Case Report

Quetiapine-induced Diabetic Ketoacidosis

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ABSTRACT

Psychomotor retardation and extrapyramidal symptoms have limited the conventional antipsychotic use. Atypical antipsychotics though widely prescribed with good tolerability and efficacy, the metabolic complications associated with them are of clinical importance. Diabetic ketoacidosis (DKA) is a fatal complication of atypical antipsychotic use. We report a case of new-onset diabetes presenting as DKA with quetiapine use.

Key words: Diabetic ketoacidosis, new-onset diabetes mellitus, quetiapine

INTRODUCTION

During the past 20 years, several case reports have emerged in the literature associating the onset of diabetes mellitus with the use of new atypical antipsychotic medications. The occurrence of diabetic ketoacidosis (DKA) raises concern over the possible causal mechanisms on its pathophysiology. We report the case of a patient with bipolar depression who developed new-onset diabetes mellitus and associated ketoacidosis several months after starting quetiapine.

CASE REPORT

A 40-year-old woman on treatment for bipolar depression attended the psychiatry outpatient department on May 10, 2014. She complained of excessive tiredness for the past few days and was admitted for evaluation in view of her multiple admissions in the past. She was afebrile with normal vitals and Glasgow Coma Scale of 15. Her psychiatric history revealed bipolar depression for the past 5 years with an episode of depression in 2013. She was on tablet quetiapine 400 mg and tablet valproate 500 mg for July 15, 2013. There was no medical history of diabetes in her or her first-degree relatives. Ten months after the initiation of medication, her weight was 231 lbs (105 kg) with body mass index of 40.92 kg/m² (height 5 feet 3 inches) indicating class III obesity.

Laboratory investigations revealed an elevated random blood sugar (RBS) value of 443 mg/dl. Urine acetone was positive (+++). Arterial blood gas analysis revealed pH 7.1 and bicarbonate 10.54 mEq/L (normal 22–26 mEq/L) and PaCO₂ 30 (normal 35–45) revealing a picture of uncompensated metabolic acidosis. Next day fasting lipid profile was done which showed...
Diagnosis of DKA was made. After consultation with the physician, the patient was aggressively managed with 10 units regular insulin as bolus injection followed by 15 units plain insulin in 500 ml of 0.9% saline given as intravenous infusion at the rate of 15 drops per minute. She was also given intensive fluid management with normal saline and dextrose normal saline. When her blood glucose became 261 mg/dl, the insulin infusion was stopped, and plain insulin 8 units was given eighth hourly subcutaneously. Her fasting and postprandial blood sugars remained high on the consecutive days, and the insulin therapy was stepped up to 14 units in morning, 14 units in afternoon and 10 units at night (14-14-10) on May 17, 2014. Tablet atorvastatin 20 mg once daily was initiated in view of her deranged lipid profile. The dose of quetiapine was stepped down (18th - 300 mg, 20th - 250 mg, and 21st - 100 mg) and stopped on May 22, 2014. The RBS values on 22nd and 23rd were 76 and 90 mg%, respectively, and the patient was discharged with tablet amisulpride 200 mg twice daily and tablet metformin 1000 mg once daily.

DISCUSSION

The acceptance of atypical antipsychotics ever since they have marketed in terms of improvement in the positive and negative symptoms of schizophrenia is remarkable. The lower propensity to cause extrapyramidal symptoms has earned them the preferred drug status among the prescribers than the conventional antipsychotics. However, the increasing evidence of metabolic derangement caused by them during the postmarketing surveillance has raised several areas of concern. Limitations in the medical service to the chronic mentally ill patients make the impact of these derangements on subsequent morbidity and quality of life profound. Younger age group, female gender, and less overweight before the antipsychotic treatment have been identified as risk factors in DKA cohorts. Antipsychotics implicated in DKA are clozapine, olanzapine, risperidone, aripiprazole, and quetiapine with the most common association being for clozapine and olanzapine. DKA is a medical emergency with considerable mortality and morbidity. It is typically characterized by hyperglycemia over 250 mg/dL, a bicarbonate level <18 mEq/L, and a pH <7.30, with ketonemia and ketonuria. While definitions vary, moderate DKA can be categorized by a pH between 7.0 and 7.24 and a serum bicarbonate level of 10–<15 mEq/L. This patient was suffering from moderate DKA. Despite the aggressive management, the glycemic control was poor as the drug was only tapered initially. The temporal relation between the onset of diabetes and ketoacidosis in a previously nondiabetic patient who showed poor glycemic control until the drug was stopped is indicative of drug-induced DKA. Causality assessment using Naranjo algorithm showed a score of 6 indicating a “probable” relation of quetiapine with her DKA. The World Health Organization-Uppsala Monitoring Centre causality assessment revealed that DKA was “probable/likely” due to quetiapine intake. Severity assessment using the modified Hartwig and Siegel scale showed that it was of level 5 severe adverse drug reaction and was life-threatening in terms of seriousness.

Although antipsychotic-associated DKA is uncommon, hyperglycemia associated with these medications is commonplace. The first report of quetiapine-induced DKA was published in 1999 by Sobel et al. The occurrence of DKA in patients with new-onset type 2 diabetes has led to main theories. Insulin resistance is commonly cited as the mechanism for hyperglycemia, a theory supported by the efficacy of insulin-sensitizing medications in reported cases. However, insulin resistance associated with weight gain cannot explain the frequent occurrence DKA. The proposed mechanisms are decrease in insulin output, toxic effect on pancreatic islet cells, sympathetic nervous system dysregulation, or physiologic effect of serotonin antagonism on the beta cells. The administration of an atypical antipsychotic has been identified as metabolic stressor which can trigger the onset of DKA in patients. Clinical trials with quetiapine have reported increased levels of triglycerides, low-density lipoprotein, and total cholesterol and decrease in high-density lipoprotein cholesterol as common adverse effects (more than in 10%).

CONCLUSION

The psychiatrist should be vigilant concerning the possible diabetogenic effect of quetiapine, and the patients should be meticulously screened for new-onset diabetes. DKA due to atypical antipsychotics should be managed aggressively with concomitant withdrawal of the suspected drug.

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Conflicts of interest
There are no conflicts of interest.

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