri, MD[1],
Mina Tanios, MD[1],
Joseph S. Herron, MD[1],
Maxwell Cooper, MD[1],
Mustafa Khan, MD[2]

[1]University of Toledo Medical Center, Toledo, Ohio

[2]Milwaukee Orthopedic Group, Milwaukee, Wisconsin

E-mail address for A. Kouri:
Anthony.kouri@utoledo.edu

ORCID iD for A. Kouri:
0000-0002-5671-7540
ORCID iD for M. Tanios:
0000-0002-6622-9399
ORCID iD for J.S. Herron:
0000-0002-1859-4658
ORCID iD for M. Cooper:
0000-0003-3521-751X
ORCID iD for M. Khan:
0000-0002-8633-396X

References

1. Kim DH, Vaccaro AR, Henderson FC, Benzel EC. Molecular biology of cervical myelopathy and spinal cord injury: role of oligodendrocyte apoptosis. Spine J. 2003 Nov-Dec;3(6):510-9.

2. Rhee JM, Heflin JA, Hamasaki T, Freedman B. Prevalence of physical signs in cervical myelopathy: a prospective, controlled study. Spine (Phila Pa 1976). 2009 Apr 20;34(9): 890-5.

3. Ono K, Ebara S, Fuji T, Yonenobu K, Yamashit K. Myelopathy hand. New clinical signs of cervical cord damage. J Bone Joint Surg Br. 1987 Mar;69(2):215-9.

4. Baptiste DC, Fehlings MG. Pathophysiology of cervical myelopathy. Spine J. 2006 Nov-Dec; 6(6 Suppl):190S-7S.

5. Teresi LM, Lufkin RB, Reicher MA, Moffit BJ, Vinuela FV, Wilson GM, Bentson JR, Hanafee WN. Asymptomatic degenerative disk disease and spondylosis of the cervical spine: MR imaging. Radiology. 1987 Jul;164(1):83-8.

6. de Oliveira Vilaça C, Orsini M, Leite MA, de Freitas MR, Davidovich E, Fiorelli R, Fiorelli S, Fiorelli C, Oliveira AB, Pessoa BL. Cervical spondylotic myelopathy: what the neurologist should know. Neurol Int. 2016 Nov 23;8(4):6330.

7. Calabresi PA. Diagnosis and management of multiple sclerosis. Am Fam Physician. 2004 Nov 15;70(10):1935-44.

8. Hauser SL, Goodwin DS. Multiple sclerosis and other demyelinating diseases. In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, editors. Harrison's principles of internal medicine. 17th ed. New York: McGraw-Hill Medical; 2008. p 2611-21.

9. Goldenberg MM. Multiple sclerosis review. P T. 2012 Mar;37(3):175-84.

10. Mills RJ, Young CA, Pallant JF, Tennant A. Development of a patient reported outcome scale for fatigue in multiple sclerosis: the Neurological Fatigue Index (NFI-MS). Health Qual Life Outcomes. 2010 Feb 12;8:22.

11. Rowland LP, Shneider NA. Amyotrophic lateral sclerosis. N Engl J Med. 2001 May 31; 344(22):1688-700.

12. Rowland LP, Mitsumoto H, Przedborski S. Amyotrophic lateral sclerosis, progressive muscular atrophy, and primary lateral sclerosis. In: Rowland LP, Pedley TA, editors. Merritt's neurology. 12th ed. Philadelphia: Lippincott, Williams & Wilkins; 2010. p 802-8.

13. Chiò A, Logroscino G, Hardiman O, Swingler R, Mitchell D, Beghi E, Traynor BG; Eurals Consortium. Prognostic factors in ALS: a critical review. Amyotroph Lateral Scler. 2009 Oct-Dec; 10(5-6):310-23.

14. Gordon PH. Amyotrophic lateral sclerosis: an update for 2013 clinical features, pathophysiology, management and therapeutic trials. Aging Dis. 2013 Oct 1;4(5): 295-310.

15. Brooks DJ. Diagnosis and management of atypical Parkinsonian syndromes. J Neurol Neurosurg Psychiatry. 2002 Mar;72(Suppl 1): I10-6.

16. Sveinbjornsdottir S. The clinical symptoms of Parkinson's disease. J Neurochem. 2016 Oct; 139(Suppl 1):318-24. Epub 2016 Jul 11.

17. Brooks DJ. Morphological and functional imaging studies on the diagnosis and progression of Parkinson's disease. J Neurol. 2000 Apr;247(Suppl 2):II11-8.

18. Bland JD. Carpal tunnel syndrome. BMJ. 2007 Aug 18;335(7615):343-6.

19. Bland JD. The value of the history in the diagnosis of carpal tunnel syndrome. J Hand Surg Br. 2000 Oct;25(5):445-50.

20. Wojewnik B, Bindra R. Cubital tunnel syndrome - review of current literature on causes, diagnosis and treatment. J Hand Microsurg. 2009 Dec;1(2):76-81. Epub 2010 Jan 8.

21. Alter M. The digiti quinti sign of mild hemiparesis. Neurology. 1973 May;23(5):503-5.

22. Rittenberg JD, Burns SP, Little JW. Worsening myelopathy masked by peripheral nerve disorders. J Spinal Cord Med. 2004;27(1): 72-7.

23. Cohen BH, Gaspar MP, Daniels AH, Akelman E, Kane PM. Multifocal neuropathy: expanding the scope of double crush syndrome. J Hand Surg Am. 2016 Dec;41(12):1171-5. Epub 2016 Oct 15.

24. Osterman AL. The double crush syndrome. Orthop Clin North Am. 1988 Jan;19(1):147-55.

25. Kane PM, Daniels AH, Akelman E. Double crush syndrome. J Am Acad Orthop Surg. 2015 Sep;23(9):558-62.

26. Petito CK, Navia BA, Cho ES, Jordan BD, George DC, Price RW. Vacuolar myelopathy pathologically resembling subacute combined degeneration in patients with the acquired immunodeficiency syndrome. N Engl J Med. 1985 Apr 4;312(14):874-9.

27. Di Rocco A. Diseases of the spinal cord in human immunodeficiency virus infection. Semin Neurol. 1999;19(2):151-5.

28. Tagliati M, Di Rocco A, Danisi F, Simpson DM. The role of somatosensory evoked potentials in the diagnosis of AIDS-associated myelopathy. Neurology. 2000 Apr 11;54(7): 1477-82.

29. Gessain A, Barin F, Vernant JC, Gout O, Maurs L, Calender A, de Thé G. Antibodies to human T-lymphotropic virus type-I in patients with tropical spastic paraparesis. Lancet. 1985 Aug 24;2(8452):407-10.

30. Vernant JC, Maurs L, Gessain A, Barin F, Gout O, Delaporte JM, Sanhadji K, Buisson G, de-Thé G. Endemic tropical spastic paraparesis associated with human T-lymphotropic virus type I: a clinical and seroepidemiological study of 25 cases. Ann Neurol. 1987 Feb;21(2):123-30.

31. World Health Organization. Virus diseases: human T-lymphotropic virus type I, HTLV-I. Wkly Epidemiol Rec. 1989;64(49):382-3.

32. Puccioni-Sohler M, Rios M, Carvalho SM, Gonçalves RR, Oliveira C, Correa RB, Novis S, de Oliveira MS, Bianco C. Diagnosis of HAM/TSP based on CSF proviral HTLV-I DNA and HTLV-I antibody index. Neurology. 2001 Aug 28;57(4):725-7.

33. Berger JR, Sabet A. Infectious myelopathies. Semin Neurol. 2002 Jun;22(2):133-42.

34. Yuki N, Hartung HP. Guillain-Barré syndrome. N Engl J Med. 2012 Jun 14;366(24): 2294-304.

35. Winer J. An update in Guillain-Barré syndrome. Autoimmune Diseases. 2014 Jan; 2014(2014):793024.

36. Rees JH, Thompson RD, Smeeton NC, Hughes RA. Epidemiological study of Guillain-Barré syndrome in south east England. J Neurol Neurosurg Psychiatry. 1998 Jan;64(1):74-7.

37. Visser LH, Schmitz PI, Meulstee J, van Doorn PA, van der Meché FG; Dutch Guillain-Barré Study Group. Prognostic factors of Guillain-Barré syndrome after intravenous immunoglobulin or plasma exchange. Neurology. 1999 Aug 11;53(3):598-604.

38. al Deeb SM, Yaqub BA, Bruyn GW, Biary NM. Acute transverse myelitis. A localized form of postinfectious encephalomyelitis. Brain. 1997 Jul;120(Pt 7):1115-22.

39. Kerr D, Krishnan C, Pidcock F. Acute transverse myelitis. In: Singer HS, Kossoff EH, Hartman AL, Crawford WO, editors. Treatment of pediatric neurologic disorders. 1st ed. Boca Raton: CRC Press; 2005. p 445-51.

40. Thurnher MM, Cartes-Zumelzu F, Mueller-Mang C. Demyelinating and infectious diseases of the spinal cord. Neuroimaging Clin N Am. 2007 Feb;17(1):37-55.

41. Jacob A, Weinshenker BG. An approach to the diagnosis of acute transverse myelitis. Semin Neurol. 2008 Feb;28(1):105-20.

42. Reynolds E. Vitamin B12, folic acid, and the nervous system. Lancet Neurol. 2006 Nov;5(11): 949-60.

43. Dharmarajan TS, Norkus EP. Approaches to vitamin B12 deficiency. Early treatment may

prevent devastating complications. Postgrad Med. 2001 Jul;110(1):99-105; quiz 106.

44. Healton EB, Savage DG, Brust JC, Garrett TJ, Lindenbaum J. Neurologic aspects of cobalamin deficiency. Medicine (Baltimore). 1991 Jul;70(4):229-45.

45. Singer MA, Lazaridis C, Nations SP, Wolfe GI. Reversible nitrous oxide-induced myeloneuropathy with pernicious anemia: case report and literature review. Muscle Nerve. 2008 Jan;37(1):125-9.

46. Metz J. Cobalamin deficiency and the pathogenesis of nervous system disease. Annu Rev Nutr. 1992;12:59-79.

47. Srikanth SG, Jayakumar PN, Vasudev MK, Taly AB, Chandrashekar HS. MRI in subacute combined degeneration of spinal cord: a case report and review of literature. Neurol India. 2002 Sep;50(3):310-2.

48. Zager EL, Ojemann RG, Poletti CE. Acute presentations of syringomyelia. Report of three cases. J Neurosurg. 1990 Jan;72(1):133-8.

49. Zadeh HG, Sakka SA, Powell MP, Mehta MH. Absent superficial abdominal reflexes in children with scoliosis. An early indicator of syringomyelia. J Bone Joint Surg Br. 1995 Sep;77(5):762-7.

50. Sanchez A, Posada L, Toscano C, Lopez A. Diagnostic approach to myelopathies. Rev Colorab Radiol. 2011;22(3):1-21.

51. Anwer UE, Fisher M. Acute and atypical presentations of syringomyelia. Eur Neurol. 1996;36(4):215-8.

52. DeSanto J, Ross JS. Spine infection/inflammation. Radiol Clin North Am. 2011 Jan;49(1):105-27.

53. Steinbok P. Clinical features of Chiari I malformations. Childs Nerv Syst. 2004 May;20(5):329-31. Epub 2004 Feb 14.

54. Kadir T, Sarica FB, Ozgur K, Cekinmez M, Nur AM. Delayed radiation myelopathy: differential diagnosis with positron emission tomography/computed tomography examination. Asian J Neurosurg. 2012 Oct;7(4):206-9.

55. Hauser SL. Diseases of the spinal cord. In: Harrison's principles of internal medicine. 16th ed. New York: McGraw-Hill; 2005. p 2438-47.

56. Flanagan EP, Keegan BM. Paraneoplastic myelopathy. Neurol Clin. 2013 Feb;31(1):307-18.

57. Caragine LP Jr, Halbach VV, Ng PP, Dowd CF. Vascular myelopathies-vascular malformations of the spinal cord: presentation and endovascular surgical management. Semin Neurol. 2002 Jun;22(2):123-32.

58. Riche MC, Reizine D, Melki JP, Merland JJ. Classification of spinal cord vascular malformations. Radiat Med. 1985 Jan-Mar;3(1):17-24.

59. de Seze J, Stojkovic T, Breteau G, Lucas C, Michon-Pasturel U, Gauvrit JY, Hachulla E, Mounier-Vehier F, Pruvo JP, Leys D, Destée A, Hatron PY, Vermersch P. Acute myelopathies: clinical, laboratory and outcome profiles in 79 cases. Brain. 2001 Aug;124(Pt 8):1509-21.

60. Masson C, Pruvo JP, Meder JF, Cordonnier C, Touzé E, De La Sayette V, Giroud M, Mas JL, Leys D; Study Group on Spinal Cord Infarction of the French Neurovascular Society. Spinal cord infarction: clinical and magnetic resonance imaging findings and short term outcome. J Neurol Neurosurg Psychiatry. 2004 Oct;75(10):1431-5.

61. Premkumar M, Bagchi A, Kapoor N, Gupta A, Maurya G, Vatsya S, Kapahtia S, Kar P. Hepatic myelopathy in a patient with decompensated alcoholic cirrhosis and portal colopathy. Case Reports Hepatol. 2012;2012:735906. Epub 2012 Dec 18.

62. Mendoza G, Marti-Fàbregas J, Kulisevsky J, Escartín A. Hepatic myelopathy: a rare complication of portacaval shunt. Eur Neurol. 1994;34(4):209-12.

63. Panicker J, Sinha S, Taly AB, Ravishankar S, Arunodaya GR. Hepatic myelopathy: a rare complication following extrahepatic portal vein occlusion and lienorenal shunt. Neurol India. 2006 Sep;54(3):298-300.

64. Campellone JV, Lacomis D, Giuliani MJ, Kroboth FJ. Hepatic myelopathy. Case report with review of the literature. Clin Neurol Neurosurg. 1996 Aug;98(3):242-6.

65. Weissenborn K, Tietge UJ, Bokemeyer M, Mohammadi B, Bode U, Manns MP, Caselitz M. Liver transplantation improves hepatic myelopathy: evidence by three cases. Gastroenterology. 2003 Feb;124(2):346-51.

66. Lefer LG, Vogel FS. Encephalomyelopathy with hepatic cirrhosis following portosystemic venous shunts. Arch Pathol. 1972 Feb;93(2):91-7.

67. Demirci M, Tan E, Elibol B, Gedikoğlu G, Saribaş O. Spastic paraparesis associated with portal-systemic venous shunting due to congenital hepatic fibrosis. Neurology. 1992 May;42(5):983-5.

68. Mandal K, Chopra N. Acute transverse myelitis following hepatitis E virus infection. Indian Pediatr. 2006 Apr;43(4):365-6.

69. Zieve L, Mendelson DF, Goepfert M. Shunt encephalomyelopathy. II. Occurrence of permanent myelopathy. Ann Intern Med. 1960 Jul;53:53-63.

70. Brust JCM. Alcoholism. In: Rowland LP, editor. Merritt's neurology. 10th ed. Philadelphia: Lippincott Williams & Wilkins; 2000. p 921-9.

71. Liversedge LA, Rawson MD. Myelopathy in hepatic disease and portosystemic venous anastomosis. Lancet. 1966 Feb 5;1(7432):277-9.

72. Sage JI, Van Uitert RL, Lepore FE. Alcoholic myelopathy without substantial liver disease. A syndrome of progressive dorsal and lateral column dysfunction. Arch Neurol. 1984 Sep;41(9):999-1001.

73. Dreyfus PM. Disease of the nervous system in chronic alcoholics. In: Kissin B, Begleiter H, editors. The biology of alcoholism. New York: Plenum Press; 1974. p 265-90.