

# Olanzapine-Induced Hypertriglyceridemia Resulting in Necrotizing Pancreatitis

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## ABSTRACT

Olanzapine is an atypical antipsychotic agent that was approved by the Food and Drug Administration in 1996 for treatment of psychotic disorders, bipolar disorder, and schizophrenia. Since that time, numerous case reports have been published that describe the association of olanzapine and the development of pancreatitis. Furthermore, 3 reports suggest the mechanism of olanzapine-induced hypertriglyceridemia as the etiology of this progression. We report a case of a 36-year-old man who developed necrotizing pancreatitis secondary to olanzapine-induced hypertriglyceridemia. This case, to our knowledge, is the most severe case of this progression and the first case requiring plasmapheresis for acute management.

## INTRODUCTION

Olanzapine (Eli Lilly, Indianapolis, IN) is an atypical antipsychotic agent in the thienobenzodiazepine class that was approved by the Food and Drug Administration in 1996 for treatment of psychotic disorders, bipolar disorder, and schizophrenia. It was modeled after a precursor agent, clozapine, which was found to be associated with acute pancreatitis in 1992.<sup>1</sup> Since that time, numerous case reports have been published with the association of olanzapine and pancreatitis, with the first report of this association published in 2000.<sup>2-4</sup> To our knowledge, 3 of these reports have discussed the mechanism of olanzapine-induced hypertriglyceridemia as the etiology of this progression.<sup>2-3,5</sup>

## CASE REPORT

A 36-year-old man with a significant past medical history of bipolar disorder, previous alcohol abuse, hypertension, recent onset diabetes, and hyperlipidemia presented to an outside hospital with a week-long history of left upper quadrant and epigastric pain. The patient reported consumption of his last alcoholic beverage 2 years prior to admission. Labs on admission to the outside hospital were significant for a lipase level of 1322 U/L, a glucose level of 290 mg/dL with a hemoglobin A1c of 11.4%, and a triglyceride level of 5185 mg/dL with a total cholesterol of 677 mg/dL and an high-density lipoprotein (HDL) of 16 mg/dL. On exam, the patient was morbidly obese, with a body mass index (BMI) of 40 kg/m<sup>2</sup>, tachycardic, and febrile to 102.1°F. Prior abdominal/pelvic computed tomography with contrast had demonstrated findings consistent with underlying acute pancreatitis, no findings of necrotizing or hemorrhagic pancreatitis, and a normal-appearing gallbladder with no signs of cholelithiasis. The patient was diagnosed with acute pancreatitis secondary to hypertriglyceridemia and required plasmapheresis for acute management. Plasmapheresis was not available at the outside facility, so the patient was transferred to our center for treatment.

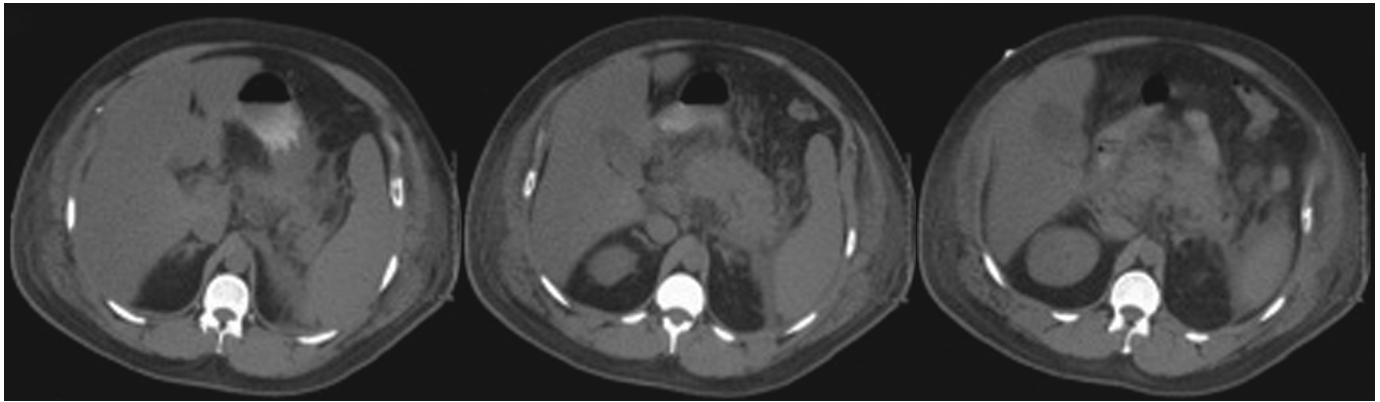
Six weeks prior to admission, the patient began a new medication regimen for his bipolar disorder, consisting of sertraline 200 mg every day, buspirone 15 mg 3 times a day, and olanzapine 20 mg at bedtime. The patient had a history of mild hypertriglyceridemia and was compliant with fibrate therapy. His last lipid panel was performed

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**Figure 1.** Abdominal/pelvic computed tomography without contrast demonstrated extensive acute pancreatitis with suspicion of necrotizing pancreatitis.

5 years prior to admission. Three weeks prior to admission, the patient was diagnosed with diabetes mellitus Type II and was started on metformin.

While in the hospital, the patient required plasmapheresis twice. His triglyceride level trended downward from 5185 mg/dL on admission to 195 mg/dL by discharge on hospital day 15. His olanzapine was stopped on hospital day 3 because of its association with pancreatitis. He resumed oral food intake on hospital day 4, but became symptomatic again on hospital day 7, and a nasojejunal feeding tube was placed. Abdominal/pelvic computed tomography without contrast demonstrated extensive acute pancreatitis with suspicion of necrotizing pancreatitis (Figure 1). His lipid panel normalized by hospital day 8, and he was discharged on hospital day 16 to a skilled nursing facility on clonazepam for his bipolar disorder. Following his discharge, the patient continued to recover and was eventually discharged home and established care with a psychiatrist for medication management.

## DISCUSSION

The most common causes of acute pancreatitis include biliary tract disease, alcohol, trauma, and drugs. When a patient presents with the signs and symptoms of acute pancreatitis, it is imperative to take a careful history to search for causative etiologies not only with prescription medications but also with herbal medications and supplements. The differential diagnosis for acute pancreatitis is broad and includes lung etiologies, gallbladder etiologies, and occult malignancies. About 1% of new-onset diabetes cases in adults are related to an occult pancreatic malignancy.<sup>6</sup> With this patient's presentation of new onset diabetes and acute pancreatitis, consideration of a possibly neoplasm is warranted.

Olanzapine has been known to cause fatigue, dry mouth, restlessness, and numerous gastrointestinal complaints.<sup>7</sup> Additionally, there have been numerous studies linking

this atypical antipsychotic to the predisposition of hyperglycemia leading to the development of diabetes mellitus, hypertriglyceridemia, and metabolic syndrome.<sup>8,9</sup> The exact mechanism of action of olanzapine leading to these reported side effects is not certain; however, many hypotheses exist. One potential hypothesis is olanzapine's potential effect on adipocyte function promoting fat deposition and a possible role of leptin leading to weight gain.<sup>10-12</sup> Additionally, olanzapine may directly increase triglyceride levels with or without weight gain,<sup>6</sup> or may potentially alter appetite-signaling leading to hyperphagia, resulting in weight gain.<sup>13</sup> Furthermore, olanzapine may lead to the development of insulin resistance from a high-residual carbohydrate load due to preferential metabolism of fat.<sup>10</sup> Finally, olanzapine may inhibit M<sub>3</sub> muscarinic receptors leading to altered pancreatic insulin secretion.<sup>11</sup>

A handful of prior case studies have reported olanzapine causing hypertriglyceridemia leading to acute pancreatitis<sup>2,4-5</sup>; however, to our knowledge, our patient is the first in the literature to require plasmapheresis. Suggested guidelines for the use of plasmapheresis to treat hypertriglyceridemia include determining whether the patient has a serum triglyceride level >1000 mg/dL plus lipase >3 times the upper limit of normal AND signs of hypocalcemia, lactic acidosis, or signs of worsening inflammation or organ dysfunction and whether there are contraindications to apheresis.<sup>14</sup>

An association has been made between patients with a preexisting diagnosis of hypertriglyceridemia and their development of worsening lipid levels after the initiation of olanzapine therapy.<sup>15</sup> This relationship should be taken into consideration when determining if a patient is a good candidate for olanzapine therapy, and all patients should have a screening lipid panel before beginning their therapy. Further investigation is needed into the mechanism of action resulting in the metabolic changes with the use of atypical antipsychotic agents.

## DISCLOSURES

Author contributions: SM Buszek researched the case and wrote the manuscript. P. Roy-Chaudhury and G. Yadlapalli edited and supervised the manuscript. G. Yadlapalli is the article guarantor.

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