SHORT REPORT

Proximal diabetic neuropathy presenting with respiratory weakness

Thomas H Brannagan, Robert A Promisloff, Leo F McCluskey, Kathleen A Mitz

Abstract

A patient is described with proximal diabetic neuropathy presenting with respiratory weakness. A 50 year old man developed progressive shortness of breath over 2 months. He also had weakness of hip flexion. Phrenic nerve responses were absent, and spontaneous activity was seen in the intercostal and lumbar paraspinal muscles with long duration neurogenic MUPs and reduced recruitment in the diaphragm. Without treatment, the patient began to improve with resolution of his proximal leg weakness and breathing difficulties. Proximal diabetic neuropathy is another cause of neuromuscular respiratory weakness.

(*J Neurol Neurosurg Psychiatry* 1999;**67**:539–541)

Keywords: proximal diabetic neuropathy; diabetic amyotrophy; respiratory weakness; phrenic nerve; diaphragm

MCP-Hahnemann University School of Medicine, Department of Neurology
T H Brannagan
K A Mitz

Department of Internal Medicine, Division of Pulmonary and Critical Care Medicine, Pennsylvania, USA
R A Promisloff

Department of Neurology, University of Pennsylvania Medical Center, Pennsylvania Hospital, Pennsylvania, USA
Leo F McCluskey

Correspondence to:
Dr Thomas Brannagan, MCP, Hahnemann University School of Medicine, Department of Neurology, Broad and Vine, Mail Stop 308, Philadelphia, PA 19102, USA. Telephone 001 215 762 5036; fax 001 215 762 1537; email Brannagan@drexel.edu

Received 23 February 1999
Accepted 7 April 1999

Diabetes mellitus is the most common cause of peripheral neuropathy.[1] Most patients develop a symmetric axonal distal neuropathy, but proximal diabetic neuropathy[2–4] and thoracic radiculopathy[5] have also been recognised. Diabetic neuropathy is not among the neuromuscular diseases that result in respiratory failure.[6–8] A patient with a diabetic proximal polyradiculoneuropathy and respiratory weakness was studied. His dominant symptoms were dyspnoea and orthopnoea.

Case report

A 50 year old man with a 47 year history of insulin dependent diabetes mellitus, presented with 2 months of progressive dyspnoea and orthopnea. These symptoms led to a cardiac catheterisation, which showed severe three vessel coronary artery disease and preserved left ventricular function (LVF) with an estimated ejection fraction of 60%. Coronary artery bypass surgery (CABG) was performed. Topical cooling with ice slush was not used. Postoperatively, shortness of breath and orthopnea continued to progress. He could not lie flat in bed and slept upright in a chair. He said that this pattern started several months before surgery. He denied diplopia, difficulty chewing, fasciculations, ptosis. For 1 year, he noted paraesthesias in the feet, which was attributed to diabetic neuropathy. He had also had carpal tunnel surgery and an ulnar nerve transposition, with improvement of sensory symptoms on the right.

On examination, 9 days after the CABG, he could not lie flat because of severe dyspnoea. Ocular motion was normal without fatiguing weakness. He could count only to 3 on a single breath, before his voice faded out. He had no ptosis, facial or jaw weakness, tongue fasciculations, or atrophy. Strength was normal in the arms. Strength in the hip flexors was MRC 4. Other muscle groups in the legs were full strength. He had difficulty rising from a low chair and doing a deep knee bend. His gait was normal. Tendon reflexes were absent and his toes were down going. Pain perception was impaired in the feet. Position sense testing was normal.

Pulmonary function tests were compatible with neuromuscular weakness. Forced vital capacity was 1.85 l (38% predicted). Maximal inspiratory pressure was 28 cm H_2O (37%). Maximal expiratory pressure was 62 cm H_2O (44%). There was no improvement after intramuscular injection of 1.5 mg neostigmine. Chest *x* ray performed before and after surgery was normal. There were no signs of congestive heart failure. An echocardiogram 6 days after surgery showed normal left ventricular size and normal left ventricular function with an ejection fraction of 55%-60%. An arterial blood gas showed a pCO_2 of 51 with a bicarbonate of 36. Fluoroscopy showed normal diaphragmatic motion.

Motor nerve conduction studies disclosed low evoked response amplitudes in the left ulnar and tibial nerves and borderline amplitude responses stimulating the left median and peroneal nerves (table). Phrenic nerve responses were absent bilaterally (using both the modified Markand and Newsome-Davis methods). Sensory evoked responses were absent stimulating the left median, ulnar, and sural nerve. Repetitive stimulation of the median/abductor pollicis brevis and accessory/trapezius system disclosed no abnormal increment or decrement. Needle EMG showed abundant spontaneous activity in the form of fibrillations, positive sharp waves and complex repetitive discharges (CRDS) in the lumbar paraspinal muscles and right intercostal muscles. Needle EMG of the right diaphragm

Nerve conduction and EMG data

	September 1997	*September 1998*
Median nerve:		
Distal motor latency	**5.0 ms** (left)	**5.1 ms** (right)
Motor amplitude, wrist	6.5 mV	11.3
Motor conduction velocity	51 m/s	**44 m/s**
F wave latency	31.4 ms	
SNAP	**Absent** (digits 2,3,4)	
Ulnar nerve:		
Distal motor latency	**3.7 ms** (left)	
Motor amplitude, wrist	1.5 mV	
Motor conduction velocity	46 m/s	
F wave latency	30.9 ms	
SNAP	**Absent**	
Radial nerve, right:		
SNAP amplitude		**7.6 µV**
Sensory conduction velocity		**35 m/s**
Peroneal nerve:		
Distal motor latency	4.0 ms (left)	3.4 ms (right)
Motor amplitude, ankle	3.0 mV	684 µV
Motor conduction velocity	**33 m/s**	**35 m/s**
Tibial nerve:		
Distal motor latency	4.9 ms (left)	5.1 ms (right)
Motor amplitude, ankle	**2.7 mV**	4.8 mV
Motor conduction velocity	**32 m/s**	**32 m/s**
F wave latency	**65.7 ms**	
Sural nerve:		
SNAP	**Absent** (left)	**Absent** (right)
Phrenic nerve, right:		
Motor amplitude	**Absent**	**Absent**
Phrenic nerve, left:		
Distal motor latency	—	5.9 ms
Motor amplitude	**Absent**	**59 µV**

Muscle: Left	*fib/PSW*		*MUP morphology*		*Recruitment*	
	9/97	*9/98*	*9/97*	*9/98*	*9/97*	*9/98*
Vastus lateralis	0		**Poly**		↓	
Tibialis anterior	**1+**		**Poly**		↓	
Gastrocnemius, medial head	0		**Poly,↑amp**		↓	
First dorsal interossei	0		**Poly**		↓	
Deltoid	0		Normal		Full	
Cervical paraspinals	0					
Lumbar paraspinals	**4+**					
Right						
Intercostals	**3+**	0				
Diaphragm	0		**Poly↑dur**		↓	
Tibialis anterior		0	**Poly↑dur, amp**		↓	
Gastrocnemius medial head		**1+ (CRDS)**	**Poly↑dur, amp**		↓	
Vastus medialis		0	**Poly↑amp**		Full	
Deltoid		0	Normal		Full	
Triceps		0	Normal		Full	
Biceps		0	Normal		Full	
Thoracic paraspinals		0				

Abnormal values are bold or underlined; amp=amplitude; CRDS= complex repetitive discharges; dur=duration; poly=polyphasic; SNAP=sensory nerve action potential; MUP=motor unit potential; fib/PSW=fibrillations/positive sharp waves.

showed long duration motor unit potentials with an increased number of polyphasic potentials and reduced recruitment. No abnormal spontaneous activity was seen in the cervical paraspinal muscles. Rare fibrillations and positive sharp waves were seen in the tibialis anterior, but not other distal and proximal muscles in the arms and legs. Long duration neurogenic motor unit potentials with reduced recruitment was seen in distal muscles in the arms and legs. A quantitative EMG of 20 motor unit potentials in the left vastus lateralis showed a normal mean duration of 16.8 ms (normal 11.7–17.5 ms) and an increase in polyphasic potentials (20% (normal <12%)), compared with age matched normal subjects.[9]

The erythrocyte sedimentation rate was 75. Antinuclear antibody titre was 1:640. The following laboratory tests were normal or negative: blood urea nitrogen, creatinine, creatine kinase 126 (<160), aldolase 11 (0–11), acetyl choline receptor antibodies, rheumatoid factor, SS-A, SS-B, C3, C4, anti-SM, anti-dsDNA, antiribonucleoprotein, and thyroid function tests.

The patient began to improve while in hospital, after several days. He could lie down without difficulty breathing, although dyspnoea remained. On physical examination he no longer had iliopsoas weakness, could do deep knee bends, and rise from a seated position. Fourteen months after the onset of his symptoms he remains with dyspnoea on minimal exertion. Forced vital capacity remained reduced at 2.39 l (50% of predicted). Nerve conduction studies showed an absent right phrenic evoked response and a low amplitude left phrenic response (modified Markand method). He has been able to return to work.

Discussion

A limited number of neuromuscular diseases cause respiratory weakness. These include motor neuron diseases such as amyotrophic lateral sclerosis or poliomyelitis; peripheral neuropathy such as the Guillain Barré syndrome; critical illness neuropathy; or neuropathy related to porphyria, diphtheria, or toxins; defects of neuromuscular transmission such as myasthenia gravis or botulism; and

myopathies such as acid maltase deficiency, polymyositis, or acute tetraplegic steroid myopathy.[6–8]

This patient had diabetes and coronary artery disease, after CABG with respiratory muscle weakness and orthopnoea predating cardiac surgery. After CABG, orthopnoea without congestive heart failure is often due to diaphragmatic paralysis caused by cooling of the phrenic nerve during surgery.[10 11] But in the present case, symptoms started before surgery. In addition, there were signs of chronic denervation during needle EMG of the diaphragm, which would not be expected after only 13 days, if the nerve injury occurred during surgery.

The laboratory evaluations and neurophysiology identified a peripheral neuropathy as the cause of the respiratory weakness and orthopnoea. Any cause of neuropathy other than diabetes is unlikely. The course of progression and recovery was typical of proximal diabetic neuropathy. Progression for 2 to 18 months has been noted in several large series.[2 3] The symptoms of our patient progressed for almost 3 months, unlike Guillain-Barre syndrome, in which patients reach a nadir by 1 month. No electrophysiological features of demyelination were present. Examination of CSF and a nerve biopsy was not obtained to exclude other causes of neuropathy, because the patient began to improve just after the beginning of our evaluation; however, no laboratory evidence of other autoimmune disease was seen. The erythrocyte sedimentation rate was raised, which has been described in other patients with proximal diabetic neuropathy[12 13] or may occur after a pericardotomy. Peripheral nerve vasculitis is rarely a cause of respiratory failure, reported in one patient with systemic lupus erythematosus[14]; our patient did not have other systemic manifestations to fulfill this diagnosis. Spontaneous recovery without treatment would also be unusual for a vasculitic process. Our patient did not have pain, which is encountered by most patients with diabetic proximal neuropathy, although it is not universal. In one series,[3] only 28 of 44 patients noted pain.

Some patients with prolonged progression have been said to improve after immunosuppressive treatment including corticosteroids or intravenous immune globulin (IVIg).[3 13 15 16] Our patient improved before any specific treatment, as in other reports.[3 17 18]

Possible sites of diabetic proximal neuropathy have been controversial[19]; root, plexus, nerve and motor terminal branches have all been proposed. In our patient the clinical and electrophysiological involvement of the diaphragm would implicate cervical roots or the phrenic nerve. The denervation seen in the lumbosacral paraspinal and intercostal muscles would favour thoracic and lumbar root localisation. Weakness of the iliopsoas is typical of the proximal leg weakness in proximal diabetic neuropathy (diabetic amyotrophy). One patient had both diabetic thoracic radiculopathy and amyotrophy.[20]

Some investigators have divided proximal diabetic neuropathy into those with and without an associated distal symmetric neuropathy.[4 17] Those with an associated neuropathy tend to have a gradual onset, bilateral proximal symptoms, insulin dependency, and paraspinal denervation on EMG. Our patient, who had a preceding distal symmetric neuropathy, fits this profile.

First described by Bruns in 1890 and expanded upon by Garland, diabetic proximal neuropathy has been widely recognised.[21 22] Prominent bulbar symptoms have been described.[23] Respiratory weakness may also be the initial manifestation of diabetic proximal neuropathy.

We thank Dr Lewis P Rowland for helpful comments on this manuscript. This work was presented in part in abstract form at the 45th Annual meeting of the American Association of Electrodiagnostic Medicine. Orlando, Florida, 14–18 October, 1998.

1 Martyn CN, Hughes RAC. Epidemiology of peripheral neuropathy. *J Neurol Neurosurg Psychiatry* 1997;**62**:310–18.
2 Barohn RJ, Sahenk Z, Warmolts JR, *et al*. The Bruns-Garland syndrome (diabetic amyotrophy) revisited 100 years later. *Arch Neurol* 1991;**48**:1130–5.
3 Pascoe MK, Low PA, Windebank AJ, *et al*. Subacute diabetic proximal neuropathy. *Mayo Clin Proc* 1997;**72**: 1123–32.
4 Subramony SH, Wilbourn AJ. Diabetic proximal neuropathy clinical and electromyographic studies. *J Neurol Sci* 1982;**53**:293–304.
5 Kitka DG, Breuer AC, Wilbourn AJ. Thoracic root pain in diabetes: the spectrum of clinical and electromyographic findings. *Ann Neurol* 1982;**11**:80–5.
6 Bolton CF. Clinical neurophysiology of the respiratory system. *Muscle Nerve* 1993;**16**:809–18.
7 Hughes RAC, Bihari BD. Acute neuromuscular respiratory paralysis. *J Neurol Neurosurg Psychiatry* 1993;**56**:334–43.
8 Raps EC, Bird SJ, Hansen-Flaschen J. Prolonged muscle weakness after neuromuscular block in the intensive care unit. *Crit Care Clin* 1994;**10**:799–813.
9 Rosenfalck P, Rosenfalck A. *Electromyography, sensory and motor conduction: findings in normal subjects*. Copenhagen: Laboratory of Clinical Neurophysiology, Rigshospitalet, 1975:1–49.
10 Dimopoulou I, Daganou M, Dafni U, *et al*. Phrenic nerve dysfunction after cardiac operations. Electro-physiologic evaluation of risk factors. *Chest* 1998;**113**:8–14.
11 Mills GH, Khan ZP, Moxham J, *et al*. Effects of temperature on phrenic nerve and diaphragmatic function during cardiac surgery. *Br J Anaesth* 1997;**79**:726–32.
12 Bradley WG, Chad D, Verghese JP, *et al*. Painful lumbosacral plexopathy with elevated erthrocyte sedimentation rate: a treatable inflammatory syndrome. *Ann Neurol* 1984;**15**: 457–64.
13 Younger DS, Rosoklija G, Hays AP, *et al*. Diabetic peripheral neuropathy: a clinicopathologic and immunohistochemical analysis of sural nerve biopsies. *Muscle Nerve* 1996;**19**:722–7.
14 Hughes RAC, Cameron JS, Hall SM, *et al*. Multiple mononeuropathy as the initial presentation of systemic lupus erythematosus-nerve biopsy and response to plasma exchange. *J Neurol* 1982;**228**:239–347.
15 Said G, Goulon-Goeau C, Lacroix C, *et al*. Nerve biopsy findings in different patterns of proximal diabetic neuropathy. *Ann Neurol* 1994;**35**:559–69.
16 Krendal DA, Costigan CD, Hopkins LC. Successful treatment of neuropathies in patients with diabetes mellitus. *Arch Neurol* 1995;**52**:1053–61.
17 Asbury AK. Proximal diabetic neuropathy. *Ann Neurol* 1977;**2**:179–80.
18 Said G, Elgrably F, Lacroix C, *et al*. Painful proximal diabetic neuropathy: inflammatory nerve lesions and spontaneous favorable outcome. *Ann Neurol* 1997;**41**:762–70.
19 Sander HW, Chokroverty S. Diabetic amyotrophy: current concepts. *Semin Neurol* 1996;**16**:173–8.
20 Anderson T, Carroll G, Avery S. Combined diabetic thoracic radiculopathy and amyotrophy. *N Z Med J* 1991;**104**:475–6.
21 Bruns L. Ueber neuritische Lähmungen beim diabetes mellitus. *Berliner Klinische Wochenschrift* 1890;**27**:509–15.
22 Garland H. Diabetic amyotrophy. *BMJ* 1955;ii:1287–90.
23 Di Biagio F. L'amiotrofia diabetica (con un caso personale di amiotrofia bulbare a tipodi SLA). *Rivista di Neurologia* 1959;**29**:457–70.