

## OBSERVATIONS

## Liraglutide Treatment in a Patient With HIV and Uncontrolled Insulin-Treated Type 2 Diabetes

Combination antiretroviral therapy has improved survival in human immunodeficiency virus (HIV)-infected patients but has become associated with altered body fat distribution, type 2 diabetes, and increased cardiovascular risk (1). Both the protease inhibitors and nucleotide reverse transcriptase inhibitors have been implicated (1). Management of HIV-associated type 2 diabetes may be challenging because of severe insulin resistance, which—in spite of the initial use of insulin sensitizers—often requires a high dose of insulin, causing additional weight gain (1). The glucagon-like peptide-1 receptor agonists lower glucose, reduce weight, and improve the cardiovascular risk profile in type 2 diabetes (2,3). Recently, exenatide use in an HIV-associated type 2 diabetic case and in a type 1 diabetic HIV patient was reported (4,5). Here, we report the first successful liraglutide use in an HIV patient with type 2 diabetes.

A 57-year-old man regularly visited the outpatient clinic since 2003 because of an HIV infection, which was diagnosed in 1995. Initial treatment consisted of zidovudine, then dual-therapy zidovudine and zalcitabine. From 1997–2003 he received zidovudine and lamivudine, then triple-therapy with efavirenz, didanosine, and lamivudine, which was discontinued because of dizziness, rash, and depression. Then, atazanavir, tenofovir, and lamivudine were given. In 2005, because of a progressive abdominal distention, the protease inhibitor atazanavir was replaced by raltegravir, an integrase inhibitor with a better metabolic profile.

In 2005, at a weight of 105 kg, compatible with a 15-kg weight gain in 2 years, type 2 diabetes was diagnosed. After lifestyle consultation, metformin (1,000 mg b.i.d.) was initiated. Since A1C rose to 8.8%, NPH insulin was started (November 2007). Body weight increased by 5 kg in 6 months with little glycemic improvement. Insulin treatment was replaced by glimepiride (up to 6 mg q.i.d.), but A1C remained 8.3%. He could be persuaded to start insulin glargine (September 2010), titrated to 60 U/day, while glimepiride was discontinued. Unfortunately, weight increased by 7 kg in 6 months without glycemic improvement. In May 2011, at a weight of 116 kg (BMI 35.1 kg/m<sup>2</sup>) and A1C 8.1%, off-label liraglutide was initiated at 0.6 mg/day, and uptitrated to 1.8 mg/day. He consulted a dietitian and diabetes educator and was advised to lower daily insulin dose by 10 U when self-monitored blood glucose was <5 mmol/L. After 3 weeks of liraglutide therapy, body weight dropped to 110 kg, insulin dose was reduced to 30 U/day, and discontinued altogether after 6 weeks. Fasting glucose decreased from 12.3 to 7.0 mmol/L. The patient reported no side-effects or hypoglycemia, rather less fatigue and overall improved quality of life. Self-monitored blood glucose varied between 5.6–8.3 mmol/L, HIV-RNA remained undetectable. Four months after liraglutide initiation, A1C decreased to 6.8% and body weight to 102 kg, but body weight rose slightly to 108 kg at 7 months, while A1C remained 6.8%. Previously elevated liver enzymes normalized while his lipid profile improved significantly (total cholesterol from 5.6 to 4.9 mmol/L, HDL cholesterol from 0.79 to 1.0 mmol/L, triglycerides from 6.6 to 3.1 mmol/L). This case illustrates that glucagon-like peptide-1 receptor agonists, possibly by improving weight control, body fat distribution, and cardiovascular markers (3), may be a valuable tool in the treatment of HIV-associated type 2 diabetes, which is characterized by central obesity, lipodystrophy, and insulin resistance.

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M.D. advised regarding the therapy and the clinical data to be collected and wrote the manuscript. M.v.A. is the treating physician of the patient described in this case report, performed the practical collection of the clinical data, edited the manuscript, and contributed to discussion.

The patient described in this case-report has given written informed consent to publish his case anonymously.

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