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Case Reports

Quetiapine-Induced Hyperglycemic Crisis and Severe Hyperlipidemia: A Case Report and Review of the Literature

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Introduction

Quetiapine, dispensed as *Seroquel*, has become 1 of the 100 most commonly prescribed medications in the United States in the past 10 years.[1] It has fewer extrapyramidal side effects than first-generation antipsychotics, but it has been associated with low to moderate weight gain, hyperlipidemia/hypercholesterolemia, and new-onset diabetes, with half of these cases manifesting as diabetic ketoacidosis (DKA).[2–7] We present a case of a middle-aged man who developed diabetes mellitus (DM) manifesting as hyperglycemic crisis and severe reversible hyperlipidemia. Literature on antipsychotic-associated metabolic adverse effects and clinical recommendations is presented.

Case Report

Mr. H, a 39-year-old man with bipolar I disorder and hyperlipidemia, was brought to the emergency department after being found minimally responsive at his apartment. He was noted to be acidotic and severely hyperglycemic, with a pH of 7.24, a serum glucose level of 1966 mg/dL, an anion gap of 22 ($[Na^+]$ level of 125 mEq/L, $[Cl^-]$ level of 79 mEq/L, and a [bicarbonate] level of 24 mEq/L), and a significant ketonuria. Serum osmolality was 399 mOsm/kg. Medical complications at the time of admission included hypercarbia and hypoxia (requiring intubation), electrolyte abnormalities, prerenal azotemia, and a triglyceride level of 2942 mg/dL. He reportedly had been drinking increasing amounts of sweetened beverages in the weeks before admission, including fruit juices, sports drinks, and soda. His body mass index on admission was 38.7 (130 kg). Pertinent admission medications included 700 mg of quetiapine, 2500 mg of valproic acid, and 0.5 mg of lorazepam (all administered before bedtime). He had no history of glucose intolerance but did have a family history of diet-controlled diabetes in his father. Before admission, he had attended weekly appointments with his outpatient psychiatrist, and no metabolic implicative signs or symptoms (such as polyuria/polydipsia or eruptive xanthomas) had been noted.

Mr. H was stabilized medically, and his condition improved steadily. A lipid panel obtained on the second day of admission showed a cholesterol level of 365 mg/dL, triglycerides level of 1918 mg/dL, and high-density lipoprotein level of 16 mg/dL. His hemoglobin A1c was 14.2. Treatment with quetiapine was stopped because of metabolic concerns and medication with 15 mg of aripiprazole daily was started; no change was made to his valproic acid regimen. Treatment with 600 mg of gemfibrozil given twice a day was

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begun for hyperlipidemia, and administration of insulin was continued to maintain glycemic control. He was discharged after 13 days in the hospital. At outpatient follow-up, 1 week after discharge, his daily insulin dosage was decreased and his cholesterol and triglyceride levels were within the normal range.

Mr. H's last hospitalization had been 16 months earlier for acute mania in the setting of medication noncompliance. During that admission, his nightly quetiapine dosage of 150 mg was increased to a nightly 800 mg dosage. At that time, his blood glucose levels were within the normal range, whereas lipids levels were elevated, with a cholesterol level of 225 mg/dL, a triglyceride level of 764 mg/dL, a high-density lipoprotein level of 43 mg/dL, and a low-density lipoprotein level of 120 mg/dL. He had been taking 800 mg of quetiapine before bedtime for 8 days before the aforementioned lipid panel was drawn. His body mass index at that time was 35.8 (120 kg). There was no evidence that laboratory metabolic monitoring was performed in the intervening 16 months between Mr. H's hospitalizations nor were medications given to lower his lipid or cholesterol levels.

Discussion

Quetiapine is an atypical antipsychotic originally approved in the United States in 1997 for the treatment of schizophrenia and currently also approved by the Food and Drug Administration for the treatment of bipolar disorder and major depressive disorder; its off-label uses include generalized anxiety disorder, dementia, obsessive-compulsive disorder, and psychosis in patients with Parkinson disease.[8] Quetiapine, and atypical antipsychotics as a class, has better side-effect profiles than typical antipsychotics do and is thus much more widely prescribed. However, metabolic complications are more common with atypical antipsychotics; these typically include hyperglycemia, weight gain, hypertriglyceridemia, elevated low-density lipoprotein level, and decreased high-density lipoprotein level.[2,4] Hypertension is another metabolic risk factor, although it is not typically mentioned secondary to atypical antipsychotics.[9] These metabolic complications can be used to diagnose metabolic syndromes when 3 or more risk factors are present, with clinical significance attributed to its causal relationship with heart disease, diabetes, and stroke.[9] There are 2 case reports of rapid simultaneous development of hypertriglyceridemia and DM due to quetiapine usage.[4,6,10] Aripiprazole and ziprasidone appear to have less metabolic risk than the other atypical antipsychotics do.[5]

Our case features a young white man who developed progressive hypertriglyceridemia and new-onset DM discovered during hospitalization for hyperglycemic emergency in the setting of high-dose quetiapine augmentation of valproic acid for the treatment of bipolar I disorder. In the 16 months that Mr. H was taking 700-800 mg of quetiapine nightly, he gained 10 kg and his triglyceride level increased from 764 mg/dL to 2942 mg/dL. His initial triglyceride level of 764 mg/dL suggests he was already developing metabolic complications from quetiapine at the time of the dose increase.

Quetiapine usage commonly results in dyslipidemia, with increased levels of triglycerides, low-density lipoprotein, and total cholesterol and decreased high-density lipoprotein level.[4] Severe hypertriglyceridemia (>600 mg/dL) has been associated with quetiapine usage, with new-onset diabetes developing in some of these patients as well.[5,6] The etiology of this severe hypertriglyceridemia is unclear.[6] The highest level of triglycerides reported was 9450 mg/dL in a patient who was taking both quetiapine and olanzapine.[11] There have also been several incidences of acute pancreatitis resulting from the extreme triglyceride level induced by quetiapine.[4,6] Our case shows that the dyslipidemia that occurs with quetiapine usage is progressive. Mr. H's triglyceride level increased from 764 mg/dL to 2942 mg/dL in the 16 months while he was taking high dose quetiapine. His triglyceride level decreased to 1918 mg/dL after initiation of insulin therapy. In this same time interval, he also gained 10 kg and became diabetic (hemoglobin A1c of 14.2), which suggests development of more global metabolic complications that likely exacerbated his dyslipidemia.

The proper characterization of Mr. H's hyperglycemic emergency is not known with absolute clarity. DKA and hyperglycemic hyperosmolar state (HHS) are nondistinct and both may result from atypical antipsychotic usage.[5] In fact, patients presenting with hyperglycemic crisis have features of both in more than 30% of cases.[12] DKA is defined by the clinical triad of hyperglycemia (>250 mg/dL), ketonemia, and metabolic acidosis and usually occurs with type 1 DM; meanwhile, HHS has more severe hyperglycemia (blood glucose level at an average of