

## CASE REPORT

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# Elevated Lipase and Diabetic Ketoacidosis Associated with Aripiprazole

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### ABSTRACT

**Context** Atypical antipsychotic agents are associated with diabetes mellitus and pancreatitis. Aripiprazole, a new antipsychotic, has never been implicated to cause either diabetes mellitus or pancreatitis. We present a patient who developed diabetes mellitus after being started on aripiprazole.

**Case report:** A 33 year-old male with schizophrenia presented with fatigue, dyspepsia and epigastric pain. Patient was found to have hyperglycemia, diabetic ketoacidosis, and hyperlipasemia. Imaging studies of the pancreas were normal. Patient was started on aripiprazole treatment 18 months prior to this episode and had experienced progressive weight gain since then. Work up for other causes of pancreatitis was negative.

**Conclusions** Diabetes mellitus in this patient was probably a complication of aripiprazole due to progressive weight gain. In the absence of radiologic evidence of pancreatitis, hyperlipasemia was probably secondary to diabetic ketoacidosis. Possible causes of hyperlipasemia and its significance in diabetic ketoacidosis are discussed.

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### INTRODUCTION

Aripiprazole is a relatively new antipsychotic drug approved to treat schizophrenia and

considered to have the least side effects among all the atypical antipsychotics [1, 2]. Other atypical antipsychotic agents including clozapine, olanzapine, quetiapine, risperidone, and ziprasidone are associated with diabetes, neuroleptic malignant syndrome, pancreatitis and weight gain [3]. We present a patient who had diabetic ketoacidosis and elevated lipase with aripiprazole.

### CASE REPORT

A 33-year-old African American male with schizophrenia presented to the Emergency Department with complains of fatigue, dyspepsia and epigastric abdominal pain. At presentation his body mass index (BMI) was 41 kg/m<sup>2</sup> (reference range: 18.5-24.9 kg/m<sup>2</sup>) and he had a blood glucose of 1,769 mg/dL (reference range: 70-105 mg/dL), anion gap of 32 mmol/L (reference range: 8-16 mmol/L), serum osmolality 373 mOsm/kg (reference range: 275-300 mOsm/kg), CO<sub>2</sub> 6 mmol/L (reference range: 18-29 mmol/L), amylase 182 IU/L (reference range: 20-125 IU/L), lipase 4,068 IU/L (reference range: 8-78 IU/L), serum triglycerides 184 mg/dL (reference range: 40-150 mg/dL), calcium 8.5 mg/dL (reference range: 8.9-10 mg/dL). Thyroid function tests were normal. No prior history of diabetes mellitus, pancreatitis, cholelithiasis or substance abuse was obtained. Family history for diabetes mellitus was negative. Treatment with aripiprazole (Abilify<sup>®</sup>) was initiated 18 months ago prior to admission. Since that time, the patient had

experienced progressive weight gain. His BMI was 32 kg/m<sup>2</sup> prior to starting the medication. Computerized tomography (CT) and ultrasound of the abdomen were negative for pancreatitis and gallstones. Patient was treated with intravenous fluids and insulin. Aripiprazole was discontinued. Patient was discharged home on haloperidol and insulin glargine. Diagnosis was diabetes induced by aripiprazole and elevated lipase secondary to diabetic ketoacidosis. After 6 months off of aripiprazole his BMI decreased to 33 kg/m<sup>2</sup>. Although he continued to be a diabetic, his insulin requirements came down.

## DISCUSSION

The pathophysiology of new onset diabetes in atypical antipsychotic drug use is not clear. A possible mechanism is insulin resistance due to weight gain induced by these drugs [3]. The patient presented above had been gaining weight ever since aripiprazole therapy was initiated, which may explain his new onset diabetes mellitus and diabetic ketoacidosis. Incidence of diabetes mellitus is lowest with aripiprazole, when compared to other antipsychotics [1, 2, 4]. Timing of onset of diabetes mellitus may vary from a few days up to 4 years [4]. Metabolic complications with atypical antipsychotics have commonly been reported in African American patients and often presentation is with diabetic ketoacidosis, as in our patient [4, 5, 6, 7, 8]. We know of no studies that confirm this association. Slightly elevated amylase and grossly elevated lipase in our patient could indicate pancreatitis, but negative imaging studies of the pancreas weigh against this diagnosis. It has been proposed that amylase and lipase levels are elevated in 16-25% of patients with diabetic ketoacidosis, especially lipase. Elevated lipase in diabetic ketoacidosis is not a reliable indicator of pancreatitis in the presence of normal imaging studies of the pancreas [9, 10]. There is a direct correlation between the lipase level and the serum osmolality in diabetic ketoacidosis [9], as in this patient. There is no clear explanation for the hyperlipasemia in diabetic ketoacidosis.

Possible mechanisms involved include decreased excretion of lipase due to a lower glomerular filtration rate in diabetic ketoacidosis [11]. Non pancreatic lipolytic enzymes produced by stomach, liver, small intestine, or esophagus might be released into circulation causing a elevated lipase level [12]. We conclude that aripiprazole might induce diabetes mellitus by causing weight gain and it would be prudent to constantly monitor patients weight and blood sugars as long as the patient is on this drug. Hyperlipasemia in this patient was due to diabetic ketoacidosis and not secondary to aripiprazole. In the absence of any structural abnormalities of the pancreas, elevated lipase is a non-specific indicator of pancreatitis in diabetic ketoacidosis.

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**Keywords** aripiprazole; Diabetic Ketoacidosis; Lipase; Pancreatitis

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