Acute Painful Neuropathy Restricted to the Abdomen Following Rapid Glycaemic Control in Type 2 Diabetes

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A 46-year-old Japanese man with type 2 diabetes mellitus, whose only diabetic complication was simple retinopathy, developed acute painful neuropathy. This presented as paresthesia and hyperesthesia restricted to the abdomen. The patient’s haemoglobin A1c had dropped from 12% to 7.5% within 5 months, following a rapid improvement in glycaemic control. On investigation, there were no indications of disease in the intra-abdominal area. Nerve conduction studies were consistent with mild sensorimotor peripheral and autonomic neuropathy. The patient required medication (mexiteline, sulpiride and imipramine hydrochloride) to control the pain. Four months after presentation, the symptoms showed a dramatic improvement and the treatment for pain relief was discontinued without any recurrence of paresthesia or hyperesthesia in the patient’s abdomen. This was a very unusual case of diabetic post-treatment painful neuropathy in which the prominent features were severe pain, paresthesia and hyperesthesia restricted to the abdomen.

KEY WORDS: TYPE 2 DIABETES; HYPERESTHESIA; PAIN; PARESTHESIA; NEUROPATHY

Introduction

In patients with diabetes mellitus, painful sensation and/or paresthesia are sometimes precipitated by insulin treatment or strict glycaemic control. The phenomenon is generally called ‘post-treatment painful neuropathy’, and it is regarded as an entity of diabetic neuropathy.1,2 The cause of post-treatment painful neuropathy and the reason why an individual might be predisposed to develop it are unknown; the prevalence is generally thought to be low.2 One hypothesis suggests that post-treatment painful neuropathy results from adequate diabetic control promoting nerve regeneration and that the pain may be related to the ectopic generation of impulses in regenerating axon sprouts.3 Post-treatment painful neuropathy usually develops several weeks after a rapid improvement in glycaemic control, and presents as dramatic and severe pain in the lower extremities. This usually subsides within a year.2

This paper presents a very unusual case of acute painful neuropathy following a rapid improvement in glycaemic control in which the prominent feature was a severe pain restricted to the abdomen.
Case report

A Japanese man aged 46 years was diagnosed with type 2 diabetes in 1999. He drank alcohol and did not smoke. He was treated with glimepiride (3 mg/day), voglibose (0.2 mg/day) and buformine (50 mg/day), but his haemoglobin A1c (HbA1c) was 9 – 12% because he did not control his diet. In April 2003, he adopted a healthier lifestyle by commencing a strict diet and omitting alcohol. Subsequently, his HbA1c had fallen from 12% to 7.5% by August 2003, and he developed pain, paresthesia and hyperesthesia in his abdomen; these symptoms did not affect other areas (end of June 2003). In August 2003, the patient underwent general clinical examination, an abdominal ultrasound examination and assessment for tumour markers (α-fetoprotein [AFP], carcinoembryonic antigen [CEA] and carbohydrate antigenic determinant 19-9 [CA19-9]), which revealed no intra-abdominal pathology.

On neurological examination, his cranial nerve, knee jerk reflex and Achilles tendon reflex were normal. In terms of the sensory system, Fig. 1 shows that the dermatome involved in the abnormal sensation (paresthesia and hyperesthesia) was both anterior sides of the thoracic (Th) spinal nerves at levels 8 – 11. There were no other areas with

FIGURE 1: The distribution of thoracic (Th) spinal nerves showing the abnormal sensation (paresthesia and hyperesthesia) dermatome at levels 8 – 11 (shaded area) associated with post-treatment painful neuropathy in a 46-year-old Japanese man with type 2 diabetes following a rapid improvement in glycaemic control.
abnormal sensation. There were no eruptions on the skin of his trunk. Nerve conduction studies were consistent with mild sensorimotor peripheral neuropathy (motor nerve conduction velocity: right ulnar nerve 43.0 m/s, right peroneal nerve 42.8 m/s; sensory nerve conduction velocity: right ulnar nerve 48.6 m/s, right sural nerve 46.5 m/s), and there was a dysfunction of the autonomic nervous system (heart rate variation on deep breathing: 9 beats/min). There was an osteophyte at the Th10 level, but no evidence of spinal cord compression on magnetic resonance imaging (MRI) of the thoracic spine. With regard to other diabetic complications, simple retinopathy was found, but there was no evidence of nephropathy.

At the end of August 2003, the patient commenced treatment with mexiletine (150 mg/day), sulpiride (150 mg/day) and imipramine hydrochloride (30 mg/day) for pain relief. Three weeks after treatment, his symptoms showed a dramatic improvement, and these drugs were discontinued at the end of November 2003. There was no subsequent recurrence of paresthesia and hyperesthesia in his abdomen.

Discussion

This is a very unusual case of acute painful neuropathy following a rapid improvement in glycaemic control (HbA1c reduced from 12% to 7.5% within 5 months); the prominent features were severe pain, paresthesia and hyperesthesia restricted to the abdomen. We speculate that the symptoms in this case may have been caused by diabetic post-treatment painful neuropathy.

The aetiology and pathogenesis of post-treatment painful neuropathy are still unclear. Previous studies have reported arterio-venous shunting and proliferating new vessels in acute painful neuropathy following rapid glycaemic control. Suzuki et al.6 reported that all five patients with diabetic post-treatment painful neuropathy in their study were identified as having a mitochondrial tRNA (Leu) mutation at position 3243. These observations cannot completely explain the clinical course and sites of pain sensation associated with post-treatment painful neuropathy, however. Greater care should be taken when commencing strict glycaemic control in diabetic patients with prolonged hyperglycaemia and previous neuropathy.2,7

In this case, we had to discriminate between a diagnosis of post-treatment painful neuropathy or one of truncal neuropathy. The latter usually presents with pain and dysesthesia in areas of the chest or abdomen or both.8 The pathogenesis of diabetic truncal neuropathy is also not known with certainty, although it is widely thought to be due to an ischaemic change because it frequently has a sudden onset.9 Clinically, the differential diagnosis of diabetic truncal or post-treatment painful neuropathy is very difficult. This is because the clinical courses of diabetic truncal and post-treatment painful neuropathy are very similar and the symptoms of both often subside within a year without medication. In this particular case, it was also difficult to differentiate between diabetic truncal neuropathy and post-treatment painful neuropathy. It is clear that symptoms of each of these types of diabetic neuropathy are triggered by a rapid improvement in glycaemic control.

Polyneuropathy affecting the limbs, usually in a distal or ‘stocking and glove’ distribution, has long been recognized in diabetes mellitus.10 Usual painful diabetic neuropathy is just one of a myriad of secondary conditions that may result from poor glycaemic control. The sites of symptoms of usual painful diabetic neuropathy also
show a distal or ‘stocking and glove’ distribution. The symptom (pain) areas associated with post-treatment painful neuropathy not only have a distal distribution, however, but they may often be found in other areas. Takahashi et al.\textsuperscript{2} reported that the pain sites of post-treatment painful neuropathy were the lower extremities, with pain spreading evenly throughout the body. Patients with post-treatment painful neuropathy were significantly thinner than patients without post-treatment painful neuropathy at the beginning of diabetic treatment. They also had a greater impairment of the patella tendon reflex and motor nerve conduction velocity in the ulnar and peroneal nerves and more sensory nerve symptoms.\textsuperscript{11} The present case is very unusual in terms of the localization of the symptoms of pain.

Painful neuropathy is the transmission of painful stimuli from the peripheral nerve fibres (C-fibres) to the higher centres. A recent study reported that pain from the abnormal stimulation of C-fibres was caused by an abnormality of the tetrodotoxin-resistant sodium channels in post-treatment painful neuropathy.\textsuperscript{12} Alternatively, abnormal opioid receptors in higher centres have been shown to influence pain sensitivity in chronic hyperglycaemia.\textsuperscript{13} It is not known which of these theories is correct, and we also do not know which peripheral nerve C-fibres may influence the painful stimulation associated with post-treatment painful neuropathy. In this case, there was an osteophyte at the Th10 level, but there was no evidence of spinal cord compression on MRI and the symptoms of pain were not stimulated by exercise. The osteophyte was not considered to influence the symptoms, therefore.

There is still much to learn about post-treatment painful neuropathy and diabetes, including which peripheral nerve C-fibres may influence the painful stimulation.

References


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