Diabetic Neuropathic Cachexia in a 50-Year-Old Woman with Type 2 Diabetes: First Case Report in Korea

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Abstract

Diabetic neuropathic cachexia (DNC) is one of the rarest presentations of diabetic neuropathy associated with profound weight loss. A 50-year-old Korean woman with poorly controlled type 2 diabetes complained of intractable pain in the trunk and lower extremities, and total body weight loss of 17% over a 6 month period. The patient’s symptoms persisted after glucose control and various medications for neuropathic pain. A diagnosis of DNC was made based on the rapid onset of severe pain, polyneuropathy, and marked weight loss without evidence of end organ disease other than mild retinopathy, and the exclusion of other possible causes. Spontaneous improvement of the patient’s neuropathic pain and gradual weight gain occurred after 6 months of supportive care. Since the original report of DNC, 31 cases have been published in the English-language literature; however, ours is the first reported case in Korea. Clinicians must be aware of this debilitating complication of diabetes because of its severity and rapid progression.

Keywords: Cachexia, Diabetic neuropathies, Korea
INTRODUCTION

In 1974, Ellenberg[1] described a group of patients with diabetes mellitus who complained of profound involuntary weight loss and neuropathic pain. The patients were all in their sixth to seventh decade of life. The neuropathic pain was bilateral involving the anterior thighs and was associated with anorexia, emotional disturbances, and unexplained weight loss. All of the patients recovered spontaneously in 1 or 2 years. The term diabetic neuropathic cachexia (DNC) was given to these patients. Since that original report, 31 cases have been reported in the English-language literature[2].

Here, we present an additional case of DNC in Korea. This is the first such case from an East Asian population. Although DNC is considered the least common form of diabetic neuropathy, clinicians must be aware of this debilitating complication because of its severity and rapid progression.

CASE REPORT

A 50-year-old woman who was diagnosed with type 2 diabetes 10 years ago, visited our clinic. She had been prescribed an antidiabetic medication at another diabetes clinic, but had refused to take her medication for more than a year. Her random blood glucose level was 457 mg/dL and her HbA1c level was over 15%. The patient complained of recent weight loss and severe pain in her trunk and lower extremities. The pain, which was sharp and burning in nature, had started in the pelvic area and then spread to the thighs, knees, lower extremities, and feet over a period of 2 months. Initially, 16~20 units of basal insulin, metformin and nateglinide were used to control the patient’s glucose level. After 4 months, the patient’s HbA1c level decreased to 6.8% but she experienced additional weight loss. She tried non-steroidal anti-inflammatory drugs, pregabalin, and a nerve block to control her lower extremity pain without success. Ultimately, the patient was admitted for further evaluation of her weight loss and pain.

At the time of admission, the patient’s blood pressure was 160/90 mmHg in the supine position and 140/76 mmHg in the standing position, indicating postural hypotension. Her body weight was 37 kg and her height was 158 cm with a body mass index (BMI) of 14.8 kg/m². Previously, the patient weighed 57 kg and had a BMI of 22.8 kg/m², but she had 10 kg of unintentional weight loss over 6 months. The patient did not smoke or consume alcohol.

The patient complained of numbness and a severe burning sensation across the left inguinal area that extended symmetrically to her lower abdomen, back, hips, thighs, lateral aspect of the calves, knees, ankles and feet. The severity of pain was estimated to be 8/10 using a visual analog scale (VAS). The patient also suffered from generalized weakness, fatigue, insomnia, emotional instability, severe anorexia associated with poor oral intake, and difficulty in going from sitting to standing.

On physical exam, the patient appeared to have a depressed mood. There was diffuse symmetrical muscle wasting and a bilateral decrease in ability to sense touch, vibration, temperature, and pain, which was more pronounced in the proximal and lower extremities than in the distal and upper extremities. The patient’s deep tendon reflex was diminished at both the knee and ankle; the dorsalis pedis pulse was intact but weak.

A laboratory examination showed an HbA1c level of 7.6%, hemoglobin level of 12.3 g/dL, blood urea

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Case Report

A diagnosis of DNC was made based on the rapid onset of severe pain, polyneuropathy, and marked weight loss without evidence of end organ disease other than mild NPDR, and the exclusion of other known causes such as malignancy, neuropathic carcinomatosis, and toxic or alcoholic neuropathy.

During the hospitalization period, we consulted with the psychiatric department for emotional support and a dietitian for nutritional support. Nortriptyline and gabapentin were administered for pain. The patient’s blood glucose level was well controlled with metformin and sitagliptin. We withheld metformin as a possible cause of anorexia and gliclazide was prescribed instead. After several days of supportive care, the patient’s neuropathic pain improved gradually and her VAS score decreased to 4/10 by the time of discharge. The patient was discharged with sitagliptin and gliclazide for diabetes and gabapentin, nortriptyline, acetaminophen and tramadol for neuropathic pain.

About 6 months later, the patient’s weight had increased to 48kg and her neuropathic pain resolved gradually. The patient’s blood glucose level was well controlled with sitagliptin monotherapy with HbA1c of 5.7%. She continued to experience mild pain but was well controlled with small doses of gabapentin (100 mg, three times a day).

DISCUSSION

DNC is characterized by the subacute onset of a painful, sensory-predominant polyneuropathy associated with rapid profound weight loss. It is most common in middle-aged males with newly diagnosed type 2 diabetes, but also occurs less commonly in women and, in rare cases, has been observed in patients...
with type 1 diabetes[3,4]. Most of DNC patients complain of varying degrees of bilateral symmetrical sensory-motor peripheral neuropathy which eventually extends to the lower and upper extremities, chest, and abdomen[1]. Autonomic neuropathy, including constipation, diarrhea, gastroparesis and impotence is another recognizable finding in DNC patients[1]. Motor manifestations include generalized wasting and decreased muscle strength, which is more pronounced in the proximal lower extremities than in the upper extremities, thus resembling proximal diabetic neuropathy. Deep tendon reflexes and positional and vibratory sensations are usually decreased or absent symmetrically. Most DNC patients experience a single episode and recover fully, but recurrent cases have been reported[5]. DNC is a diagnosis of exclusion: an extensive check-up must be performed to rule out any occult malignancy, neuropathic carcinomatosis, toxic or alcoholic neuropathy, porphyria or chronic relapsing Guillain–Barre syndrome[6].

Weight loss is often severe, in some cases reaching as much as 60% of the patient’s total body weight[7]. However, patients typically regain weight spontaneously. The underlying mechanism of weight loss is unclear. Several reports have demonstrated marked hyperglycemia in patients with DNC: therefore, caloric loss from glycosuria may be a contributing factor. In some cases, dramatic weight loss has been explained as a result of anorexia due to massive pain and depression[1]. In one report, malabsorption related to an exocrine pancreatic insufficiency was found in four DNC patients[8].

Archer et al.[9] reported nerve biopsies of patients with DNC showed axonal degeneration of myelinated nerve fibers as well as unmyelinated fibers, while Jackson and Barohn[5] reported a profound loss of myelinated axons without axonal degeneration. The extreme rarity of microangiopathic end-organ complications of diabetes, including retinopathy or nephropathy[10,11], speaks against a vascular cause of the neuropathy. Some reports have suggested that pain in patients with DNC is due to paradoxical hypoxic nerve fiber damage caused by intensive insulin administration to control hyperglycemia[12-14]. When insulin therapy is initiated with the rapid establishment of normoglycemia, epineural arteriovenous shunting occurs leading to a ‘steal’ effect and endoneurial ischemia[15]. Subsequent acute endoneurial hypoxia may account for the deterioration of neuropathic symptoms. However, the definite etiology of neuropathic pain remains unknown.

Treatment is supportive and focuses on symptomatic care as the disorder is typically self-limited. Agents such as gabapentin, pregabalin, tricyclic antidepressants, phenytoin, carbamazepine, tramadol, topical capsaicin and clonidines have shown limited benefit in DNC[9,13]. Gamma-linolenic acid was shown to be effective for leg pain in one report[3]. Strict diabetic control with or without insulin is usually necessary. A recurrent form of DNC with an asymptomatic period of 7 years between two episodes was previously reported[5]. The prognosis is usually good and patients typically recover their baseline weight with resolution of the painful sensory symptoms and muscle weakness within 1 or 2 years[12]. Psychiatric consultation may be helpful for emotional support, and the selection of an appropriate agent for both mood stabilization and neuropathic pain control is important[16].

In summary, we report a middle aged Korean woman who was diagnosed with DNC. This is the first such
case in East Asia. Sudden weight loss reaching 17.5\% of the patient’s total body weight and intractable neuropathic pain improved spontaneously over several months. In contrast to other typical cases in patients with recently diagnosed diabetes, our patient had a long duration of diabetes and mild NPDR as a microvascular complication. As DNC is one of the rarest presentations of diabetic neuropathy and shows a rapid course with severe symptoms, clinicians must understand the natural course of this syndrome and offer multidisciplinary support while excluding other possible underlying causes.

**CONFLICTS OF INTEREST**

No potential conflict of interest relevant to this article was reported.

**REFERENCES**

1. Ellenberg M. Diabetic neuropathic cachexia. Diabetes 1974;23:418-23.
2. Naccache DD, Nseir WB, Herskovitz MZ, Khamaisi MH. Diabetic neuropathic cachexia: a case report. J Med Case Rep 2014;8:20.
3. Weintrob N, Josefberg Z, Galazer A, Vardi P, Karp M. Acute painful neuropathic cachexia in a young type 1 diabetic woman. A case report. Diabetes Care 1997;20:290-1.
4. Deorchis VS, Herskovitz S, Laureta E, Heptulla RA. Neuropathic cachexia associated with type 1 diabetes in an adolescent girl. Pediatr Neurol 2013;49:282-5.
5. Jackson CE, Barohn RJ. Diabetic neuropathic cachexia: report of a recurrent case. J Neurol Neurosurg Psychiatry 1998;64:785-7.
6. Chandler PT, Singh RS, Schwetschenau RP. Diabetic neuropathic cachexia. Acta Diabetol Lat 1978;15:212-6.
7. Blau RH. Diabetic neuropathic cachexia. Report of a woman with this syndrome and review of the literature. Arch Intern Med 1983;143:2011-2.
8. D’Costa DF, Price DE, Burden AC. Diabetic neuropathic cachexia associated with malabsorption. Diabet Med 1992;9:203-5.
9. Archer AG, Watkins PJ, Thomas PK, Sharma AK, Payan J. The natural history of acute painful neuropathy in diabetes mellitus. J Neurol Neurosurg Psychiatry 1983;46:491-9.
10. Godil A, Berrieman D, Knapij S, Norman M, Godil F, Firek AF. Diabetic neuropathic cachexia. West J Med 1996;165:382-5.
11. Neal JM. Diabetic neuropathic cachexia: a rare manifestation of diabetic neuropathy. South Med J 2009;102:327-9.
12. Grewal J, Bril V, Lewis GF, Perkins BA. Objective evidence for the reversibility of nerve injury in diabetic neuropathic cachexia. Diabetes Care 2006;29:473-4.
13. Yuen KC, Day JL, Flanagan DW, Rayman G. Diabetic neuropathic cachexia and acute bilateral cataract formation following rapid glycaemic control in a newly diagnosed type 1 diabetic patient. Diabet Med 2001;18:854-7.
14. Kihara M, Zollman PJ, Smithson IL, Lagerlund TD, Low PA. Hypoxic effect of exogenous insulin on normal and diabetic peripheral nerve. Am J Physiol 1994;266:E980-5.
15. Tesfaye S, Malik R, Harris N, Jakubowski JJ, Mody C, Rennie IG, Ward JD. Arterio-venous shunting and proliferating new vessels in acute painful neuropathy of rapid glycaemic control (insulin neuritis). Diabetologia 1996;39:329-35.
16. Jain R, Jain S, Raison CL, Malevic T. Painful diabetic neuropathy is more than pain alone: examining the role of anxiety and depression as mediators and complicators. Curr Diab Rep 2011;11:275-84.