Diabetic amyotrophy: a painful radiculoplexus neuropathy

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ABSTRACT

Diabetic lumbosacral radiculoplexus neuropathy is a monophasic syndrome of diffuse pain and weakness that typically affects the lower limbs asymmetrically and is often associated with significant weight loss. Recovery can be prolonged and unpredictable. It is a clinical diagnosis and investigations are performed mainly to exclude other causes. Although it is most likely caused by a microvasculitis, there is no evidence to support using intravenous immunoglobulin or any long-term immunosuppression. Pulsed methylprednisolone may help pain if given within 2–3 months of symptom onset.

INTRODUCTION

Historical perspective

Bruns, a German neuropathologist first described the syndrome in 1890; Garland coined the term ‘diabetic amyotrophy’ in the 1950s. It is characterised by diffuse pain, weakness and areflexia that typically affects the lower limbs and is asymmetric. Garland commented that the condition was always reversible by full diabetic control. We now use the term Bruns-Garland syndrome, along with diabetic lumbosacral radiculoplexus neuropathy (DLRPN), defining the extent of pathological involvement.

Although rare and affecting fewer than 1% of patients with diabetes (compared with distal sensory neuropathy, which affects up to half of patients with diabetes), the increasing worldwide prevalence of diabetes (over 3.5 million in the UK alone) makes DLRPN a significant cause of morbidity and health burden.

Clinical phenotype

DLRPN typically affects men aged over 50 years with type 2 diabetes mellitus but also occurs in women and younger people. It may occur as a complication of a prediabetic state or may follow tight glycaemic control in someone with newly diagnosed diabetes.

It begins with unilateral pain in the thigh or buttock, typically spreading to other regions of the same leg, and then the opposite leg due to involvement of the lumbosacral roots, plexus and peripheral nerves. The pain is followed a few weeks later by weakness and then muscle wasting; weight loss is characteristic (box 1).

By the time the patient seeks medical attention, the symptoms and signs may be more symmetric, and a careful history is required to ascertain the asymmetry at onset.

What features point to a radiculoplexus neuropathy? It is the pattern of weakness, the loss of reflexes and the finding that the sensory disturbance is more extensive than could be localised to a single nerve root or peripheral nerve distribution. Lumbar plexus lesions tend to cause weakness of hip flexion and hip adduction and/or knee extension, while lumbosacral trunk and upper sacral plexus lesions result in foot drop and weakness of knee flexion or hip abduction. Patterns of sensory disturbance are less reliable, as it is difficult to delineate clinically between dermatomal and nerve trunk sensory loss. In general, sensory change over the anterior and medial thigh and medial leg...
Box 1  Key clinical features

**Symptoms**
- Pain: severe and deep; asymmetric onset with variable distribution.
- Weakness: asymmetric.
- Weight loss: can be up to 20–30 kg.

**Clinical signs**
- Asymmetric wasting and weakness.
- Loss of reflexes: knee and ankle.
- Minimal sensory loss, unless there is a coexisting distal sensory neuropathy.

Box 2  Differential diagnosis of a lumbosacral radiculoplexus neuropathy in a patient with diabetes

**Compression/infiltration**
- Nerve root compression, neoplastic invasion/compression, retroperitoneal haematoma, arterial (pseudoaneurysm), abscess (eg, tuberculosis and salmonella) and prolonged labour.

**Iatrogenic**
- Postradiotherapy, postoperative and obstetric instrumentation.

**Vasculitides/connective tissue disorders and sarcoidosis.**

**Infection (eg, HIV, Epstein-Barr virus, cytomegalovirus, varicella zoster virus, Lyme disease and syphilis).**

**Amyloidosis and carcinomatous meningitis.**

Box 3  Important investigations

**Blood tests**
- Full blood count, urea and electrolytes, liver function tests, HbA1c, serum calcium, serum C reactive protein, erythrocyte sedimentation rate, serum antinuclear antibody (other tests depending on risk factors, eg, HIV).

**MR scan of lumbosacral spine.**

**CT scan of pelvis.**

**Neurophysiology.**

typically represents lumbar plexus involvement, while sensory disturbance involving the dorsum of the foot, back of the thigh and perineum suggests a lumbosacral trunk and/or sacral plexus lesion.

Most patients will have had MRI of the lumbosacral spine, and in this middle-aged patient population, it inevitably shows degenerative change. It is important to ask, ‘Does the pattern of motor deficit match the changes on imaging?’.

**Clinical variants and associations**

i. Painless diabetic motor neuropathy is characterised by more symmetric weakness affecting the chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). Nerve pathology shows the same changes as in DLRPN, and so it is considered to be a painless form of this.7

ii. Diabetic cervical radiculoplexus neuropathy shares many of the clinical and pathological features of DLRPN, providing evidence that these conditions are best categorised together within the spectrum of diabetic radiculoplexus neuropathies.8

iii. Thoracoabdominal neuropathy may occur in isolation or be associated with DLRPN and the common diabetic sensory polyneuropathy.

**Differential diagnosis**

Having excluded nerve root compression, the main differential diagnosis to consider is infiltrative pelvic malignancy, particularly when there is profound weight loss and unilateral weakness. A similar picture can develop as a complication of radiotherapy. Multiple mononeuropathies due to vasculitis are often painful with weakness and sensory loss in a specific peripheral nerve distribution. Painless progressive asymmetric leg weakness would make one consider CIDP. Box 2 outlines less common causes.

**Investigations**

The diagnosis of DLRPN relies mostly on clinical suspicion, as there is no single definitive test. Imaging can exclude compressive lesions, and neurophysiology may provide supportive findings.9 Cerebrospinal fluid (CSF) examination is not usually needed in typical cases but may show elevated protein of up to 2 g/L without cells; oligoclonal bands are negative. In general, CSF examination or nerve biopsy should only be considered if an alternative diagnosis such as carcinomatous meningitis is likely (box 3).

How does neurophysiology help with localisation to the lumbosacral plexus as opposed to nerve roots or peripheral nerves? In most spinal segments, the dorsal root ganglion lies lateral to and outside the intervertebral foramen (figure 1). Knowing this helps to distinguish a preganglionic process (nerve root) from a postganglionic process (plexus or individual peripheral nerves). The key point is that in most patients with a lumbosacralplexopathy, the problem is postganglionic, and therefore the sensory nerve action potential amplitudes are small. However, normal sensory nerve action potentials do not completely exclude a plexopathy. Motor nerve conduction studies often show reduced compound muscle action potential amplitudes, as well as mild slowing of conduction velocity, in keeping with a loss of axons.

Because the nerve conduction changes in a radiculoplexopathy are unreliable, needle electromyographic examination is a more useful component of neurophysiology testing. Fibrillation potentials and...
How to understand it

Figure 1 Anatomy of the dorsal root ganglion. SNAP, sensory nerve action potential.

long duration, high amplitude motor unit action potentials are commonly found, extending from the lumbar paraspinal muscles to the distal leg muscles and involving multiple myotomes (more than two nerve roots). These denervation changes in paraspinal muscles indicate involvement at nerve root level (ie, a radiculoplexopathy) as this would not occur in a pureplexopathy. Examination of both lower limbs is often required to document the extent of involvement.

Neuropathology

Although DLRPN is motor predominant, there is unequivocal evidence that autonomic and sensory nerves are also involved. Cutaneous nerves from patients with DLRPN show pathological evidence of ischaemic injury and microvasculitis.

Management

The finding of microvasculitis and endoneurial inflammatory infiltration on nerve biopsy has not led to a major change in management, as there have been no trials to answer the question of whether immunosuppression (corticosteroids, cyclophosphamide or intravenous immunoglobulin) has a role to play in improving outcome. Nearly all patients have some recovery of function without medical treatment but may be slow and incomplete (box 4).

Pain control is difficult and often requires opiates. Physiotherapy and orthotic assessment can help in selected, often more severely affected cases. Diabetes control should be optimal, but there is no evidence that patients who are well controlled on oral hypoglycaemic agents should be switched to insulin.

The possible use of corticosteroids in pain management is intriguing with a few reports of improvement with oral prednisolone and intravenous methylprednisolone. However, there are no controlled trials to recommend using corticosteroids routinely.

Prognosis

The time course for this condition is prolonged. While it usually begins in one leg, it commonly spreads to the other leg within weeks or months. It can worsen in a slowly progressive or stepwise manner over up to 18 months and in 30% of cases may spread to involve the upper limbs. Eventually, the process stabilises and gradually improves, although recovery may take many months. Patients should be informed that some degree of permanent weakness may persist.

Summary

We do not have defined clinical criteria for diagnosing DLRPN, which can be variable in its severity. Those patients requiring input from a neurologist tend to be at the more severe end of the clinical spectrum. The condition involves the nerve roots, plexus and peripheral nerves and pathologically results from ischaemic injury secondary to a microscopic vasculitis.

The diagnosis is largely clinical, and investigations are focused on ruling out other pathologies. It is recognised as a complication of a prediabetic state, following tight glycaemic control in a patient with newly diagnosed diabetes and after bariatric surgery in a patient with diabetes. Management includes pain

Box 4 Management

- Pain control: opiates may be needed at onset, amitriptyline 10–75 mg at night to help pain and insomnia. Regular paracetamol/non-steroidal anti-inflammatory drug. Gabapentinoids. Consider a short course of corticosteroids* if pain remains unremitting.
- Physiotherapy.
- Maintaining good diabetic control: no evidence that switching to insulin is helpful.

*Oral/intravenous methylprednisolone 500 mg/day for 2 days, repeated every 2 weeks for 2–3 months.
control and physiotherapy along with maintaining optimal diabetic control.

To date, there is no evidence to support using intravenous immunoglobulin, plasma exchange or cyclophosphamide. As for corticosteroids, small case studies have produced conflicting outcomes, with a suggestion that pulsed oral or intravenous methylprednisolone may help pain if given within 2–3 months of onset of symptoms.

What do we recommend regarding corticosteroids? In patients where the pain and weakness has plateaued, corticosteroids would not be indicated as we know that the natural history will be of some degree of recovery. The situation becomes difficult in the patient with severe unremitting pain. There would need to be a careful discussion with the patient on the possible use of pulsed corticosteroids and its complications. A regimen of pulsed methylprednisolone (500 mg/day for 2 days, repeating every 2 weeks for 8–12 weeks) is reasonable but is based on reports from uncontrolled studies.

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