

Large, Small Fiber Neuropathy: Know the Signs and Symptoms

Obtain detailed patient history and identify specific neuropathy to prescribe treatment.

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It is known that 50% of patients with diabetes typically develop neuropathy.¹ Because this complication is associated with hyperglycemia, controlling glycemia is the mainstay of diabetes treatment in regard to neuropathy and in patient's overall treatment.

I presented a lecture at the 2005 Annual Scientific Meeting of the American Podiatric Medical Association where I discussed the various types of neuropathy. In addition to glycemic control, proper treatment for diabetic neuropathy requires that the specific type of neuropathy be diagnosed.

The epidemiology and natural history of diabetic neuropathy are poorly understood. Because there are several classifications – some which may not be directly related to diabetes – it is important to individualize diagnosis. In most instances the cause of neuropathy is diabetes; neuropathy is related to other causes in 10% of diabetes patients.²

Treatments should only be prescribed after the true cause and type of neuropathy are known. The first consideration is patient history. A complete examination and detailed history promotes a more accurate description of neuropathy. The treatment can then be targeted to the patient's specific symptoms. Questions to ask include: How well controlled is your glucose, and does it fluctuate during the day? Do you get dizzy with standing? Do you experience intermittent diarrhea or constipation? Is there a history of sexual dysfunction? Do you have any eye or kidney problems?

There are many classifications of diabetic neuropathy. For the purpose of this article, we will focus in generalized symmetrical polyneuropathy. Generalized symmetrical polyneuropathy is the type of neuropathy that most of us refer as diabetic neuropathy. Acute sensory neuropathy and chronic sensorimotor neuropathy are two the subtypes.

Acute sensory neuropathy. Presents as a rapid onset, clinical triad of burning sensation, depression and weight loss. The clinical presentation is mild sensory manifestations, and nerve conduction velocity may be either normal or with

minor abnormalities. It will resolve spontaneously within 12 months if hyperglycemia is controlled.

Chronic sensorimotor neuropathy. Presents with a gradual onset of paresthesias, burning pain and/or numbness. These symptoms are usually mild to moderate, and may persist for several years. Nerve conduction velocity is usually normal with minor abnormalities as well. Either subtype can involve large or small fibers nerves.

In order to understand the symptomatology of diabetic neuropathy, the reader needs to understand the anatomical distribution of the peripheral nervous system. The peripheral nervous system can be classified into large fibers and small fibers. These are respectively known as A-fibers and C-fibers, both causing a unique set of neuropathic symptoms. It is very important to assess what type of neuropathy the patient may have. When a lower extremity neurological exam is performed, the clinical tools used to assess neuropathy evaluate large fibers only. A good patient history such as asking the patient if he/she has cold/hot feet at times, periods of dizziness with sudden standing (orthostatic hypotension), and period of diarrhea and constipation (gastroparesis) will assess for autonomic neuropathy.

SMALL FIBER NEUROPATHY

Small fibers (C-fibers) provide mostly sensory and autonomic innervations. The sensory fibers (unmyelinated and thinly myelinated) perceive pain and temperature changes. The autonomic fibers controls for heart rate, blood pressure, sudomotor function and gut function. Small fiber neuropathy mostly involves thermal perception, which means that pain is in the form of cold, warm and hot. Clinical presentations of small fiber neuropathy include hyperesthesias, hyperalgesia, excess sweating and impaired microcirculation.

These patients will have normal strength and reflexes, however they are at risk for ulceration, gangrene and eventually amputation. In small fiber neuropathy, the defective

TABLE 1. SIGNS AND SYMPTOMS OF NEUROPATHY

Stage of neuropathy	Characteristics
• No neuropathy	No signs and symptoms
• Clinical neuropathy	
Chronic painful	Burning, shooting, stabbing pains that are worst at night; absent sensation to several modalities, absent reduced reflexes
Acute painful	Severe symptoms as above, may be related to initiation of insulin in poorly controlled diabetes
• Painless with complete/partial sensory loss	Numbness of feet, loss of sensation, absent reflexes decrease thermal sensitivity
• Late complications	Ulcerations, neuropathic deformity, amputations

function of C-fibers causes abnormal blood flow.³ In patients with diabetes and small fiber neuropathy, blood is shunted away from the skin causing a low oxygen tension to the area. In the presence of a wound, a poor oxygen tension will lead to a problem wound. Therefore, a complete patient history and clinical examination should lead us to an accurate classification of diabetic neuropathy.

LARGE FIBER NEUROPATHY

The large fibers are myelinated motor fibers. These fibers are responsible for motion control, touch, proprioception and vibration. The myelinated sensory fibers also perceive for touch, proprioception and vibration. The clinical presentation in patients with large fibers neuropathy are impaired vibration, gait instability, weakness, numbness, small muscle wasting and commonly radiating or cramping pain at night.

On the other hand, the clinical presentation in patients with small fibers neuropathy is different. A warm, erythematous, hypohidrotic foot is noticed with normal deep tendon reflexes, normal muscle tone with impaired thermal and pain threshold. Both types of neuropathies have been advocated as possible causes of Charcot neuroarthropathy. Another indication of large fiber neuropathy is that the patient's hands will demonstrate thenar muscle atrophy.

Electrophysiology is helpful when ruling out other causes of neuropathy. It is also helpful in following the progression of neuropathy and providing information of the severity of it.

The initial management of diabetic neuropathy is three-fold. First, etiologies such as malignancy, toxic, infective or

medications need to be ruled out. Second, physicians need to target for optimal glucose control. Finally, we can consider pharmacological treatment for painful symptoms.

The physician should not mask painful symptoms with pharmacological treatments prior to achieving glucose control. The patient may ignore the importance of controlling glucose if their symptoms were relieved, and therefore, they become numb in the presence of hyperglycemia.

The medical treatment of diabetic neuropathy can be divided into drugs for the treatment of pain and drugs to change the natural history of neuropathy. *See the article on page 22 for more information.*

Ruboxistaurin (Eli Lilly and Company) may slow the natural history of diabetic neuropathy by protein kinase-C (PKC) beta inhibition. It has been advocated that PKC-beta activation may play a role in the development of microvascular damage that may lead to neuropathy. In a randomized, placebo-controlled trial, vibration perception threshold and neuropathic symptoms statistically improved in the ruboxistaurin group.

Alpha-lipoic acid is an antioxidant that has demonstrated improvement in symptoms in two large clinical trials. It has been tested intravenously and orally with minimal side effects, and it looks like a promising treatment to slow the progression of neuropathy.

While making a distinction of neuropathy type, consider the diabetic peripheral neuropathy stages. A patient may have any symptom associated with neuropathy including burning, shooting pain, pins and needles, severe hyperesthesias, numbness, reduced sensitivity or ulcers. The symptoms with which a patient presents will aid in the diagnosis.

The understanding of stage of diabetic neuropathy is helpful in identifying patients at risk for ulceration. Dyck et al² demonstrated the severity and stages of polyneuropathy. We need to understand that this staging system does not signify that every patient goes from one stage to the next.

Understanding the anatomy and the physiology of diabetic neuropathy will enable us to provide excellent care for our patients. Paying close attention to the clinical symptoms of each will aid in choosing the appropriate medication for controlling painful symptoms. ■

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