CASE REPORTS

Resolution of diabetic autonomic neuropathy

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Many consider diabetic autonomic neuropathy to be an irreversible complication of diabetes of long duration. Three patients developed symptoms of autonomic neuropathy which subsequently resolved. Their autonomic neuropathy was not associated with long duration of diabetes, but with weight loss. Each had marked weight loss and resolution occurred on regaining remembered premonitory weight. A woman aged 20 was admitted with anorexia nervosa (weight loss 6 kg). She complained of feeling bloated. Gastroenterological investigations showed delayed gastric emptying. RR ratio (respiration and standing) was abnormal. Resolution occurred after two years. A male aged 18 developed diabetic symptoms, which were overlooked. Twelve months later he presented underweight and ketonuric; insulin treatment was started but within one month he became impotent. Resolution occurred after 18 months. An 80 year old man presented after six months trial of diet and sulphonylurea therapy. He was underweight, had ketonuria, and such muscle loss that he was unable to sit unaided. Insulin treatment was started. He developed severe symptomatic postural hypotension. This resolved six months later by which time he had regained his normal weight. These cases illustrated symptomatic autonomic neuropathy occurring in relation to weight loss with resolution on recovery of normal weight, a temporal pattern mimicking that of acute cachectic painful neuropathy. Treatment of autonomic neuropathy should be like that of cachectic neuropathy, that is with an expectation of recovery and should include strategies to regain premonitory weight and achieve glycaemic control

Autonomic neuropathy due to diabetes has long been recognised. It can be asymptomatic but may be the cause of crippling disability. It can affect any organ that receives autonomic innervation and the symptoms that

patients suffer are numerous and include postural hypotension, diarrhoea, gustatory sweating, problems from “neuropathic bladder”, and impotence. Gastric stasis can produce feelings of fullness, and bad taste, but can also be found on investigations such as endoscopy. Investigative evidence includes lack of beat to beat cardiac variation with position or respiration. It is usually described in textbooks as permanent¹ and occurring in patients with long standing diabetes.² However Isotani and Fukumoto have described the reversibility of autonomic nerve function in relation to rapid improvement of glycaemic control in 54 patients with type 2 diabetes of short duration.³ Despite this, a book recently published aimed at the diabetes primary care team reiterates the view that autonomic neuropathy is irreversible: “autonomic neuropathy is an irreversible progressive form (of neuropathy)”.⁴ We wish to describe three patients who developed autonomic neuropathy after a varying but short duration of diabetes and in whom their signs and symptoms subsequently resolved. The three all have type 1 diabetes, and their clinical features are summarised in table 1.

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Case 1

A 20 year old woman fashion designer with a duration of type 1 diabetes for five years was experiencing some social problems and was admitted to hospital with anorexia nervosa/bulimia. Her recent weight loss was at least 6 kg and her glycated haemoglobin (HbA_{1c}, high pressure liquid chromatography method) was higher than the assay range (that is more than 19%). She complained of feeling bloated and unable to eat and had symptoms of acute painful peripheral neuropathy, that is burning sensation with pins and needles in both feet and legs that was worsened by touch. She had gustatory sweating with excessive sweating after food, particularly over head and chest and it was noted she had a postural blood pressure drop of 15 mm Hg. She had no evidence of retinopathy or microalbuminuria, she retained vibration and light touch sensation and her reflexes were

Table 1 Features of clinical presentation, symptoms and signs of autonomic neuropathy

	1	2	3
Patients	Female aged 20, 5 year duration of type 1	Male, aged 18, with newly diagnosed type 1 diabetes	Male aged 80, with 6 months' duration of type 1 diabetes
Associated features	Anorexia nervosa with weight loss (6 kg) Peripheral neuropathic pain	Weight loss (22 kg) Peripheral neuropathic pain	Weight loss (10 kg) Peripheral neuropathic pain
Symptoms of autonomic neuropathy	Bloating Gustatory sweating Dizzy on standing	Bloating Gustatory sweating – Impotence	Bloating Gustatory sweating Marked dizziness on standing
Signs of autonomic neuropathy	Postural drop >15 mm Hg RR ratios (lying/standing) = 1 (Inspiration/expiration) = 1	Postural drop >10 mm Hg RR ratios not done	Postural drop >26 mm Hg RR ratios (lying/standing) = 1 (Inspiration/expiration) = 1

present. Gastroenterological investigations included ultrasound, endoscopy, and barium studies. These revealed delayed gastric emptying with food debris, no pyloric stenosis, and fluid filled loops of small bowel. The electrocardiogram showed that the RR ratio on respiration and standing were abnormal: standing/lying = 1; inspiration/expiration = 1. During her long hospital stay (18 months), she received medical and psychiatric support. The treatment included behavioural therapy, encouragement to eat, increased insulin dosages, and therapy for painful neuropathy with paracetamol and amitriptyline. On discharge, she was pain free, her HbA1c had improved to 9.0% (normal up to 8.5%) and she was regularly taking her insulin. At two years after admission both signs and symptoms of autonomic neuropathy had resolved; RR intervals on standing from lying changed to 0.8 and inspiration to expiration became 0.85. She maintained acceptable glycaemic control (HbA1c less than 9.5%). Ten years have since elapsed and she remains free of symptoms of autonomic neuropathy.

Case 2

A young male of 18 years presented to his general practitioner complaining of polyuria, balanitis, painful feet, and thirst. No investigations were undertaken and he was referred non-urgently to the urologist who had a six month waiting list. At the first urological consultation glycosuria was found and he was referred urgently to the diabetic clinic. At presentation he was markedly underweight and ketonuric. Insulin therapy was started and he managed well. Within one month of diagnosis however, he complained of impotence, with no nocturnal erections. At the same time he developed worsened symptoms of painful peripheral neuropathy and gustatory sweating, similar in nature to case 1. No specific tests of autonomic function were performed. The plan to improve his glycaemic control was continued. His HbA1c became normal in two months (8.2%), premorbid weight was achieved at six months with an increase of 22 kg and the symptoms of painful neuropathy disappeared at 12 months. Much to his relief after 18 months his impotence resolved. Twelve years have elapsed and he remains potent with no other symptoms of autonomic neuropathy.

Case 3

An 80 year old man presented having been diagnosed with diabetes by his general practitioner six months previously. He said he had lost 10 kg over the last two years. On diagnosis he had been started on a "diabetic" diet with sulphonylurea therapy. On admission, six months later he was markedly underweight, ketonuric, with muscle loss so marked he was unable to sit unaided and could not stand. His HbA1c (DCA method) was 5.9% (normal up to 6.5%). He had a postural systolic blood pressure drop of between 25 and 88 mm Hg and felt dizzy when he stood up. He complained of burning pains in his feet and autonomic function tests showed RR intervals on standing/lying and inspiration/expiration of 1. Insulin therapy was started but he developed worsened severe symptomatic postural hypotension. The care plan was to treat hypotensive symptoms, with fludrocortisone, with elevation of the head of the bed during the night and the day time spent in a chair if not mobilising, to improve glycaemic control but encourage a high calorie diet that included fat and sugar. At six months he had regained his premorbid weight, his HbA1c remained normal (6.2%) and his painful neuropathy and symptoms and signs of postural hypotension had resolved.

DISCUSSION

All three patients had subjective and some objective evidence of autonomic neuropathy (see table 1). This was not associated with long duration of diabetes but was associated with weight

loss, and in one with improved diabetic control. The symptoms of autonomic neuropathy resolved. It is unclear whether the time that had elapsed, continued improved glycaemic control, improved nutrition, or a combination of these brought about the resolution. In all three the autonomic neuropathy accompanied painful neuropathy. In two this was acute neuropathic cachexia⁵ and in one the symptoms worsened with improved glycaemic control.⁶ These painful neuropathies are known to resolve over time, and neuropathic cachexia is resolved by regaining premorbid weight.⁷ This resolution may even happen with some worsening of glycaemic control provided weight is increased. However as well as overall nutrition being important, glycaemic control has been shown to be important.⁸ Nerve function, particularly autonomic, improves with improved glycaemic control—most noticeably from pancreatic transplantation.⁹

The pattern of resolution of autonomic neuropathy in these patients over time mimicked that of painful neuropathic cachectic neuropathy. Consequently it seems reasonable to manage acute autonomic neuropathy symptomatically, with the expectation of improvement or recovery. Weight gain to the premorbid state should be encouraged with attention to glycaemic control. These strategies can be confusing for patients and health care professionals alike because it seemingly contradicts the usual standards of diabetes care, with their emphasis on a "prudent diet" and lifestyle advice. Careful education and support is required for patients and their carers and families, since at first sight it would seem that the patient is not complying with usual advice and may even be blamed for bringing these distressing symptoms on themselves. All these patients benefited from having their symptoms treated, eating whatever they could and covering the consequent hyperglycaemia with increasing amounts of insulin. All health care professionals should be persuaded that autonomic neuropathy can be reversible and not the inevitable consequence of long standing diabetes.

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