

PERIPHERAL NEUROPATHY

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Peripheral neuropathy is a general term for any disorder affecting the peripheral nerves. Since peripheral neuropathy can be caused by numerous factors, an investigation into the cause of the neuropathy should be undertaken as soon as the diagnosis of neuropathy is made.

CLINICAL FEATURES

Symptoms

Since the peripheral nervous system consists of motor, sensory and autonomic nerves, symptoms can fall into all three of these categories.

- Sensory symptoms include distal dysesthesias, pain and numbness. A characteristic pattern of numbness is one in which the distal portions of the nerves are first affected, the so-called "stocking-glove" pattern. This pattern occurs because nerve fibers are affected according to length of axon, without regard to root or nerve trunk distribution.
- Motor symptoms include weakness, which once again is distal, and typically involves extensor groups rather than flexor groups of muscles.
- Autonomic dysfunction is common and includes orthostasis, impotence in males and gastroparesis.

Signs

Signs of peripheral neuropathy also include sensory, motor and autonomic components.

- Sensory disturbance is manifest as distal loss of pin, temperature and vibratory perception as well as proprioception. Initial signs are frequently confined to the toes and feet. A positive Romberg sign is frequently present due to proprioceptive loss in the lower extremities.
- Motor signs include distal weakness, primarily in extensor groups, and most prominent in the lower extremities initially. Distal muscles are often atrophic, and one should carefully assess the bulk of the extensor digitorum brevis muscles in the feet and of the intrinsic muscles of the hands. Muscle tone is reduced and often is flaccid.
- Muscle stretch reflexes are frequently lost, and most patients with peripheral neuropathy have absent ankle jerks as one of the first signs of the disorder.
- The most prominent autonomic sign of neuropathy is orthostatic hypotension.

CLASSIFICATION

There are many ways to classify peripheral neuropathy. One helpful method is to consider four categories, namely etiology, distribution, pathology and modality.

Etiology

Most peripheral neuropathies fall into three etiologic categories, namely hereditary, toxic/metabolic, and those associated with systemic disease.

Hereditary:

This is a large group of disorders in which the onset of symptoms is insidious and progression is indolent over years or decades. Three of these hereditary neuropathies will be discussed:

- **Charcot-Marie-Tooth Disease** (Hereditary Sensory-Motor Neuropathy [HSMN] I). This is the most common hereditary neuropathy that has an autosomal dominant pattern of inheritance. Phenotypic expression is often variable, such that affected family members of a propositus may have no symptoms and minimal neurologic findings. Characteristic clinical findings include striking atrophy of the calves, resulting in an inverted "champagne-bottle" appearance to the lower extremities. Peripheral nerves are often palpably enlarged. Large fiber sensory loss is present, with a marked reduction in vibratory perception and proprioception. Ankle jerk reflexes are lost. Since this is a demyelinating polyneuropathy, nerve conduction velocity measurements are characteristically slow, at approximately 50% of normal values.
- **Dejerine-Sottas Disease** (HSMN III). This is a rare pediatric disorder with autosomal recessive inheritance that causes severe weakness and numbness, markedly enlarged peripheral nerves with "onion-bulb" formation and markedly slowed conduction velocities.
- **Refsum's Disease** (HSMN IV). This autosomal recessive disorder is caused by an enzymatic defect that results in accumulation of phytanic acid. The clinical triad includes peripheral neuropathy, retinitis pigmentosa and dry, scaly skin. Treatment includes dietary restriction of phytanic acid and plasmapheresis.

Toxic/Metabolic:

Numerous drugs and toxins can cause peripheral neuropathy. A partial list follows:

- **Drugs:** amiodarone, cis-platinum, dapson, INH, phenytoin, pyridoxine, vincristine, nitrofurantoin, ddl, ddC.
- **Toxins:** heavy metals including mercury, arsenic, lead, zinc and thallium; alcohol; and the organophosphates.

Neuropathy Associated with Systemic Diseases:

- Numerous systemic diseases are associated with neuropathy. Among the most common systemic disorders are: uremia; porphyria; vitamin B₁₂ deficiency; amyloidosis; hypothyroidism; lymphoma, including Hodgkins' disease; multiple myeloma; cryoglobulinemia; vasculitis, including systemic lupus erythematosus (SLE), rheumatoid arthritis and polyarteritis nodosa; sarcoidosis; and benign monoclonal gammopathy, including IgG, IgA and IgM.
- A purely sensory neuropathy can be seen with several carcinomas, especially oat cell carcinoma of the lung.
- Four systemic infections have a high incidence of neuropathy, including leprosy, syphilis, HIV and diphtheria.
- Diabetes mellitus is perhaps the most common cause of neuropathy in the United States. Both symmetric and asymmetric diabetic neuropathies can occur, as follows:
 - Symmetric polyneuropathies: These are the most common and include a sensory/motor polyneuropathy and an autonomic neuropathy.
 - Asymmetric neuropathies are less common. Mononeuropathy multiplex results in simultaneous dysfunction of several peripheral nerves, and is due to ischemic infarction of the vasa nervorum. Cranial neuropathies, truncal radiculopathies and diabetic amyotrophy (ischemic infarction of the lumbosacral plexus) are other forms of asymmetric neuropathies. Entrapment neuropathies, including carpal tunnel syndrome, are also commonly seen in diabetics.

Distribution

Nerve damage in peripheral neuropathy may be symmetrical generalized, multifocal or focal.

- **Symmetrical generalized polyneuropathies** produce signs and symptoms in a distal-to-proximal gradient, the so-called "stocking-glove" pattern. The reason for this is that the "offending agent" causing the neuropathy affects protein synthesis in the cell body of the peripheral nerve. Hence, neuronal dysfunction will first occur in the distal portions of the longest axons, and thus produce symptoms of weakness and numbness in the most distal portions of the extremities, i.e. the feet and hands.
- **Multifocal Neuropathies (Mononeuropathy Multiplex)**: Patients with these forms of neuropathy develop more-or-less simultaneous dysfunction of several peripheral nerves. The underlying pathologic mechanism is felt to be ischemic infarction of the vasa nervorum due to vasculitis, as can occur with SLE, rheumatoid arthritis, polyarteritis nodosa and diabetes mellitus. These neuropathies are frequently painful and cause profound weakness. Prognosis for recovery is good, assuming that the underlying disease process leading to nerve infarction can be suppressed.

- **Focal Neuropathies (Mononeuropathies):** Traumatic injuries and entrapment of peripheral nerves at the usual sites of compression are the most common causes of focal mononeuropathy. The most frequently seen entrapment neuropathies include:
 - Compression of the median nerve across the wrist (carpal tunnel syndrome)
 - Compression of the ulnar nerve across the elbow (tardy ulnar palsy)
 - Compression of the radial nerve at the spiral groove (Saturday night palsy)
 - Compression of the peroneal nerve at the fibular head (peroneal nerve palsy)
 - Compression of the distal branches of the tibial nerve at the ankle (tarsal tunnel syndrome)

Pathology

There are three major pathologic mechanisms causing peripheral neuropathy: distal axonopathy, myelinopathy, and neuronopathy.

Distal Axonopathy:

In this form of neuropathy, a metabolic abnormality causes failure of protein synthesis and axonal transport, resulting in degeneration of distal regions of axons. For this reason, axonal neuropathies characteristically produce a "stocking-glove" distribution of numbness and weakness.

Small-diameter axons are most susceptible to metabolic injury because of their small neuronal size and lack of "reserve". Hence, initial symptoms of an axonal neuropathy typically include autonomic dysfunction and small-fiber sensory modalities, including loss of pain and temperature perception, since these modalities are subserved by small, unmyelinated or thinly myelinated axons.

Myelinopathy:

An immune-mediated attack on peripheral nervous system myelin is the characteristic pathologic change in this group of neuropathies. Guillain-Barre syndrome (GBS) and chronic inflammatory demyelinating polyneuropathy (CIDP) are the two most common forms of demyelinating polyneuropathy.

GBS is a monophasic, immune-mediated demyelinating neuropathy that frequently follows a viral infection and causes an acute and frequently severe progression of weakness and numbness over several weeks. CIDP is a chronic demyelinating polyneuropathy that can have a slowly progressive or a relapsing course. In both of these neuropathies antibodies have been found that cross-react with peripheral nerve myelin. Elevated CSF protein and slowed nerve conduction velocities are characteristic of the demyelinating neuropathies.

In general, demyelinating neuropathies affect large-diameter, myelinated axons at the start of the illness, and hence produce significant motor weakness and large-fiber sensory loss, including loss of vibratory perception and proprioception.

In diphtheritic neuropathy, the bacterium produces a toxin that inhibits Schwann cell synthesis of myelin constituents, producing severe weakness and large-fiber sensory loss.

Neuronopathy:

Selective involvement of the cell bodies of motor, sensory and autonomic nerves is the hallmark of this group of neuropathies.

- **Somatic motor neuronopathies** result from isolated involvement of the anterior horn cells. Amyotrophic lateral sclerosis and the spinal muscular atrophies are two examples of somatic motor neuronopathies.
- **Somatic sensory neuronopathies** result from disruption of the metabolism of sensory nerve cell bodies, followed by degeneration of their processes. Special permeability of the blood vessels in the dorsal root and Gasserian ganglia make these neurons particularly vulnerable to certain toxins. Two common examples of somatic sensory neuronopathies include the paraneoplastic subacute sensory neuropathy seen with oat-cell carcinoma of the lung, and the sensory neuronopathy associated with Sjogren's syndrome.
- **Autonomic Neuronopathy:** This unusual group of neuropathies results from isolated involvement of post-ganglionic autonomic neurons and causes idiopathic orthostatic hypotension.

Modality

Peripheral neuropathies can be sub-classified based on their involvement of motor, sensory or autonomic neurons.

- **Modality-Specific Neuropathies:** The somatic motor, somatic sensory and autonomic neuronopathies described above are examples of modality-specific neuropathies. The pathologic lesion in this group of neuropathies is confined to the cell bodies.
- **Mixed-Modality Neuropathies:** The majority of peripheral neuropathies is not modality-specific, and includes various combinations of motor, sensory and autonomic dysfunction. The reason for this finding is that most peripheral nerves include a mixture of motor, sensory and autonomic axons. Hence, axonal neuropathies typically present with mixed symptomatology. Likewise, since most axons are myelinated to a greater or lesser extent, demyelinating neuropathies also produce a mixture of motor, sensory and autonomic symptoms.

The mnemonic **DANG THERAPIST** is helpful in recalling the more common causes of peripheral neuropathy:

D Diabetes Mellitus
A Alcohol
Nutritional (B₁₂ deficiency)
Guillain-Barre Syndrome
Toxins (Pb, As, Zn, Hg)
Hematologic (paraproteins)
Endocrine (hypothyroid)
Rheumatologic (SLE, rheumatoid arthritis, vasculitis)
Amyloid
Porphyrin
Infectious (syphilis, HIV)
Sarcoid
Tumor (paraneoplastic neuropathy)

LABORATORY INVESTIGATION

Laboratory studies play an important role in diagnosing and categorizing the peripheral neuropathies. Electrodiagnostic studies are helpful in quantitating the neuropathy, while blood and urine studies are helpful in identifying an etiology.

Electrodiagnostic Studies

Nerve Conduction Study:

The recording and measurement of the compound nerve and muscle action potential elicited in response to a single supramaximal electrical stimulus, to measure the terminal latency, amplitude and duration of the evoked potential, as well as the conduction velocity.

Nerve conduction studies are helpful in documenting that a neuropathy exists, quantitating the severity, and noting the distribution of the neuropathy, i.e. whether it is distal, proximal or diffuse. In addition, nerve conduction studies can provide information on the modality involved, i.e. motor versus sensory, and can also give clues as to the underlying pathology, whether axonal or demyelinating.

Demyelinating neuropathies (neuropathies due to loss or destruction of myelin) result in slowed conduction velocities and prolonged distal latencies, because conduction velocity is proportional to the velocity of the largest-diameter myelinated fibers. Dispersion of evoked compound action potentials (CAP) can also be seen in demyelinating neuropathies, because all of the action potentials elicited in response to a single electrical stimulus will not reach the recording potential at the same time.

Severe demyelinating neuropathies can also produce conduction block, which is a major decrease in amplitude of the muscle CAP upon proximal stimulation of its nerve as compared to distal stimulation.

Axonal neuropathies (neuropathies due to loss of axons or their cell bodies) generally result in a reduced amplitude of the compound motor or sensory nerve action potentials.

Electromyography (EMG):

The recording and study of insertional, spontaneous, and voluntary electrical activity of muscle.

This test allows one to physiologically evaluate the motor unit, including the anterior horn cell, peripheral nerve, and muscle. EMG is helpful when evaluating patients with weakness, in that it can help one determine whether weakness is due to anterior horn cell disease, nerve root compression, peripheral neuropathy, or an intrinsic disease of muscle itself (myopathy).

EMG can differentiate acute denervation from chronic denervation, and may thus give an indication as to the time course of the lesion causing the neuropathy.

- **Acute Denervation:** Fibrillations and positive waves are present indicating spontaneous discharge of individual muscle fibers.
- **Chronic Denervation:** Voluntary motor unit potentials are of large amplitude and long duration, and are frequently polyphasic, because the motor units are enlarged as a result of re-innervation of adjacent previously denervated muscle fibers. Recruitment of additional motor units in response to increasing the force of muscular contraction is reduced for the same reason.
- **Demyelinating Neuropathy:** A decreased recruitment pattern is seen, since demyelination interferes with conduction of individual action potentials along the course of a peripheral nerve. Because denervation and reinnervation of muscle fibers are not features of demyelinating neuropathies, the configuration of the voluntary motor unit potentials is usually normal, and fibrillation potentials are not seen.

Nerve Biopsy

There are few indications for nerve biopsy when evaluating peripheral neuropathy. In general, a nerve biopsy is performed to evaluate asymmetric, multi-focal neuropathies. The sural nerve is frequently biopsied, since this is a purely sensory nerve that is easily obtained. In the upper extremity, the superficial radial nerve may be biopsied if necessary.

The nerve specimen is typically evaluated by means of light and electron microscopy. Semi-thin plastic embedded sections, stained with toluidine blue, are helpful for evaluating the myelin sheaths. Teased nerve fiber preparations are also helpful to look for demyelination and remyelination.

Sural nerve biopsies are particularly helpful when evaluating patients with a clinical picture of mononeuropathy multiplex, the basis of which is still unclear after other laboratory investigations are complete. Vasculitis, amyloidosis, leprosy and sarcoidosis can be accurately diagnosed by means of nerve biopsy.

Performing a nerve biopsy routinely in the evaluation of symmetric, distal polyneuropathies is usually fruitless, in that the pathologic diagnosis most often reveals "chronic neuropathy with mixed axonal-demyelinating features", a non-specific finding of little clinical benefit.

Blood Studies

Routine blood studies should be obtained in all patients with peripheral neuropathy in order to screen for reversible causes. The following blood tests are recommended:

- Complete blood count
- Chemistry profile
- Sedimentation rate
- Thyroid studies
- Vitamin B₁₂ level
- ANA, rheumatoid factor
- Serum protein electrophoresis, serum immuno-electrophoresis
- RPR and HIV (if the clinical situation warrants)

Urine Studies

The following studies are recommended to screen for reversible causes of neuropathy:

- Heavy metal screen (Hg, Pb, Zn, As)
- Urine protein electrophoresis, urine immuno-electrophoresis
- Watson-Schwartz test (qualitative test for porphobilinogen)

Chest x-ray, helpful to screen for asymptomatic lung cancer that can sometimes cause a purely sensory neuropathy.

TREATMENT

Neuropathy Associated With Systemic Illness

Treatment of the systemic illness frequently results in improvement in neuropathic symptoms. Since nerves regenerate slowly, at a rate of about one mm per day, recovery is often prolonged and may take months to years.

Immune-mediated Neuropathies

The immune-mediated neuropathies include those associated with vasculitis (SLE, rheumatoid arthritis or polyarteritis nodosa), and the immune-mediated demyelinating neuropathies (Guillain-Barre syndrome and CIDP).

Corticosteroids:

By virtue of their immunosuppressive effects, corticosteroids have been found to be effective in treating the vasculitic neuropathies as well as CIDP. Corticosteroids may be given daily or on an every-other-day regimen, depending on the severity and tempo of the disease. The typical initial dose of corticosteroids for the treatment of these neuropathies is 1 mg/kg/day of prednisone (or 2 mg/kg every-other-day).

Corticosteroids have never been proven to be effective in treating Guillain-Barre syndrome, and hence are not recommended for this disorder.

Immunosuppressives:

Azathioprine, cyclophosphamide, cyclosporine, mycophenolate and methotrexate are all used in the treatment of autoimmune diseases. Each of these medications has potential serious toxicity.

Azathioprine is frequently used, in combination with steroids, to treat autoimmune neuropathies because of its steroid-sparing effect. Concurrent use of these two medications allows corticosteroids to be tapered more quickly and more completely once the neuropathy is brought under control.

The usual dosage of azathioprine is 2-3 mg/kg/day given in divided doses. This medication has a delayed beneficial effect and several months are required before an effect may be seen. The erythrocyte mean cell volume (MCV) provides an index of therapeutic effect: a slight elevation in MCV suggests that the dose of azathioprine is appropriate.

Azathioprine is metabolized by xanthine oxidase, and medications that block this enzyme, such as allopurinol, should be avoided since concurrent use can cause azathioprine toxicity.

Plasmapheresis:

In this procedure, blood is removed from the patient, plasma is separated from blood cells and discarded, and blood cells are resuspended in colloid solution and reinfused. Plasmapheresis is effective in treating patients with immune-mediated neuropathies such as those caused by cryoglobulins, SLE, rheumatoid arthritis or polyarteritis nodosa. In addition, individuals with GBS and a large subset of patients with CIDP benefit from this procedure.

The effects of plasma exchange can be summarized as "fast, temporary, and expensive". This procedure does not, by itself, induce permanent remission, and the

ideal application is therefore in acute, self-limited disorders such as GBS. Plasma exchange may also have application in chronic diseases, such as CIDP, where rapid therapeutic effects may occasionally be required.

Intravenous Immunoglobulin (IVIg):

IVIg is pooled, human IgG in a form that is safe for intravenous administration. How IVIg affects immunologic function is unknown, but three putative mechanisms have been postulated:

- Administration of IVIg floods the recipient with an enormously diverse array of antibody molecules, some of which are anti-idiotypic antibodies which may neutralize auto-antibodies in the patient, thereby increasing their clearance and perhaps down-regulating their production.
- IVIg inhibits the binding of activated complement to target cells, thus reducing complement-mediated damage to cell membranes.
- IVIg infusion is a potent stimulus that down-regulates immunologic production.

To date, IVIg has been found to be as effective as plasma exchange in treating many immunologic disorders, including Guillain-Barre syndrome and CIDP. IVIg is also reported to be beneficial in treating the polyneuropathy associated with IgG or IgM paraproteins.

Side effects of IVIg include fever, myalgia, headache, rash, and occasionally aseptic meningitis and renal failure. The cost of IVIg is equivalent to that of plasma exchange.

Symptomatic Treatment

Numerous symptomatic treatments for the pain of peripheral neuropathy are available, and all have their relative risks and benefits.

Tricyclic Compounds:

Drugs in this category include amitriptyline, nortriptyline, desipramine, imipramine and duloxetine. These drugs inhibit the re-uptake of the catecholamine neurotransmitters epinephrine and norepinephrine as well as serotonin, and thus may enhance central pathways that suppress pain transmission. The tricyclic compounds are quite useful for treatment of the burning, dysesthetic pains seen with peripheral neuropathies. Most of these drugs are sedating and, when given at bedtime, promote sleep.

Effective dosages of these drugs for treating chronic neuropathic pain are typically lower than the dosages used for treating depression. We recommend starting with a low single dose at bedtime and slowly increasing the dose over several weeks. Patients should be informed that it may take several weeks before full therapeutic effects are realized.

Anticonvulsants:

Drugs in this category include carbamazepine, phenytoin, gabapentin and lamotrigine. These drugs stabilize neuronal membranes and may thus prevent neuronal “short-circuits” that lead to neuropathic pain. The anticonvulsant drugs are quite useful in treating the lancinating pains frequently seen with trigeminal neuralgia and in some other peripheral neuropathies.

Effective dosages for treating neuropathic pain are similar to the dosages used for treating seizures. Blood levels of these drugs may be monitored and dosages adjusted as needed.

Lamotrigine, a new anti-seizure drug effective for primary generalized seizures, can cause a severe and fatal cutaneous hypersensitivity reaction if the starting dosage is high, and therefore must be started at a very low dose with a very gradual dosage escalation.

Topicals:

Capsaicin, a drug that impedes pain transmission by depleting substance P from sensory nerve fibers, has been found effective in treating refractory neuralgia in several studies. The cream must be applied several times daily to be effective, and patients frequently experience severe burning following each application for one or two weeks following initiation of treatment.

Transdermal lidocaine (Lidoderm), a local anesthetic, also appears to be effective for some patients with neuropathic pain syndromes. This drug is available as an adhesive patch that may be cut to size and replaced every 12 hours.

Surgery

Surgical release of tendons, scar tissue and bony ridges is beneficial in treating many forms of entrapment neuropathy. Nerve transposition may play a role as well in certain clinical circumstances.

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Case 1

A 23-year-old, right-handed college student and summer waitress was well until one month ago when she developed tingling in both hands, primarily in the thumb, second and third digits, and worse on the right. It frequently awoke her from sleep. She occasionally noted pain in her right forearm. She denied any hand weakness. No history of neck pain.

She started to work as a waitress 2 months ago. She had no tingling when waiting on tables or when mowing the lawn but developed the tingling afterwards.

Past Medical History: Herniated lumbar disk following a fall; s/p right L5 laminectomy

Medications: Oral contraceptives

Family History: Unremarkable

Physical Examination:

- P=108/min; BP=110/80 mm Hg
- Neck ROM full
- Tinel sign negative bilaterally
- Phalen sign positive bilaterally

Neurologic Examination:

- Motor exam: Slight weakness of the right APB muscle
- Sensory exam: normal, including hands and feet
- MSR: 3+ bilaterally, including ankle jerks
- Romberg: negative

Case 2

A 56-year-old mechanical engineer was referred for evaluation of numb toes that came on gradually and painlessly 12 years ago. The numbness is most pronounced when he is trying to fall asleep and is made worse by cold weather; warm weather improves the sensation in his feet. He has decreased sensation on the soles of his feet when he is stepping on the pedals in his car. Walking barefoot produces intense pain. The numbness has progressed to involve the distal feet.

He denies weakness in his feet, walking difficulty, bowel or bladder difficulty, sexual dysfunction, or back or neck pain.

Past Medical History: Hypertension, meralgia paresthetica, s/p appendectomy

Medications: captopril, potassium, aspirin

Habits: occasional EtOH, no tobacco

Family History: unremarkable

Physical examination:

- P=60/min, BP=160/100 mm Hg
- Moderately obese, lipoma over right lateral hip
- Neck and back ROM intact; SLR negative

Neurologic examination:

- Motor: atrophy of EDB muscles in both feet; unable to fully cock up his toes
- Sensory: reduced pin sensation in toes; absent vibration and position sense in feet
- Reflexes: Absent ankle jerks

Case 3

A 70-year-old woman developed numbness in her feet and upper back pain. The following month she developed a left Bell's palsy that was treated with a seven day course of prednisone. She then developed progressive numbness and pain in her feet and hands in a stocking-glove distribution. Distal weakness developed after this. She was treated with amitriptyline which helped the pain but not the numbness or weakness. Over the past two weeks her weakness worsened to the point that she had difficulty walking because of bilateral foot drop. She was therefore admitted for further evaluation.

Past Medical History: Hypertension

Medications: HCTZ, nifedipine, ranitidine, ASA

Physical Examination:

- P=84/min; BP=140/82 mm Hg; T=37°C
- Grade 2/6 SEM present

Neurologic Examination:

- Motor: unable to stand on heels or toes; grade 4 weakness in biceps, wrist extensors and flexors, finger flexors and psoas muscles; grade 2 weakness in interossei and dorsi and plantar flexor muscles
- Sensory: light touch, temperature and pin reduced in a stocking-glove distribution; vibration and position sense absent at the toes;
- Reflexes: UE 2+; knees 1+; ankles absent
- Gait: bilateral steppage

Case 4

A 63-year-old school bus driver noted tingling and numbness in her limbs two months ago. The tingling first began in her left arm and leg. Her gait is unsteady and she fell 3 times. She has exquisite pain in her feet when she steps on a sharp object. She also feels that her lower limbs are weak.

Past Medical History:

- s/p cervical laminectomy in 1994 for severe spinal stenosis
- s/p left 6th nerve palsy one year ago with resolution
- Stage 2 endometrial cancer in 2001, s/p surgery, pelvic irradiation and chemotherapy (carboplatin / paclitaxel)
- Hypothyroidism

Medications: diltiazem, l-thyroxine, ASA

Physical Examination:

- P=76/min, BP=142/80 mm Hg
- Neck ROM reduced in all directions

Neurologic Examination:

- Motor: Essentially normal
- Sensory: Absent vibration in hands and feet, ↓ position sense in toes, pin and temperature reduced distal to mid forearms and calves and at umbilicus
- Coordination: ataxia with heel-to-shin testing
- Reflexes: MSR absent, plantar responses flexor
- Romberg unsteady, wide based gait