

A Case of Insulin Induced Peripheral Neuropathy

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Case Report

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Abstract

A 24-year-old man with type 1 diabetes, presented with neuropathic pain and severe postural hypotension, was diagnosed with insulin-induced peripheral neuropathy which mimicking diabetic peripheral neuropathy following a rapid improvement in glycaemic control. HbA1c was reduced from 17.5% to 7.4 % within two months. A decrease in insulin dosage with a relaxing glycaemic target improved his condition. In conclusion, clinicians should have a high index of suspicion of this condition in a patient presenting with neuropathic pain and autonomic dysfunction following rigorous glycaemic control.

Introduction

Insulin-induced peripheral neuropathy, also known as treatment-induced diabetic neuropathy (TIDN), is an uncommon treatment-induced neuropathic pain and/or autonomic dysfunction that occurs in diabetic patients after a rapid improvement in glycaemic control.⁽¹⁾⁽²⁾⁽³⁾ TIDN is often mistaken for diabetic neuropathic pain as it is more common than TIDN and their clinical features are almost similar. To date, there is no guideline on management of TIDN, and only a few case reports have been published. We report a patient who has developed TIDN after a rapid improvement in glycaemic control. He developed severe neuropathic pain and autonomic dysfunction manifesting as severe postural hypotension resulting in postural giddiness and unsteady gait.

Case Report

A 24-year-old man, with underlying type 1 diabetes diagnosed in 2018, developed diabetic ketoacidosis (DKA) with an HbA1C of 17.5% on admission. Following rigorous treatment for DKA, he was discharged with both short-acting (Actrapid® 14 units TDS) and long-acting (Insulatard® 18 units ON) subcutaneous insulin injection.

One month later, he began to experience pain in his feet that affected his daily activities and sleep. The pain was described as persistent pricking in nature with a pain score of 9 out of 10. It originated from the toes and radiated to the medial side of thigh regions. He also developed a few episodes of postural giddiness which led to unsteady gait. Besides that, he also had a loss of appetite and significant weight loss about 15kg over two months, that led to a drop in his BMI to 17.6 kg/m². However, unlike in diabetic neuropathy cachexic, his mood was not affected.

The physical examination revealed a significant drop in blood pressure from sitting to standing. His blood pressure was 141/110 mmHg lying and 113/67 mmHg standing. Heart rate was 140 beats per minute when lying, but it dropped to 92 beats per minute when standing. His neurological examination of bilateral lower limb showed that hyporeflexia for ankle reflex and hyperesthesia in dermatome L2 and below with absence of proprioception of big toes for bilateral lower limbs. Other neurological and organ system examination were normal.

Short synacthen test showed an adequate response, excluding the diagnosis of adrenal insufficiency. The thyroid function test, folate and vitamin B12 were within the normal range. Chest x-ray finding was unremarkable. Nerve conduction test indicated that length-dependent sensorimotor axonal polyneuropathy, which is most likely due to the underlying diabetes mellitus. With that, the patient was initially diagnosed with diabetic neuropathy and started on tablet gabapentin and mecabalamin. Fludrocortisone 0.1 mg OD was also prescribed for postural hypotension.

His neuropathic pain initially improved with gabapentin; however, the pain subsequently became worse despite the high dosage of gabapentin given. The pain was so severe that he had difficulty to bear weight or walk. The postural giddiness also persisted despite taking Fludrocortisone 0.1 mg OD. In the meantime, we noticed that his HbA1C reduced from 17.5–7.4% over the past two months. Coupling the rapid reduction in HbA1c with his clinical presentations of pain and autonomic dysfunction that were not improving with the treatment plan for diabetic neuropathy, the diagnosis of TIDN was made.

Considering TIDN as the diagnosis, the patient's insulin dosage was reduced with a relaxing glycaemic target. As for postural hypotension, fludrocortisone was increased to 0.2 mg. Two weeks after the adjustment of medications, his condition improved tremendously. He had fewer episodes of postural giddiness. The pain was very much reduced and he could bear weight and walk. His latest sitting blood pressure was 130/92 mmHg with a sitting heart rate of 110 beats per minute, and the standing blood pressure was 120/87 mmHg with a standing heart rate of 130 beats per minute. His medication was then maintained with subcutaneous Actrapid® 6 units TDS, Insulatard® 6 unit ON, Tablet mecabalamin 500mcg TDS, Capsule pregabalin 75 mg BD and Fludrocortisone 0.2mg OD.

Discussion

Herein we present a case of a 24-year-old man with type 1 diabetes who developed TIDN after rigorous glycaemic control manifesting severe neuropathic pain, and postural hypotension due to autonomic dysfunction. TIDN is an uncommon iatrogenic micro-neuropathy caused by an abrupt correction in HbA1c in the setting of a long duration of hyperglycaemia. ⁽¹⁾⁽²⁾⁽³⁾ Compared to diabetic peripheral neuropathy, TIDN is more severe in terms of neuropathic pain. The onset of duration is acute and commonly happens within eight weeks of glycaemic changes. ⁽¹⁾ The patients will usually experience pain at the distal part of the limbs.

Gibbons and Freeman have proposed a set of diagnostic criteria for TIDN which includes: (i) acute onset of neuropathic pain or autonomic symptoms, (ii) a drop in HbA1c level of over 2% in 3 months, and (iii) onset of neuropathic pain and or autonomic symptoms within eight weeks of the reduction in the HbA1c level. ⁽¹⁾ This patient meets the three above proposed diagnostic criteria.

Some case reports reported that⁽⁴⁾⁽⁵⁾ stopping insulin for a few weeks might seem to be the best way of reducing the neuropathic pain. However, this does not apply to this patient as he has type 1 diabetes, where continuation of insulin therapy is mandatory for his condition to prevent severe complication like

DKA, and oral hypoglycaemia agents are not the best treatment choice. Considering all the above, a decision was made to reduce his total daily insulin level and the glycaemic target was relaxed for the treatment of TIDN.

Possible differential diagnosis pertaining to this case is the diabetic neuropathy cachexia. It is characterized by profound weight loss, autonomic dysfunction, peripheral neuropathic pain and mood instability.⁽⁶⁾ However, it is more commonly diagnosed in elderly and unrelated to the antidiabetic medications.

Conclusion

Insulin-induced peripheral neuropathy or TIDN is a rare condition. It is often misdiagnosed as other types of neuropathy as many physicians may not be aware of this condition. Possible diagnosis of TIDN must be kept in mind when treating patients who are receiving a high dose of antidiabetic agents, presented with severe neuropathic pain with or without autonomic dysfunction. This may be prevented by administering less aggressive therapy for sugar control.

Declarations

Acknowledgement

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Author Disclosure

All author declared no conflict of interest.

References

1. Gibbons CH. Treatment induced neuropathy of diabetes. Auton Neurosci Basic Clin [Internet]. 2020;226(March):102668. Available from: <https://doi.org/10.1016/j.autneu.2020.102668>
2. Gibbons CH. Treatment-Induced Neuropathy of Diabetes. Vol. 17, Current Diabetes Reports. 2017. p. 127.
3. Gibbons CH, Freeman R. Treatment-induced neuropathy of diabetes: An acute, iatrogenic complication of diabetes. Brain. 2015;138(1):43–52.
4. Cuenca Hernández R, Segura Galindo A, Martínez Acebes E. Insulin neuritis or treatment-induced diabetic neuropathy of diabetes. Neurologia. 2018;33(9):616–8.
5. Ergun B. Insulin neuropathy: Rare adverse effect of insulin therapy. Bangladesh J Med Sci. 2016;15(2):303–4.
6. Naccache DD, Nseir WB, Herskovitz MZ, Khamaisi MH. Diabetic neuropathic cachexia: A case report. J Med Case Rep. 2014;8(1):1–5.