



EMG Case No. 73, July 2005

Presenting Symptom(s):

Right thumb and bilateral ankle weakness with associated numbness, tingling, and pain

This case is no longer available for CME credit.

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Disclosures: C. Huynh, None; K. Mook, None.

Appropriate Audience: Residents and practicing physicians.

Learning Objectives: After completing this educational activity, participants will be able to: (1) formulate a differential diagnosis for peripheral neuropathies; (2) be able to formulate a NCS/EMG (nerve conduction studies/electromyography) plan of approach in evaluating peripheral neuropathy and be able to analyze NCS/EMG data in order to classify peripheral neuropathies (i.e. sensory/motor demyelinating/axonal); (3) become familiar with vincristine neuropathy, its clinical presentation and course, and NCS/EMG findings.

Level of Difficulty: Intermediate.

History

(Dates have been changed to protect the identity of the patient)

A 19 year-old right-handed white woman presents for electrodiagnostic evaluation of profound weakness in her right thumb and both ankles with bilateral numbness, tingling, and pain of the hands and feet. She had a rhabdomyosarcoma removed from her lower back (two excisions in January then March) and then received adjuvant chemotherapy and radiation therapy from April to the end of September. Her symptoms started in the beginning of September. At the time the patient is seen for electrodiagnostic testing, her symptoms have been present for 2 months.

- Prior to continuing, please develop a differential diagnosis and list each possible diagnosis in order of likelihood.
- Is there any additional information regarding the clinical history that might be helpful in clarifying your differential list or changing its order of priority?

Commentary I

As the patient has concomitant, nearly symmetrical symptoms in the lower and upper extremities, one would suspect a diffuse process. Distal muscle weakness with associated distal sensory changes would likely be a polyneuropathy. Differential diagnosis of the neuropathy includes chemotherapy, cancer/paraneoplastic, radiation, metabolic (diabetes, vitamin deficiency), hereditary, infectious, inflammatory, autoimmune, vascular, and idiopathic. Other considerations are compressive myelopathy from metastases, multiple sclerosis, transverse myelitis, myopathy, neuromuscular junction disease, and polyradiculopathy.



As there are so many etiologies to consider in polyneuropathy, the approach to evaluation starts with a good patient history. Important questions to clarify include the specific chemotherapy agents she has received, the area of radiation to her body, specifics on the rhabdomyosarcoma's tissue infiltration and surgical excision, pertinent positives for metabolic disorders, any cold/flu symptoms, and family history of neuropathic conditions. Classifying symptoms (motor vs. sensory vs. motor/sensory, symmetric vs. asymmetric, acute vs. subacute vs. chronic) can also help with narrowing the differential diagnosis.

At this point, toxicity from chemotherapy is a high on the list considering the temporal relation of her symptoms.

In any case of cancer, metastases or recurrent cancer should always be considered and ruled out.

As a surgical procedure occurred to the lower back as well as radiation to the area, polyradiculopathy or nerve injury has to be considered. However, it would be difficult to explain her upper extremity symptoms if the lower back is the area of excision and radiation.

Metabolic disorders are very common causes of peripheral polyneuropathies and diabetes, thyroid disease, vitamin deficiency are common examples.

Hereditary motor sensory neuropathies can be asymptomatic in a patient and acutely be expressed when there is an inciting stimulus. There have been case reports of asymptomatic patients carrying the gene for Charcot Marie Tooth who developed chronic debilitating neuropathy after receiving certain chemotherapy agents such as vincristine.

Inflammatory demyelinating neuropathies can start distally. It would be important to find out if patient has any ascending symptoms or cold/flu illness preceding the neurologic symptoms.

In a young woman who develops profound sensory/motor symptoms, multiple sclerosis should at least be considered. However, multiple sclerosis typically has an asymmetric presentation. It would be important to do a review of systems and to evaluate any other abnormalities, which may be subtle.

There are some myopathies that cause a distal rather than proximal weakness and neuromuscular junction disorders can as well. However, the patient also has associated sensory symptoms, which makes these diagnoses less likely.

History, continued

Since the weakness, numbness, and pain began 2 months ago, the symptoms progressively worsened in intensity but then reached a plateau and have not palliated with time. The numbness, tingling, and pain are intermittent, worsened with activity, and alleviated with rest. She cannot close her right thumb to hold a pencil and her feet feel like they are dragging on the floor. She reports no recent cold/flu symptoms and that she seemed to tolerate the chemotherapy agents without much nausea or vomiting. The chemotherapy agents used in this patient were vincristine and cyclophosphamide. She states that at the end of chemotherapy and radiation therapy, there were no signs of tumor recurrence on repeat radiographic studies and the oncologist told her she did not have any evidence of metastases. Basic labs were also done with her last oncology visit and those were reported to her as being normal. She is not sure how deep the tumor was but remembers being told it was about 5cm in diameter. The surgery occurred around L2-3 and she did not have any



complications. The radiation therapy was done by external beam and concentrated only over the tumor bed. Aside from the chief complaints, review of systems shows no other weakness/fatigue, sensory changes, visual changes, cognitive changes, bowel/bladder problems, or other pertinent positives. Family history and review of systems was negative for diabetes or thyroid disorders. There also is no family history of motor/sensory neuropathies. She does not smoke and does not drink any alcohol.

- If necessary, revise your differential diagnosis based on the additional clinical history.
- On which details of the physical examination should you focus at this point?

Commentary II

Vincristine has the documented side effect of causing neuropathies and this further bolsters the suspicion that she has a toxic neuropathy. Metabolic neuropathy is less likely as her symptoms developed rather acutely. The location of her surgery and radiation, even though done at around L2-3, could possibly explain her lower extremity symptoms but do not explain the upper extremity symptoms. It is good to know her oncologist has recently ruled out recurrence or metastases. However, occult reoccurrence causing paraneoplastic syndrome is still possible. Multiple sclerosis still may be considered but she does not have the common presenting symptoms and she has symmetrical symptoms. She had no prior cold/flu or symptoms ascending her extremities that usually go along with inflammatory demyelinating neuropathies. Suspicion for a hereditary neuropathy, myopathy, and neuromuscular junction disorder does not change much with the extra history.

Physical exam should evaluate for any pattern of sensory loss (dermatomal or stocking-glover) and any pattern of motor weakness (proximal or distal; myotomal or diffuse). A thorough exam would also observe for other abnormalities such as coordination and bulbar signs.

Physical Examination

She is an overweight young woman who is walking with a normal gait pattern and appeared to get up from her chair and sit without difficulty. She has a well-healed incision over her lumbar region. Sensations to light touch and pinprick show no appreciable decrement in the hands and feet compared to the rest of her extremities. Additional exam of vibratory and positional sensation was normal. There is no evidence of muscle atrophy in her upper extremities or lower extremities. Gross cranial nerve exam shows no asymmetry.

- At this point, review your differential diagnosis and revise as appropriate.
- Are there additional observations on physical examination that might be helpful in narrowing your differential list?

Commentary III

The current findings are minimally helpful with the differential diagnosis. Despite the patient stating she has symptoms of numbness in her hands and feet, the direct exam did not show any abnormalities. This can be confusing but the patient's symptoms cannot be wholly dismissed. It would be of interest to have patient outline her numbness/tingling to get an idea of the distribution.



Sometimes observation of a patient's movement can help give a quick picture of patient's weakness. Watching her movement getting out of a chair without difficulty shows her proximal muscle strength appears intact. This makes most myopathies and neuromuscular junction disorders less likely. As her cranial nerves appear to have symmetric function, multiple sclerosis may also move lower on the list of probabilities. Manual motor testing at this time can help us define if there is a pattern of weakness that follows a single/multiple nerves or single/multiple roots.

Physical Examination, continued

When asked to draw the areas where she has numbness/tingling and pain, the patient shades out a stocking/glove distribution over her bilateral feet and hands. On manual muscle testing, she is unable to abduct the R thumb (1/5 strength) but can fully adduct and flex the phalange of the thumb (4/5 strength). The rest of her right upper and left upper extremity motor strength is 5/5 including D2-5 finger adduction/abduction, finger and metacarpal flexion/extension, wrist flexion/extension, elbow flexion/extension, and shoulder movement.

In the lower extremities, she can dorsiflex ankles bilaterally 2/5 strength; extend her big toe 1/5 on right, 0/5 on left; evert her foot bilaterally 5-/5, plantar flex bilaterally 5-/5. The rest of her lower extremity manual muscle testing was 5/5 including knee and hip flexion/extension and hip abduction/adduction. Deep tendon reflexes were done on bilateral biceps brachii, knees, and ankles and were 2+ and symmetrical.

- If necessary, revise your differential diagnosis based on the additional physical findings.
- Design your approach to the electrophysiologic examination based on the existing data.

Commentary IV

The description of her sensory changes follows a stocking-glove distribution common to peripheral neuropathies. Additionally, the manual muscle test does show multiple distal muscle weakness primarily affecting bilateral peroneal nerve innervated muscles (tibialis anterior, peroneus longus, and extensor hallucis longus) and the right median nerve innervated hand muscle (abductor pollicis brevis). The findings are a bit confusing. The sensory deficit in all extremities and motor deficit in the bilateral lower extremities have symmetry but the unilateral weakness of the right abductor pollicis brevis is an outlier. Essentially, the differential diagnoses needs to fit a picture of distal diffuse neuropathy and the current differential maintains the same order as originally suggested - albeit with some diagnoses having less likelihood of being the etiology.

Electrodiagnostic studies to evaluate for peripheral neuropathy can be labor intensive and time consuming. A starting point is to evaluate sensory and motor nerves that correlate with the sensory deficits and motor deficits noted on physical exam. In this case, any upper and lower sensory nerves, the median motor nerve, and the peroneal motor nerve are the target nerves. If those nerves show abnormalities, then other nerves in the extremity need to be tested as well to see if there is a diffuse pathology or if only single nerves are affected. EMG should also be considered to rule out other differential diagnostic considerations such as polyradiculopathy. The ultimate goal of electrodiagnosis in peripheral neuropathy is to be able to characterize the neuropathy.



When a peripheral neuropathy is detected in electrodiagnostic studies, it is important to present the classification of the neuropathy in the report. The classification of peripheral neuropathies can help direct the referring physician to the underlying etiology of the peripheral neuropathy. The classification scheme involves labeling the neuropathy as affecting mainly motor fibers, sensory fibers, or both; affecting mainly axon, myelin, or both; and being segmental or uniform. Many references are available that will list electrodiagnostic findings and respective possible conditions. An example of this listing follows below (table taken from Weiss, et al, Easy EMG, split in two parts for ease of viewing):

PART I

| Uniform demyelinating mixed sensorimotor polyneuropathy | Segmental demyelinating polyneuropathy | Axon loss motor > sensory polyneuropathy |
|--|--|--|
| Hereditary motor sensory neuropathy type I, III, VI, Metachromic leukodystrophy, Krabbe’s leukodystrophy, Adrenomyelo-neuropathy, Congenital hypomyelinating neuropathy, Tangier disease, Cockayne’s syndrome, Cereotedinous xanthomatosis | AIDP, CIDP, Osteosclerotic myeloma, Leprosy, Acute arsenic polyneuropathy, Pharmaceuticals (Amiodarone, Perhexiline, Carcinoma, AIDS | Paraneoplastic motor neuronopathy, Porphyria, Axonal Guillain-Barre syndrome, HMSN type II, V, Lead neuropathy, Dapsone neuropathy |

PART II

| Sensory axon loss polyneuropathy | Axon loss mixed sensorimotor polyneropathy | Mixed axonal loss and demyelinating sensorimotor polyneuropathy |
|--|--|---|
| Paraneoplastic, Hereditary sensory neuropathy type I-IV, Friedrich’s ataxia, Spinocerebellar degeneration, Abetalipo-proteinemia, Primary biliary cirrhosis, Cis-platinum toxicity, Lymphomatous sensory | Alcoholic polyneuropathy, Vitamin (B12, thiamine) deficiency, Gouty neuropathy, Metal neuropathy (mercury, thallium, gold), Sarcoidosis, Connective tissue diseases, Gastrectomy, Chronic liver diseases, Hypothyroidism, Myonic dystrophy, AIDS, Lyme disease, Vincristine neuropathy | Diabetic polyneuropathy, Uremia |

The table is meant to only be a guide. Correlation needs to occur between the electrodiagnostic findings and the patient history. Some other useful clues that help pinpoint



the etiology of the peripheral neuropathy is considering the time course of symptom development – acute, subacute, and chronic. For example, most toxicity related neuropathies present rather acutely, whereas diabetic neuropathy may be slowly progressive.

Electrophysiologic Data

NR = no response

| SENSORY NERVE CONDUCTION STUDIES | | | | | | | |
|----------------------------------|------|-----------|--------|----|-----------------|-------------|----|
| NERVE | SIDE | STIM SITE | RECORD | cm | LAT msec (peak) | AMPL microV | CV |
| Median | R | Palm | Wrist | 8 | 1.9 | 22 | |
| Ulnar | R | Palm | Wrist | 8 | 2.0 | 15 | |
| Median | L | Palm | Wrist | 8 | 1.9 | 49 | |
| Ulnar | L | Palm | Wrist | 8 | 1.9 | 23 | |
| Sural | R | Calf | Ankle | 14 | 3.7 | 8 | |
| Sural | L | Calf | Ankle | 14 | 3.7 | 5 | |

| MOTOR NERVE CONDUCTION STUDIES | | | | | | | |
|--------------------------------|------|-----------------|---------|------|------|------|------|
| NERVE | SIDE | STIM SITE | RECORD | cm | LAT | AMPL | CV |
| Median | R | Wrist | APB | 8 | 4.4 | 0.9 | |
| Median | R | Elbow | APB | 22.5 | 9.0 | 0.8 | 48.4 |
| Ulnar | R | Wrist | ADQ | 8 | 2.9 | 6.0 | |
| Ulnar | R | B. elbow | ADQ | 21 | 6.6 | 5.8 | 57.5 |
| Ulnar | R | A. elbow | ADQ | 14.5 | 9.0 | 5.4 | 60.4 |
| Median | L | Wrist | APB | 8 | 3.9 | 5.0 | |
| Median | L | Elbow | APB | 21 | 7.9 | 4.7 | 52.5 |
| Ulnar | L | Wrist | ADQ | 8 | 3.0 | 5.1 | |
| Ulnar | L | B. elbow | ADQ | 21 | 6.5 | 4.9 | 60.0 |
| Ulnar | L | A. elbow | ADQ | 15 | 8.8 | 4.7 | 63.8 |
| Peroneal | R+L | Ankle | EDB | 8 | NR | NR | |
| Peroneal | R+L | Fib Head | EDB | | NR | NR | NR |
| Peroneal | R+L | Across Fib Head | EDB | | NR | NR | NR |
| Peroneal | R+L | Fib Head | Tib Ant | 8 | NR | NR | |
| Peroneal | R+L | Across Fib Head | Tib Ant | | NR | NR | NR |
| Tibial | R | Ankle | Abd Hal | 8 | 4.4 | 5.3 | |
| Tibial | R | Popliteal Fossa | Abd Hal | 38.5 | 12.8 | 5.4 | 45.8 |



| | | | | | | | |
|--------|---|-----------------|---------|------|------|-----|------|
| Tibial | L | Ankle | Abd Hal | 8 | 4.8 | 4.5 | |
| Tibial | L | Popliteal Fossa | Abd Hal | 38.0 | 13.5 | 3.9 | 43.7 |

NEEDLE ELECTROMYOGRAPHY

INSERtional activity: N, sust, unsust
 FIB: 0, 1+, 2+, 3+, 4+
 PSW (positive sharp wave): 0, 1+, 2+, 3+, 4+
 AMPlitude: N, inc or dec 1+, 2+, 3+, 4+
 DURation: N, inc or dec 1+, 2+, 3+, 4+
 POLyphasia: N, inc or dec 1+, 2+, 3+, 4+
 EFFort: N, decr
 RECruitment: N, inc or dec

| Side | MUSCLE | INSER | FIB | PSW | AMP | DUR | POL | EFF | REC |
|------|--------------------------|-------|-----|-----|-----|-----|-----|-----|-----|
| R | Abd Pol Brev | Incr | 2+ | 2+ | N | N | N | N | Dec |
| R | First Dors Inteross Hand | Incr | 1+ | 2+ | N | N | N | N | N |
| R | Ext Ind Prop | N | 0 | 0 | N | N | N | N | N |
| R | Pron Teres | N | 0 | 0 | N | N | N | N | N |
| R | Flex Car Uln | N | 0 | 0 | N | N | N | N | N |
| R | Bicep | N | 0 | 0 | N | N | N | N | N |
| R | Tricep | N | 0 | 0 | N | N | N | N | N |
| R | Deltoid | N | 0 | 0 | N | N | N | N | N |
| R | Cerv paraspinal | N | 0 | 0 | 0 | N | N | N | N |
| L | Abd Pol Brev | Incr | 3+ | 3+ | N | N | N | N | Dec |
| L | First Dors Inteross Hand | Incr | 2+ | 2+ | N | N | N | N | |
| L | Ext Ind Prop | N | 0 | 0 | Inc | N | N | N | N |
| L | Pron Teres | N | 0 | 0 | N | N | N | N | N |
| R | Lumbar paraspinal | N | 0 | 0 | N | N | N | N | N |
| R | Gluteus maximus | N | 0 | 0 | N | N | N | N | N |
| R | Gluteus medius | N | 0 | 0 | N | N | N | N | N |
| R | Biceps fem SH | N | 0 | 0 | N | N | N | N | N |
| R | Vastus med | N | 0 | 0 | N | N | N | N | N |
| R | Tib ant | N | 0 | 3+ | N | N | 1+ | N | Dec |
| R | Med gastroc | N | 0 | 0 | N | N | N | N | N |
| R | Ext Hall Longus | Decr | 1+ | 0 | N | N | 1+ | N | Dec |
| R | Peroneus longus | N | 0 | 1+ | N | N | N | N | Dec |
| L | Vastus med | N | 0 | 0 | N | N | N | N | N |
| L | Tib ant | N | 1+ | 1+ | N | N | 1+ | N | Dec |



| | | | | | | | | | |
|---|-----------------|------|---|----|---|---|---|---|-----|
| L | Med gastroc | N | 0 | 0 | N | N | N | N | N |
| L | Ext Hall Longus | N | 0 | 0 | N | N | N | N | Dec |
| L | Peroneus longus | Decr | 0 | 1+ | N | N | N | N | N |
| L | Biceps fem SH | N | 0 | 0 | N | N | N | N | N |

Diagnostic Impression

In this patient, her sensory nerve conduction studies in bilateral upper and lower extremities all had normal distal latencies and amplitudes. In the upper extremities, she had borderline normal/slow right median motor distal latency with low amplitude and borderline normal/slow conduction velocity across the forearm; her left median and bilateral ulnar motor studies were normal. In the lower extremities, she had normal bilateral sural sensory latencies and low normal amplitudes. Her bilateral tibial motor distal latencies, amplitude and conduction velocity were also normal. However, her bilateral common peroneal nerve showed no activity below and above the fibular head to the extensor digitorum brevis or to the tibialis anterior muscles.

The EMG studies in the upper extremity show spontaneous potentials in bilateral abductor pollicis brevis and bilateral first dorsal interossei with decreased recruitment only in the R abductor pollicis brevis. The left extensor indicis proprius had the abnormality of large amplitude motor unit potentials, which suggest neurologic recovery. Other more proximal muscles tested in the arms and the cervical paraspinals were normal. The upper extremity findings suggest a distal axonal diffuse neuropathy, affecting distal median and ulnar nerves, but also could suggest bilateral C8, T1 radiculopathy. However, with paraspinal muscles showing no abnormalities, radiculopathy is less likely (although this could also be evidence of completed sprouting and recovery).

In the lower extremities, EMG shows spontaneous potentials and decreased recruitment in distal peroneal innervated muscles (bilateral tibialis anterior, peroneus longus, and extensor hallucis longus). With normal EMG of the bilateral biceps femoris short head, which gets the peroneal division of the sciatic nerve, findings so far suggest only the distal portion of peroneal nerve at or below the knee is affected while above the knee appears to be intact. There is some evidence of reinnervation in the bilateral tibialis anterior and right extensor hallucis longus muscles. Other more proximal muscles tested in the legs and the lumbar paraspinals were normal. The overall electrodiagnostic picture is an axonal, primarily motor, distal polyneuropathy. In looking at the sural sensory studies the amplitudes are borderline normal/low. Considering the patient’s age and the clearly normal amplitudes of the other sensory studies that were done, this would suggest the sural amplitudes are abnormal. Although this is difficult to classify, the finding makes a sensorimotor peripheral polyneuropathy a consideration. Putting this, the patient history, and clinical symptoms together make vincristine neuropathy the most likely diagnosis in this patient.

- What other diagnostic procedures (laboratory tests, etc.), if any, are needed?
- What treatment would you recommend?

Commentary V

Vincristine neuropathy usually results in axonal sensorimotor injury with relative preservation of the myelin sheath; nerve conduction velocities remain normal or only mildly



delayed. In most cases, patients have distal muscle weakness, sensory loss, and complaints of associated pain. Less commonly it has been documented to cause proximal muscle weakness and myalgias. Electromyography shows fibrillations, positive sharp waves and neurogenic MUAPs in distal muscles while proximal muscles appear normal (1). After stopping vincristine, symptoms improve in most patients.

Being right handed and unable to grasp a pencil or other utensils with right abductor pollicis brevis weakness, an orthosis could help the patient use her right hand. If her dorsiflexion weakness begins to affect her gait, bilateral ankle foot orthosis would be indicated. A trial of gabapentin, tiagabine, or amitriptyline would be appropriate for her neuropathic pain.

As vincristine neuropathy typically improves with discontinuation of the chemo agent, there is a case report that suggests another underlying peripheral motor sensory neuropathy needs to be suspected in cases of severe or abnormally persisting vincristine neuropathy even when clinical and family histories are negative. Mercuri, et al, reported a case of vincristine triggering expression of HMSN type 1A in a child that was previously asymptomatic and had no family history (2). The child had received vincristine for acute lymphoblastic leukemia while 5 years old and developed severe neuropathy (inability to ambulate). After vincristine was stopped, he had very slow recovery; it took about 1 yr before he could ambulate. With a "second opinion" evaluation of the patient's weakness at age 8, he had electrodiagnostic studies showing slow conduction velocities (22-28m/s) and was tested genetically to have HSMN type1A.

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