

Recurrent Nocturnal Hypoglycemia in a Patient with Type 1 Diabetes Mellitus

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CASE

A 39-year-old man with type 1 diabetes mellitus (DM) was admitted with diabetic ketoacidosis precipitated by an upper respiratory tract infection. His admitting biochemistry showed venous plasma glucose concentration of 933 mg/dL (51.8 mmol/L) [reference: 72–140 mg/dL (4.0–7.8 mmol/L)], bicarbonate of 14.7 mmol/L (22–31 mmol/L), β -hydroxybutyrate of >6 mmol/L (<0.6 mmol/L), and arterial pH of 7.28 (7.35–7.45). He was treated with intravenous hydration and intravenous insulin infusion, and made a rapid recovery.

The patient had been diagnosed with type 1 DM at the age of 33 years when he presented with diabetic ketoacidosis. Glutamic acid decarboxylase antibody was increased at the time of diagnosis [10.6 U/mL (reference: <1 U/mL)] and postprandial C-peptide concentrations were undetectable. His subsequent glycemic control was poor [glycated hemoglobin (Hb A_{1c}) ranged from 8.9% to 15.6%], which resulted in peripheral and autonomic neuropathy manifesting as painful sensory neuropathy and erectile dysfunction, respectively. His other medical history included mitral valve prolapse, hypertension, and dyslipidemia. He was prescribed a basal-bolus insulin regimen consisting of twice-daily insulin detemir (10 U before breakfast and 7 U before dinner) and insulin aspart (5 U before breakfast, 3 U before lunch, and 4 U before dinner), simvastatin, sildenafil, pregabalin, and omeprazole. He was not prescribed sulfonylurea and denied alcohol consumption.

After resolution of diabetic ketoacidosis, the patient was restarted on his preadmission basal-bolus insulin regimen. His insulin regimen was titrated during this hospital admission, and he had wide fluctuations in blood glucose and recurrent nocturnal hypoglycemia. Typically, there was severe hyperglycemia during daytime [capillary glucose: 205–553 mg/dL (11.4–30.7 mmol/L)], particularly after meals, and symptomatic hypoglycemia that consistently occurred between 2400 and 0230 daily [capillary glucose: 34–58 mg/dL (1.9–3.2 mmol/L)], accompanied by symptoms of adrenergic response such as diaphoresis, palpitations, and anxiety.

Physical examination revealed stable vital signs and low body mass index (16.4 kg/m²). There was no abnormal hyperpigmentation typical of Addison's disease. The thyroid gland was not enlarged, and he was clinically euthyroid. Cardiovascular and respiratory

examinations were unremarkable. There was mild lipohypertrophy at the insulin injection sites.

Other relevant serum biochemistry results were albumin 4.0 g/dL (3.8–4.8 g/dL), aspartate aminotransferase 10 U/L (14–50 U/L), alanine aminotransferase 10 U/L (10–55 U/L), γ -glutamyl transferase 30 U/L (10–70 U/L), and creatinine 0.6 mg/dL (53 μ mol/L) [0.7–1.4 mg/dL (65–125 μ mol/L)]. Insulin and C-peptide concentrations measured at the time of 1 of the hypoglycemic episodes (venous glucose: 2.8 mmol/L) during this admission were 83.6 mU/L (0.0–25.0 mU/L) and 36 pmol/L (364–1655 pmol/L), respectively. He was biochemically euthyroid.

Questions to Consider

- What are the etiologies of recurrent hypoglycemia in patients on insulin therapy?
- What is the suggested approach to recurrent hypoglycemia?
- Can insulin antibodies cause hypoglycemia?

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the October 2014 issue of *Clinical Chemistry*. To view the case and comments online, go to <http://www.clinchem.org/content/vol60/issue10> and follow the link to the Clinical Case Study and Commentaries.

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