CHAPTER

25

Practical Approach to Peripheral Neuropathy

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KEY WORDS

Practical approach, neuropathy, causes, evaluation.

Peripheral neuropathy occurs as a component of several common and many rare diseases. It is heterogeneous in etiology, diverse in pathology, and varied in severity. Peripheral neuropathy is often overlooked, underestimated and not evaluated in day to day practice. The prevalence of neuropathy is well studied in patients with diabetes mellitus in most of the studies and other causes of neuropathies are not well documented. The overall prevalence of neuropathy in south Indian diabetic population is 19.1%. A practical approach is therefore necessary to identify and manage neuropathies in clinical practice. Though there are lot of algorithmic approaches, this article gives a simple bedside assessment for peripheral neuropathic symptoms.

A discussion of neuropathic disorders encompasses those diseases that affect the neuron's cell body, neuronopathies, and those affecting the peripheral process, peripheral neuropathies.

Neuronopathies can be further subdivided into those that affect only the anterior horn cells, or motor neuron disease, and those involving only the sensory neurons, also called sensory neuronopathies or ganglionopathies. Peripheral neuropathies can be broadly subdivided into those that primarily affect myelin, or myelinopathies, and those that affect the axon, or axonopathies. Each of these pathologic categories has distinct clinical and electrophysiologic features which allow the clinician to place a patient's disease into one of these groups. Therefore, the goals in the approach to a neuropathic disorder is to determine :

1. Where the lesion is? (Table 1)
2. What is the cause of the lesion? (Table 2).
3. What is the possible therapy?

The final goal in approaching the patient with a neuropathic disorder is to determine whether or not

Table 1: Pathologic Classification of Neuropathic Disorders

1. Neuronopathies (pure sensory or pure motor) :
   - Sensory neuronopathies (ganglionopathies)
   - Motor neuronopathies (motor neuron disease)
2. Peripheral neuropathies (usually sensorimotor):
   - Myelinopathies
   - Axonopathies

Table 2: Etiology of Neuropathic Disorders

I. ACQUIRED

Dysmetabolic states
- Diabetes mellitus
- Neuropathy related to renal disease
- Vitamin deficiency states (ex. Vitamin B12 deficiency)
- Primary amyloidosis

Immune-mediated
- Guillain-Barre Syndrome
- Chronic inflammatory demyelinating polyneuropathy (CIDP)
- Vasculitis

Infectious
- Herpes zoster
- Leprosy, Lyme, HIV, and Sarcoid related

Cancer related
- Lymphoma, myeloma, carcinoma related
- Paraneoplastic subacute sensory neuronopathy

Drugs or toxins
- Chemotheraphy induced
- Other drugs
- Heavy metals and industrial toxins

Mechanical /Compressive
- Radiculopathy
- Mononeuropathy

Unknown etiology
- Cryptogenic sensory and sensorimotor neuropathy
- Amyotrophic lateral sclerosis

II. HEREDITARY

Hereditary Motor Sensory Neuropathy
- (Charcot- Marie – Tooth disease)

Hereditory neuropathy with predisposition to pressure palsies

Familia! Brachial plexopathy

Familial amyloidosis

Porphyria

Other rare peripheral neuropathies
- (Fabry's, metachromatic eukodystrophy,adrenolen kodystrophy, Refsum's disease etc.)

Motor neuron disease
- Spinal muscular atrophy
- Familial amyotrophic lateral sclerosis
- X- linked bulbospinal muscular atrophy

Table 3

1. **What systems are involved?**
- Motor, sensory, autonomic, or mixed
2. **What is the distribution of weakness ?**
- Only distal Vs proximal and distal
- Focal / asymmetric Vs symmetric
3. **What is the nature of the sensory involvement ?**
- pain / burning,or stabbing
- proprioceptive loss-joint position and vibration sense
4. **Is there evidence UMN involvement?**
- without sensory loss
- with sensory loss
5. **What is the temporal evolution ?**
- Acute (days to 4 weeks)
- Subacute (4 to 8 weeks)
- Chronic (> 8 weeks)
- Preceding events, drugs, toxins
6. **Is there evidence for a hereditary neuropathy?**
- Family history of neuropathy
- Lack of sensory symptoms despite sensory signs

Table 4: Neuropathic Disorders That May Have Only Motors Symptoms At Presentation

Motor neuron disease
Lead intoxication
Acute porphyria
Guillian- Barre Syndrome
Hereditary motor sensory neuropathy*
CIDP*

therapy is possible, and if so, what the course of therapy should be. Even if a specific therapy is not available, a management plan should be developed. These final two steps are often frustrating as it is not always possible to determine the cause or alter the natural history of neuropathic disorders.

In order to accomplish the goal of determining the site and cause of the lesion, and if possible, a therapy, the clinician gathers information from the history, the neurologic examination and various laboratory studies. While gathering this information, six key questions are asked. From the answer to these six key questions, the patient is placed into 9 different phenotype patterns. Therefore, it is the 3-6-9 step clinical approach to neuropathy:

3 goals – 6 key questions- 9 phenotypic patterns.

IMPORTANT INFORMATION FROM THE HISTORY AND PHYSICAL EXAMINATION

– Six Key Questions

Table 5: Peripheral Neuropathies With Autonomic Nervous System Involvement

Diabetes mellitus
Amyloidosis (familial and acquired)
Guillain – Barre syndrome
Vincristine induced
Porphyria
HIV – related autonomic neuropathy

Table 6: Neuropathic Disorders that Produce Asymmetric/ Focal Weakness

Motor Neuron disease
Amyotrophic lateral sclerosis
Radiculopathy – cervical or lumbosacral
Plexopathy – brachial or lumbosacral
Mononeuropathy multiplex due to:
Vasculitis
Lyme disease
Sarcoid
Leprosy
HIV infection
Hereditary neuropathy with liability to pressure palsy
Entrapment mononeuropathies
Median neuropathy
Ulnar neuropathy
Peroneal neuropathy

The first step in this approach is to ask six key questions based on the patients symptoms and signs (Table 3):

1. What systems are involved?

   It is important to determine if the patients symptoms and signs are pure motor, pure sensory, or both. If the patients has only weakness without any evidence of sensory loss, a motor neuronopathy, or motor neuron disease, is the most likely diagnosis (Table 4).

*Usually has sensory signs on examination

Some peripheral neuropathies are associated with significant autonomic nervous system dysfunction (Table 5).

Inquire if the patient has fainting spells or orthostatic light headedness, sweating abnormalities or any bowel, bladder, or sexual dysfunction. These features suggest the presence of autonomic involvement.

2. What is the distribution of weakness?

   The distribution of the patient's weakness is crucial for an accurate diagnosis and In this regard two questions should be asked: (1) Is the weakness distal only or is it both proximal and distal? And

Table 7: Peripheral Neuropathies That Are Often Associated With Pain
Cryptogenic sensory or sensorimotor neuropathy
Diabetes mellitus
Vasculitis
Guillain – Barre syndrome
Amyloidosis
Toxic (arsenic, thallium)
HIV related distal symmetrical polyneuropathy
Fabry's disease

(2) is the weakness symmetric or focal, asymmetric. The finding of weakness in both proximal and distal muscle groups in a symmetric fashion is the hallmark for acquired immune demyelinating polyneuropathies, both the acute (GBS) and the chronic form (CIDP)

Asymmetry or focal nature of the weakness is also a feature that can narrow the diagnostic possibilities (Table 6).

Some neuropathic disorder may present with unilateral leg weakness. If sensory symptoms and sign are absent, patient presents with painless foot drop evolving over weeks or months, Motor neuron disease is the leading diagnostic possibility. if a patient present with subacute or acute sensory and motor symptoms of one leg, lumbosacral radiculopathies, plexopathies, vasculitis, and compressive mononeuropathy need to be considered. if the clinical manifestations are pure motor weakness in one arm or hand, motor neuron disease is probably the leading consideration. If sensory symptoms are also present, cervical radiculopathy, brachial plexopathy, or a mononeuropathy are likely. Leprosy often presents with asymmetric sensory or sensorimotor features, and one needs to have a high index of suspicion for this disorder. The importance of finding symmetric proximal and distal weakness in a patient who presents with both motor and sensory symptoms identifies the patients who may have a treatable acquired demyelinating neuropathic disorder. If a patient with both symmetric sensory and motor findings has weakness involving only the distal lower and upper extremities, reflects a primary axonal peripheral neuropathy and is much less likely to represent a treatable entity.

3. What is the nature of the sensory involvement?

   It is important to determine if the patient has loss of sensation (numbness), altered sensation (tingling), or pain. Sometimes patient may find it difficult to distinguish between uncomfortable tingling sensations (dysesthesias) and pain. Neuropathic pain be burning, dull and poorly localized (protopathic pain), or sharp and lancinating (epicritic pain). If severe pain is one of the patients symptoms, certain peripheral neuropathies should be considered (Table 7).

Table 8: Causes of Sensory Neuronopathy (Ganglionopathy)
Cancer (Paraneoplastic)
Sjogran's syndrome
Idiopathic sensory neuronpathy
Cisplatinum and other analogues
Vitamin B6 toxicity
HIV – related sensory neuronopathy

The cryptogenic sensory polyneuropathy (CSPN) and neuropathy due to diabetes are the most common neuropathies that are associated with severe pain peripheral nerve vasculitis and Guillain- Barre Syndrome (GBS) are important to recognize because these disorders are treatable. The pain in vasculitic neuropathy is generally distal and asymmetric in the most severely involved extremity. Some patients with GBS have severe back pain associated with symmetric numbness and paresthesias in the extremities. Another painful form of diabetic neuropathy is lumbosacral radiculoplexopathy (also known as diabetic amyotrophy), in which patients may present with the abrupt onset of back, hip or thigh pain that may precede weakness by days or weeks.

If the neurologic examination reveals a asymmetric loss of proprioception with significant vibration loss and normal strength consider a sensory neuro-nopathy (i.e.,ganglionopathy). The various causes of sensory neuronopathy are as follows (Table 8):

The modalitities of light touch, pain sensation, vibration and proprioception should be assessed in all four limbs in a patient with a peripheral neuropathy.

4. Is there evidence of upper motor neuron involvement?

   In patients with symptoms of signs suggestive of lower motor neuron pathology without sensory loss, the presence of concomitant upper motor neuron signs is the hallmark of amyotrophic lateral sclerosis.

   On the other hand, if the patient presents with symmetric distal sensory symptoms and signs suggestive of a distal sensory neuropathy, but there is additional evidence of symmetric upper motor involvement, the physician should consider a disorder such as combined system degeneration with neuropathy. The most common cause for this pattern is B_{12} deficiency HIV infection, severe hepatic disease, adrenomyeloneuropathy.

5. What is the temporal evolution?

   Does the disease have an acute (days to 4 weeks), subacute (4 to 8 weeks), or chronic (greater than 8 weeks) course? Is the course monophasic, progressive, or relapsing? Neuropathies with acute and subacute presentations include GBS, vasculitis, and diabetic lumbosacral radiculoplexopathy. A relapsing course can be present in CIDP and

Table 9: Nine Patterns of Neuropathic Disorders
Pattern1: Symmetric proximal and distal weakness with sensory loss
inflammatory demyelinating polyneuropathy (GBS and CIDP)
Pattern 2: Symmetric distal weakness with sensory loss
metabolic disorders, Hereditary toxins Drugs,
Pattern 3: Asymmetric distal weakness with sensory loss
Multiple nerves- vasculitis
Single nerves/regions- compressive mononeuropathy and radiculopathy
Pattern 4: Asymmetric distal weakness without sensory loss
motor neuron disease – with upper motor neuron findings
Multifocal motor neuropathy – without upper motor neuron findings
Pattern 5: Asymmetric proximal and distal weakness with sensory loss
Polyradiculopathy or plexopathy due to diabetes mellitus,
Meningeal carcinomatosis
Pattern 6 : Symmetric sensory loss without weakness
Cryptogenic sensory polyneuropathy (CSPN), metabolic (diabetes and others) drugs, toxins
Pattern 7: Symmetric sensory loss and distal areflexia with upper motor neuron findings
B_{12}deficiency, HIV, hepatic disease
Pattern 8: A symmetric proprioceptive sensory loss without weakness
sensory neuronopathy (ganglionopathy)
Pattern 9: Autonomic Symptoms and Signs
neuropathies associated with autonomic dysfunction

porphyria. Inquire about preceding or concurrent infections, associated medical conditions, drug use including over-the-counter vitamin preparations (B6), alcohol, and dietary habits.

6. Is there evidence for a hereditary neuropathy?

   In patients with a chronic, very slowly progressive distal weakness over many years, with very little in the way of sensory symptoms, pay particular attention to the family history and inquire about foot deformities in immediate relatives. episodes of recurrent compressive mononeuropathies may indicate an underlying hereditary predisposition to pressure palsies. One must look carefully at the feet for arch and toe abnormalities (high or flat arches, hammer toes scoliosis

PATTERN RECOGNITION APPROACH OF NEUROPATHIC DISORDERS

After answering the six key questions obtained from the history and neurologic examination outlined above, one can classify neuropathic disorders into several patterns based on sensory and motor involvement and distribution of signs (Table 9). A final diagnosis is arrived at by utilizing other clues such as the temporal course, presence of other disease states, and family history and information from lab tests and electrophysiology.

Electrophysiology, an extension of the clinical examination and nerve and muscle biosy, punch biopsy of the skin adds to the information derived from the above mentioned approach and helpful in planning treatment. Even then the etiology eludes in more than 1/3rd of patients presenting with peripheral neuropathy in the best of centers.

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