OBSERVATIONS

New-Onset Saquinavir-Induced Diabetes

Saquinavir is an antiviral agent FDA-approved for the treatment of HIV. It inhibits HIV protease, a crucial enzyme for the HIV life cycle that cleaves viral polypeptides into essential proteins. When used in combination with nucleoside analog reverse-transcriptase inhibitors, protease inhibitors are highly effective in reducing HIV viral loads (1,2). In general, saquinavir is safe and well tolerated. Long-term exposure to protease inhibitors is associated with moderate hyperglycemia and insulin resistance in a minority of patients (3). We here report saquinavir as a causing agent of acutely developed extreme hyperglycemia in an HIV patient.

A 35-year-old HIV-infected male originating from Ghana presented with a hyperosmolar, hyperglycemic syndrome (glucose 48 mmol/L). He had been diagnosed with HIV-1 infection 2 years previously, with tenofovir, lamivudine, and saquinavir as initial combination antiretroviral therapy. He also suffered from decompensated liver cirrhosis with hepatitis B infection (Child-Pugh C). Previous glucose levels were normal, and HbA_{1c} had not been measured before. At presentation, he used emtricitabine/tenofovir and saquinavir as combination antiretroviral therapy. He was not lipodystrophic, and there was no ketoacidosis. Signs of an acute infection were absent, and HIV viral load was 123 copies/mL (low, but not undetectable). The saquinavir concentration was 0.9 mg/L (4–5 times above the therapeutic range). Levels of HbA_{1c} and C-peptide were 15.2% and 740 pmol/L, respectively. He was treated with insulin, and saquinavir was replaced by raltegravir to reduce pill burden. At discharge, the patient used insulin aspart 20 units t.i.d. and insulin glargine 24 units once daily. One week after the saquinavir replacement, the patient discontinued his insulin therapy because he suffered from symptoms of hypoglycemia, which disappeared after cessation of insulin therapy. Glucose concentrations then varied between 4.7 and 7.0 mmol/L, HbA_{1c} had decreased from 15.2 to 8.3%, and C-peptide was 2,700 pmol/L in this normoglycemic situation. His viral load was undetectable.

In summary, we report an insulin-treated new-onset diabetes that recovered completely within 1 week after switching from saquinavir to raltegravir. The temporal relation of the development of diabetes during saquinavir therapy and the complete and prompt recovery after cessation thereof implicates saquinavir as the cause. The C-peptide level of 740 pmol/L in the hyperglycemic condition was relatively low and could suggest a diminished insulin production, while the subsequent level of 2,700 pmol/L in the later normoglycemic condition reflects a considerable insulin production. The duration of the evident hyperglycemia, which had developed while the patient used saquinavir, could not be determined retrospectively. The rapid recovery after cessation suggests a rather acute effect of saquinavir on the hyperglycemia. The elevated saquinavir concentration may have arisen as a consequence of deranged hepatic function since saquinavir is metabolized in the liver and adequate dosing is difficult. Most probably, the clinical diabetes emerged by the increasing insulin resistance and inhibition of insulin secretion by saquinavir (4,5) due to its diminished clearance and increased plasma levels. Caution and monitoring should be exercised when prescribing saquinavir in patients at high risk of developing diabetes and with liver dysfunction.

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