

CASE PRESENTATION: POLYNEUROPATHY

STEVEN DESCHNER

PART 1: CASE REPORT

Patient is a 58 year old white female with history of hyperlipidemia and bipolar disorder. She presents with complaint of burning sensation in her hands and feet. Symptoms began nine months ago. Initially, symptoms were present in her feet. Within three months, symptoms were present in her hands. Intensity has increased progressively since onset. Now, the pain is constant and very irritating to the patient. Pain is most intense at night. Symptoms are more intense in the feet than in the hands. Symptoms are equal between sides. Pain that started in the feet has ascended to the level of the knee on the left and mid-calf on the right. Pain that began in the hands had ascended to the level of the wrists bilaterally. Patient denies pain at any other location in her body. She reports mild weakness in her hands. She does not remember if she had a respiratory or gastric illness prior to onset of symptoms. She denies history of stroke. She knows of no exposure to toxin. She takes lipitor for hyperlipidemia. In the past, she took lithium for bipolar polar disorder. She stopped taking lithium six months ago and currently is taking no medication for bipolar disorder. She denies family history of neurological disease.

Physical exam revealed a moderately obese female distressed by her condition. There was no hypertension. Vital signs were normal. Physical exam proved normal. Specifically, there was no scleral icterus, facial or extremity telangiectasias, no muscle atrophy, no extremity edema, distal pulses were present in all extremities, hair was present on the hands and toes. Neurological exam revealed depressed vibratory and positional sense in the left leg to the level of the patella, in the right leg to the level of the malleoli, and in the arms to the level of the radial styloid process. Sensation to touch was reduced on the plantar surface of the feet and in the fingers to the level of the distal interphalangeal joints. Otherwise, sensation was intact. Deep tendon reflexes were reduced, being measured as 1/4 at the quadriceps, biceps, brachioradialis, and triceps - 0/4 at the soleus. Otherwise, the neurological exam was normal. Cranial nerves were normal. Extremity strength was 5/5 throughout. Toes were downgoing bilaterally. Coordination of finger-to-nose, heel-to-shin, and rapid alternating movements were intact. Gait was normal. Romberg was negative. Patient was unable to perform tandem gait. No labs or imaging was present at time of initial interview.

PART 2: DIFFERENTIAL DIAGNOSIS:

Differential for sensory changes in multiple extremities:

1. Joint inflammatory disease
2. Post stroke pain syndrome
3. Cervical spondylosis with cord impingement
4. Mononeuropathy multiplex
5. Polyneuropathy

Differential for polyneuropathy:

1. Diabetes mellitus
2. Uremia
3. Toxins - alcohol
4. Medications
5. HIV
6. Syphilis
7. Lyme disease
8. Vasculitis
9. Vitamen B12 deficiency
10. Amyloidosis
11. Paraneoplastic neuropathy
12. Chemotherapy

PART 3: FINAL DIAGNOSIS

Patient was found to have a rapidly progressing polyneuropathy secondary to adenocarcinoma in the left breast. Diagnosis was determined in the following manner. Inflammatory joint disease was ruled out because the patient did not have enlarged, painful joints. Post stroke pain syndrome was possible. While patient denied history of stroke, she did have one known risk factor for stroke in hyperlipidemia. Silent lacunes were possible. Post stroke pain may present in a stocking glove distribution, however this is usually on the same side. Though post stroke pain may have been possible, it did not seem likely. The patient did not have mononeuropathy multiplex. She never described pain that appeared concurrently in the distribution of different nerves. Furthermore, this condition is usually secondary to vasculitis. ESR was elevated slightly above normal. ANA was normal. This did not suggest a vasculitis. Unfortunately, vasculitis secondary to other connective disease processes was not evaluated. Cervical spondylosis with cord impingement was not evaluated. To determine if this condition existed, MRI C-Spine would have been necessary. Follow-up on various etiologies of polyneuropathy provided an answer before a MRI was ordered.

A tentative diagnosis of polyneuropathy was evaluated with EMG/NCS and labs to investigate etiology. EMG/NCS revealed a sensory axonopathy. Blood glucose and hemoglobin A1C were normal. Patient was not diabetic. BUN was normal. Patient was not uremic. Patient denied history of alcohol use. She had no telangiectasias. Hepatomegaly was not evaluated, however liver enzymes and coagulation panel were normal. The patient was taking lipitor for hyperlipidemia. Statins increase the risk of polyneuropathy. This may have contributed to the patient's symptoms. Lab tests for HIV, syphilis, and Lyme disease were negative. ANA was negative. ESR was mildly elevated. Vasculitis secondary to lupus did not seem likely. Vitamin B12 was normal. Patient did not have macrocytic anemia. Amyloidosis was not evaluated. If this etiology had been pursued, a SPEP to assess for monogammopathy would have been appropriate.

Patient was referred to her PCP for thorough physical exam including breast exam, chest X-ray, PAP, colonoscopy to assess for tumor. The exam found a tumor in the left breast. Biopsy revealed adenocarcinoma. The reason for the rapidly progressing painful polyneuropathy was paraneoplastic syndrome. Evaluation of anti-Hu has not been done.

PART 4: CLINICAL QUESTION

What medication most effectively treats the paresthesia of polyneuropathy?

Answer: Tricyclic antidepressants, specifically desipramine, seem to be the most effective medication for treatment of paresthesia associated with polyneuropathy.

Tricyclic antidepressants are more effective than SSRI. When used to treat diabetic neuropathy, desipramine and amitriptyline were more effective than fluoxetine (74,61,48 respectively - control 41)
Max MB, Lynch SA, Muir J, et. al. Effects of desipramine, amitriptyline and fluoxetine on pain in diabetic neuropathy. N Engl J Med 1992; 326: 1250-1255.

Tricyclic antidepressants are more effective than gabapentin. When evaluating the number of patients needed to treat (NNT) to achieve 50 percent pain reduction in one patient with polyneuropathy, NNT was lower (more favorable) for tricyclic antidepressants (NNT 2.6 for desipramine, 4.1 for gabapentin).
Sindrup SH, Jensen TS. Pharmacologic treatment of pain in polyneuropathy. Neurology 2000; 55: 915-921.

PART 5: THERAPEUTIC OPTIONS

Treatment should involve removal of the agent causing the polyneuropathy. In this case, the adenocarcinoma should be removed. Treatment of paresthesia should start with a tricyclic antidepressant such as desipramine 10-50mg qhs. If ineffective, gabapentin should be added. Third line agents include carbamazepine and phenytoin. Tramadol and NSAID can be used for breakthrough pain. Patient should be vigilant for cutaneous injury of the feet as unattended wound can lead to serious infection.

PART 6: PATIENT RESOURCES

1. Polyneuropathy Patient/Family Resources at the following E-mail address:
cchs-dl.slis.ua.edu/patient_info/neurology/pns/neuropathy.htm
2. Polyneuropathy information resource and support at the following E-mail address:
www.medhelp.org/Health_Topics/Polyneuropathy.html

PART 7: OUTCOME

With resection of the adenocarcinoma, paresthesia should stabilize. Paresthesia may resolve to some degree, however it is more likely patient will need to continue on tricyclic antidepressants.

PART 8: QUESTIONS:

1. Which statement is correct?
 - A. By definition, polyneuropathy must have sensory deficit.
 - B. The sensory modality effected initially with polyneuropathy is pain.
 - C. Allodynia is characteristic of peripheral neuropathy.
 - D. Polyneuropathy may develop in young patients.
 - E. Stocking glove distribution of pain indicates the disease must be located in the peripheral nervous system.

Discussion: The correct answer is D. Answer A is incorrect. Guillain-Barre may present as weakness only. Answer B is incorrect. The sensory modality effected initially with polyneuropathy is vibratory or positional sense. Answer C is incorrect. Allodynia or pain initiated by tactile stimulus is characteristic of central pain syndrome. Answer E is incorrect. A stocking glove paresthesia may develop from multiple sclerosis in the spinal cord.

2. Which statement is correct?
 - A. Axonopathy and demyelinating neuropathy can be distinguished clinically.
 - B. The etiology of polyneuropathy is usually nerve compression.
 - C. Hereditary polyneuropathy always present in young patients .
 - D. EMG can be used to measure pain in patients with polyneuropathy.
 - E. Charcot-Marie-Tooth disease (HMSN Type I) is the most ocmmom inherited neuropathy.

Discussion: The correct answer is E. Answer A is incorrect. Axonopathy and demyelinating neuropathy can not be distinguished clinically. NCS/EMG is used to make this distinction. Answer B is incorrect. Polyneuropathy develops from disease process, such a demyelination or injury from vascular compromise, that accumulates along the coarse of the entire nerve. As a result the signs of polyneuropathy are manifest first in the distal ends of the longest nerves. Answer C is incorrrect. Charcot-Marie-Tooth usually presents in young peoples, however it may also present for the first time in patients who are in their fifth-sixth decade. Answer D is incorrect. Pain is transmitted by A-delta and C fibers. NCS/EMG does not record transmission on C fibers. NCS/EMG records transmission on myelinated A fibers only. Therefore NCS/ EMG can not evaluate pain.

3. Which statement is correct?
 - A. There is direct correlation between abnormalities found clinically and on EMG.
 - B. Axonopathy is characterized on NCS/EMG by profound slowing of nerve conduction.
 - C. Characteristically, Guillain -Barre syndrome will relapse.
 - D. Sural nerve biopsy is a routine component in the diagnositic evaluation of polyneuropathy.
 - E. Opiate combinations, such as percocet, are not appropriate medications for treatment of pain associated with polyneuropathy.

Discussion: The correct answer is E. Answer A is incorrect. There may by significant clinical findings with minimal electrophysiologic changes and vice versa. Answer B is incorrect. Axonopathy is characterized by reduction in amplitude. There is little to no change in conduction velocity. Change in velocity is

characteristic of a demyelinating neuropathy. Answer C is incorrect. Another name for Guillain-Barre syndrome is acute inflammatory demyelinating polyneuropathy. Recurrent peripheral demyelination is called chronic inflammatory demyelinating polyneuropathy. Answer D is incorrect. Sural nerve, because it is purely sensory and has a small distribution on the leg, is the nerve harvested if biopsy is performed. However, biopsy is rarely performed. An example of need for biopsy is evaluation for amyloidosis

PART 9: COMMENTS

Effective treatment of malignancy is contingent on early detection of the tumor. Complete evaluation of polyneuropathy, a condition that many patients attempt to ignore or simply feel that they must just learn to live with, may have an impact that significantly alters or saves their life. This was my first opportunity to take the evaluation of polyneuropathy beyond the common etiologies of diabetes or alcohol toxicity.