The International Journal of Therapeutics
January-March 2019 Edition; Volume 2, Issue 1
Peer-reviewed & Indexed International Journal

PERIPHERAL NEUROPATHY- BEYOND THE USUAL SUSPECTS

Rashmi Roongta[a], Seena Sankar[a,*]

[a]*Department of General Medicine, St. Johns Medical College Hospital, Sarjapur Road, Bangalore, 560034, Karnataka, India*

Abstract

A 62-years-old male, diabetic for five years and hypertensive since three years on regular medication presented with complaints of burning pain in both lower limbs for seven months which progressed to involve the upper limbs in the last six months. On examination, there was a significant postural drop in blood pressure. Rest of the general examination was unremarkable. Fundus showed no evidence of diabetic retinopathy. Nervous system examination was suggestive of distal sensorimotor polyneuropathy. Initial workup including complete blood count, Vitamin B12, renal, liver, and thyroid function tests was normal and retroviral marker was negative. Electroneuromyography revealed bilateral common peroneal sensorimotor axonal neuropathy. Advanced work up for neuropathy in the form of autoimmune workup, Positron Emission Tomography scan, bone scan was negative. Serum protein electrophoresis revealed a doubtful M spike but bone marrow aspiration and biopsy were unremarkable. Superficial peroneal nerve biopsy showed features of amyloidotic neuropathy. The patient is being treated with lenalidomide and steroids, is symptomatically better, and is planned for a stem cell transplant.

Keywords: amyloid, diabetes, peripheral neuropathy

Introduction

Peripheral neuropathy refers to damage of the peripheral nervous system. The overall prevalence of peripheral neuropathy is 2.4%; which increases to 8% in individuals above 55 years. [1] In the developed world, diabetes mellitus is the most common cause of this disease. [2] About 60% of the diabetic population suffers from varying forms and severity of neuropathy. [3] Twenty percent of patients with neuropathy remain undiagnosed. [4] Neuropathy in a diabetic patient is very quickly attributed to the disease but about 10%-50% of them may have other causes of neuropathy. [3, 5] Hence, diabetic neuropathy is a diagnosis of exclusion. [6] Here, we report a case of distal symmetric sensorimotor polyneuropathy in a diabetic patient who had atypical features which prompted us to investigate further to make an unsuspecting diagnosis.

*Corresponding author.
Email address: seenasankar7@gmail.com (Seena Sankar)

Case Report

A 62-years-old male, known diabetic for 5 years on metformin and hypertensive since 3 years on regular follow up, presented to us with complaints of burning pain in bilateral lower limbs for 7 months which had progressed to involve the upper limbs in 6 months. It was associated with weakness of bilateral lower limbs and difficulty in walking. Recently, he had started complaining of giddiness and transient blurring of vision upon standing. Examination revealed orthostatic hypotension. His higher mental functions, cranial nerves, and fundus examination were normal. Power was 3/5 in distal lower limbs with decreased pain, temperature, touch, joint position and vibration sense below the knee. Knee reflexes were sluggish and ankle reflexes were absent bilaterally. Initial blood workup including complete blood count, Vitamin B12, renal, liver and thyroid function tests, serum electrolytes and retroviral marker were within normal limits. His sugars were under control, as evidenced by an HbA1c of 7.2%. Urine examination showed no proteinuria.

Electroneuromyography revealed bilateral common peroneal sensorimotor axonal neuropathy. Autoimmune workup in the form of Antinuclear Antibody(ANA), ANA profile, p, and c Anti-neutrophil cytoplasmic antibody were negative. Serum protein electrophoresis revealed a doubtful M spike. Beta-2 microglobulin was mildly increased. Urine was negative for Bence Jones protein. However, bone marrow aspiration and biopsy did not show evidence of dysproteinemia.

Occult malignancies were ruled out by doing a Positron Emission Tomography scan and a bone scan. Paraneoplastic antibody panel and heavy metal screening were normal.

In the background of a negative non-invasive workup, a sural nerve biopsy was done which was suggestive of amyloidotic neuropathy. The patient was treated with lenalidomide and steroids and is symptomatically better with power improving to 5/5 in all 4 limbs and resolving sensory signs. He is planned for a stem cell transplant in view of adverse effects to lenalidomide.

Discussion

Distal sensorimotor polyneuropathy has a wide range of differential diagnoses- the commonest being diabetic neuropathy. [7] This case report highlights the importance of working up a diabetic patient for other causes of polyneuropathy especially in the presence of atypical features. His history was sub-acute in nature and more rapid in progression than the normal course of diabetic neuropathy with functional limitation due to the severity of his symptoms. He had also received a trial of pregabalin and amitryptiline but his symptoms only worsened with time. These symptoms seemed disproportionate with diabetic neuropathy. In the light of well-controlled diabetes with no evidence of microvascular or macrovascular complications, causes apart from diabetic neuropathy were considered prompting further workup.

A systematic approach is required while working up a case of peripheral neuropathy due to the diverse presentation and numerous etiologies- metabolic - diabetes, uremia and hypothyroidism, autoimmune, toxic - alcohol, heavy metals and chemotherapeutic drugs, vasculitis, neoplasms- leukemias and lymphomas, familial- Charcot- Marie-Tooth, infectious

- Lyme's disease and infiltrative disorders like sarcoidosis, leprosy and amyloidosis. Few studies have been done to evaluate alternate causes of neuropathy in diabetics but amyloid has not been reported as yet. [5, 8, 9]

A detailed history of symptoms along with family and occupational history should be taken.

General and systemic examinations aided with a comprehensive neurological examination of the motor, sensory and autonomic functions are mandatory. Loss of joint position and vibration sense and sensory ataxia is seen in large fibre neuropathy, whereas small fibre neuropathy manifests as impairment of pain, temperature, and autonomic functions. Demyelinating and axonal neuropathies can be differentiated and their severity assessed using electrodiagnostic tests. Specific immunological, genetic and biochemical tests should be done when indicated.

Nerve biopsy is indicated to search for a treatable cause. Gabriel et al studied 50 consecutive patients with peripheral neuropathy who underwent the sural nerve biopsy. It revealed an otherwise unsuspected diagnosis in 14% of the patients. In 70% the biopsy confirmed the preferred diagnosis, and in 16% the biopsy findings contributed nothing. [10]

Deposition of insoluble, misassembled fibril proteins in tissues, most commonly the kidneys, liver, and heart, leads to the disruption of normal tissue structure and function causing amyloidosis. Nervous system involvement may lead to focal, multifocal, or diffuse neuropathies involving sensory, motor and/or autonomic fibres. Amyloidosis is complicated by peripheral neuropathy in 15–35% of cases. It is the commonest neurological complication and the presenting feature in 7-17% of primary amyloidosis. [11] Symptoms of neuropathy may precede the diagnosis by 48 months. [12] Dysautonomia and carpal tunnel syndrome are frequent accompaniments.

Progressive sensory or sensorimotor polyneuropathy with or without autonomic disturbances is the commonest presentation. Sensory symptoms are usually the first evidence of neuropathy. Small fibre neuropathy is commoner and usually precedes large fibre neuropathy. The distribution and progression are characteristic of a length-dependent axonal polyneuropathy. [13]

Isolated peripheral neuropathy has a better prognosis, extraneural involvement portends a worse prognosis. [14] Diagnosis is confirmed by histopathology- amyloid deposition by Congo red staining or by the presence of kappa or lambda chains by immunohistochemistry staining. [15]

The differential diagnosis for painful peripheral neuropathy is broad, and the clinician should be aware that amyloidosis may present like this due to the involvement of small diameter sensory fibres. This is often a diagnostic challenge for the clinician, leading to an erroneous diagnosis. Neuropathy in diabetics cannot be always presumed to be secondary to the disease. In case there is a clinical suspicion of other possible etiologies- like in the presence of peculiar signs, further workup should be done to look for the same.

References

[1] CN Martyn, RA Hughes. Epidemiology of peripheral neuropathy *J Neurol Neurosurg Psychiatry.* 1997;62:310-18.

[2] K Juster-Switlyk, AG Smith. Updates in diabetic peripheral neuropathy. F1000 Faculty Rev-738. 2016.

[3] Dyck PJ, Kratz KM, Karnes JL, Litchy WJ, Klein R, Pach JM, et al. The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: the Rochester Diabetic Neuropathy Study *Neurology.* ;1993:43-4.

[4] Dyck PJ, Oviatt KF, Lambert EH. Intensive evaluation of referred unclassified neuropathies yields improved diagnosis *Ann Neurol.* ;1981:10-3.

[5] *diabetes is of diabetic etiology: differential diagnosis of diabetic neuropathy.* Curr Diab Rep. 2009 Dec;9(6):423–31.

[6] Pop-Busui R, Boulton AJM, Feldman *American Diabetes Association. Diabetes Care.* ;2017:40-1.

[7] Tracy JA, Dyck PJB. The Spectrum of Diabetic Neuropathies *Phys Med Rehabil Clin N Am.* ;2008:19-1.

[8] Gorson KC, Ropper AH. Additional causes for distal sensory polyneuropathy in diabetic patients *J Neurol Neurosurg Psychiatry.* ;2006.

[9] Lozeron P, Nahum L, Lacroix C, Ropert A, Guglielmi J-M, Said G. Symptomatic diabetic and non-diabetic neuropathies in a series of 100 diabetic patients *J Neurol.* ;2002:249-5.

[10] Prospective study of the usefulness of sural nerve biopsy *J Neurol Neurosurg Psychiatry.* ;2000:69-4.

[11] Vucic S, Chong PST, Cros D. Atypical presentations of primary amyloid neuropathy. Muscle Nerve. 2003 Dec;28(6):696–702

[12] Falk RH, Comenzo RL, Skinner M. The systemic amyloidoses *N Engl J Med.* 1997;13.

[13] SC Shin, J Robinson-Papp. Amyloid neuropathies *Mt Sinai J Med N Y.* 2012;79:733-748.

[14] Transthyretin amyloid neuropathy has earlier neural involvement but better prognosis than primary amyloid counterpart: an answer to the paradox? *Ann Neurol.* ;2016:80-3.

[15] Peripheral nerve involvement in primary systemic AL amyloidosis: a clinical and electrophysiological study *Eur J Neurol.* ;2011:18-4.

Cite As:
Roongta R, Shankar S. Peripheral Neuropathy- Beyond The Usual Suspects. Int J Thera 2019;2(1): 32-35.

-Open Access Article-
Publication Services Provided by The International Journal of Therapeutics
www.ijthera.com