

Gluteal muscle damage and rhabdomyolysis after olanzapine poisoning: a case report

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Abstract

Olanzapine is a widely adopted atypical antipsychotic medication used to manage schizophrenia. Reports show that the incidence rate of adverse reactions to olanzapine is significantly lower than those of other classic antipsychotic medications. However, olanzapine overdose may be associated with severe consequences. Herein, we report a 21-year-old female patient who had taken nearly 700 mg (70 tablets) of olanzapine; she was found after 30 hours. As her condition progressed, she presented with rhabdomyolysis, swelling in the thighs and hips, paralytic ileus, digestive tract hemorrhage, and elevated serum amylase and lipase levels; notably, she recovered after treatment. This intractable case is of great clinical significance and suggests that early-phase hemoperfusion plays a critical role in olanzapine poisoning-related rhabdomyolysis.

Keywords

Olanzapine, rhabdomyolysis, neuroleptic malignant syndrome, hemoperfusion, case report, muscle damage

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Introduction

Currently, olanzapine is widely used worldwide as an atypical antipsychotic medication to manage schizophrenia, bipolar mania and depression, and other mental illnesses.¹ It was first marketed in 1996 in the United States.² Compared with other first-line, second-generation medications, olanzapine shows superior effectiveness and is associated with a lower rate of extrapyramidal side effects.³ Some of the known side effects of olanzapine include weight gain, sedation, anticholinergic effects, metabolic dysfunction (such as lipid abnormalities and hyperglycemia), extrapyramidal side effects, orthostatic hypotension, bradycardia, tachycardia, and agranulocytosis.³⁻⁵ Although well-documented reports of poisoning-related rhabdomyolysis exist, olanzapine-induced rhabdomyolysis is rare. In the present study, we report a 21-year-old female patient who attempted suicide by an oral overdose of olanzapine. Consequently, she developed rhabdomyolysis, swelling in the thighs and hips, digestive tract hemorrhage, paralytic ileus, and elevated serum amylase and lipase levels. This patient exhibited a typical case of neuroleptic malignant syndrome (NMS). To the best of our knowledge, there are few reports on the concurrence of these adverse events caused by olanzapine overdose. There are multiple other case reports on olanzapine-induced NMS, but this condition remains sufficiently uncommon to warrant further reports.

Case presentation

An unconscious 21-year-old female patient with no previous medical condition was admitted to a local hospital 30 hours after taking nearly 70 olanzapine tablets (drug specification: 10 mg/tablet, Chinese Medicine Approval: H20010799, Jiangsu Hansoh Pharmaceutical Group Co. Ltd.,

Lianyungang, China). The patient was unconscious and exhibited tachycardia. Esmolol, naloxone, and pantoprazole were administered. Gastric lavage was not performed because the patient was unconscious. She was transferred to our department approximately 9 hours later.

Upon admission, her vital signs were as follows: temperature 37.6°C, heart rate 140 beats/minute, respiratory rate 23 breaths/minute, blood pressure 135/118 mmHg, and oxygen saturation, 98%. The patient exhibited somnolence, limb weakness, grade 4 myodynamia of the upper limbs, and grade 2 myodynamia of the lower limbs. Pressure sores (stage 1) were found on her right lateral femur skin (10 × 10 cm). Her other main physical examinations were normal. The laboratory test results were as follows: arterial blood gas analysis: pH 7.4, partial carbon dioxide pressure 29 mmHg, partial oxygen pressure 101 mmHg, lactic acid 1.2 mmol/L, base excess -6.8 mmol/L, white blood cell (WBC) count $9.52 \times 10^9/L$ (reference value $3.5-9.5 \times 10^9/L$), neutrophil ratio 84.5%, alanine transaminase 66 IU/L, aspartate aminotransferase 362 IU/L, total bilirubin 21 μmol/L, creatine kinase (CK) 18,279 IU/L, CK-MB 98.8 ng/mL (reference value 0.3-4 ng/mL), lactate dehydrogenase 1515 IU/L, myoglobin (MYO) 3413 ng/mL, urea 5.1 mmol/L, creatinine 92 μmol/L, potassium 4.5 mmol/L, serum amylase 795 IU/L, lipase 255 IU/L, D-dimer 2.13 μg/mL (reference value <0.50 μg/mL), and fibrin degradation product 7.87 μg/mL. An electrocardiogram revealed sinus tachycardia. Olanzapine-related NMS was diagnosed, and the treatment included nutritional support and daily administration of medications including lansoprazole (30 mg twice a day), reduced glutathione (2.4 g), alanyl-glutamine (10 g/50 mL), flucloxacillin (1.0 g every 6 hours), and torasemide (20 mg twice a day). To eliminate the drug in the gastrointestinal tract, Smecta (Ipsen (Tianjin)

Pharmaceutical Co., Ltd., Tianjin, China) and activated charcoal (Chinese Medicine Approval: H13022797, Hebei Changtian Pharmaceutical Group Co., Ltd., Baoding, China) with mannitol were administered through a stomach tube. Hemoperfusion (Adsorba 300c, Gambro, Sweden, 2 hours/treatment) was administered. Nursing care was increased, and the patient was assisted in changing position every 2 hours. The first hemoperfusion treatment was completed nearly 5 hours after the patient was admitted; her urine volume was 450 mL. When her MYO, CK, and CK-MB levels were reassessed, values of 1847 ng/mL, 13,027 IU/L, and 52.5 ng/mL, respectively, were observed.

At approximately 17 hours after admission, a second hemoperfusion treatment was performed. The MYO, CK, and CK-MB results after hemoperfusion were 1079.1 ng/mL, 9994 IU/L, and 24.1 ng/mL, respectively. During the first 24 hours, the patient's urine volume was 3250 mL. On the third day after admission, 12 hours after the third hemoperfusion treatment, the patient was conscious and felt pain in the bilateral thighs and hips; the pain in the left hip was obvious. A physical examination revealed the following: a bulging abdomen, no hyperactive bowel sounds, no tenderness or rebound pain, significant improvement of the muscle strength of the limbs, swelling in the left hip and upper thigh, and no redness or ulceration. The repeated and expanded laboratory test results were as follows: CK 17,521 IU/L and MYO 1387.1 ng/mL. The patient's hemoglobin (91 g/L) level had significantly decreased, and no hematemesis or melena were observed. Anemia and paralytic ileus were considered.

On the fourth day, the swelling and pain in the hips and thighs increased. A physical examination showed that the end diameters of the patient's left and right thighs were 58 cm and 54 cm, respectively. Her skin temperature was normal. A bedside

ultrasound examination revealed severe gluteal muscle damage and no arteriovenous thrombosis of the lower limbs. A computed tomography (CT) scan revealed a dilated intestinal canal, multiple gas–fluid levels in the intestines, and a normal pancreas. Multiple, patchy, low-density lesions and subcutaneous soft tissue swelling were found in both hips; the swelling in the left hip and thigh muscles was obvious (Figure 1). Gluteal compartment syndrome was suspected. Fortunately, the patient did not develop sciatic nerve dysfunction. The final hemoperfusion treatment was then administered. As the disease progressed, the swelling and pain gradually decreased, and gluteal compartment syndrome did not develop.

On the seventh day, the patient appeared pale and experienced general fatigue and lassitude. She defecated a large amount of dry black stool. An abdominal examination showed active borborygmus with no tenderness and rebound pain. Moderate anemia (hemoglobin 65 g/L) and fecal occult blood were observed. Gastrointestinal bleeding was considered. In addition to transfusion of packed red blood cells, esomeprazole, octreotide, and hemostatic drugs were given. Subsequently, the patient defecated black stool, which gradually faded to a yellow color.

On the sixteenth day, the pain and particularly the hip swelling were relieved. The other physical examination results were normal. The laboratory test results were as follows: hemoglobin 89 g/L, MYO 11.6 ng/mL, CK 157 IU/L, and fecal occult blood was negative. Gastroscopy revealed non-atrophic gastritis. According to the CT results, the severity of swelling in the patient's left hip and thigh muscle was significantly reduced. One week later, her hemoglobin level increased to 107 g/L, and the other laboratory results showed no obvious abnormality. Therefore, the patient

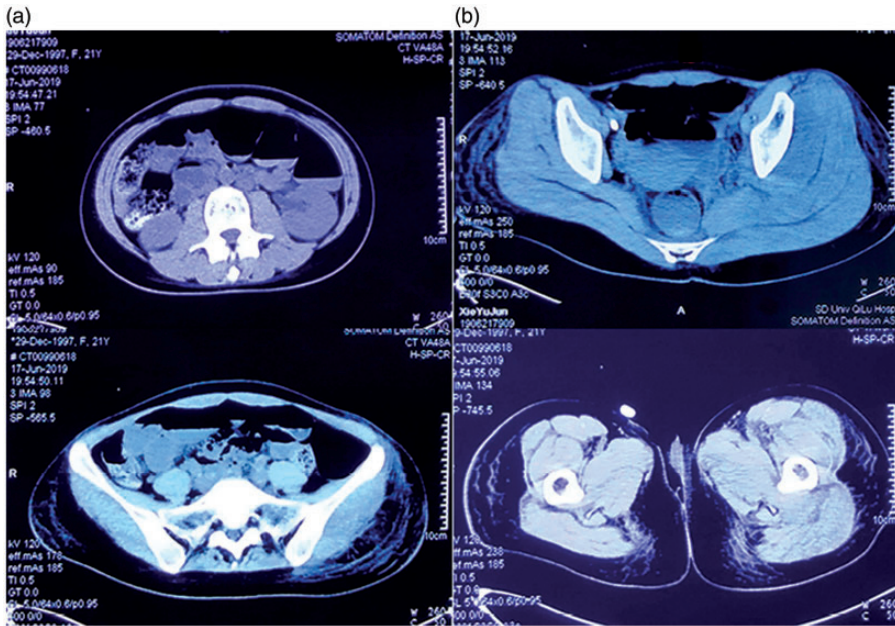


Figure 1. Computed tomography scan showing a dilated intestinal canal and multiple gas-fluid levels in the intestines. (a) Multiple, patchy, low-density lesions and subcutaneous soft tissue swelling of both hips are visible. (b) The left hip and thigh muscles exhibited obvious swelling.

was discharged and had no obvious abnormality during follow-up.

The serum olanzapine level at approximately 31 hours post-ingestion was 4.2 µg/mL (Toxicology labs of Beijing 307 Hospital, Military Medical Sciences, China).

Discussion

Rhabdomyolysis is a prevalent syndrome that poses a potential threat to humans. It is characterized by the breakdown of skeletal muscle and leakage of intracellular substances such as MYO and CK into the circulation.⁶ Laboratory diagnosis of rhabdomyolysis is based on the measurement of biomarkers of muscle injury, particularly in patients with non-traumatic rhabdomyolysis.⁷ Although unclear, the mechanism of olanzapine-related rhabdomyolysis is potentially linked to potent antagonism of serotonin (5-HT_{2A/2B/2C}), dopamine D₂,

histamine H₁, and α₁ adrenergic receptors.⁸ Histamines may promote sodium flux into cells, consequently depleting intracellular adenosine triphosphate (ATP) via the activation of energy-dependent Na⁺/K⁺-ATPase.⁹ The antagonistic activity at 5-HT_{2A} receptors can block glucose uptake by skeletal muscles and increase their permeability to CK. Therefore, 5-HT has potential toxicity to skeletal muscles, increasing their permeability to CK.¹⁰ Acute kidney injury is the main complication that dramatically worsens the prognosis of rhabdomyolysis.¹¹

Drug-induced akinesia can potentially cause pressure ulcers.¹² Somnolence is the predominant adverse effect of olanzapine. In general, the daily dose of olanzapine for patients is 5 to 20 mg per day, and some evidence supports a dose up to 40 mg/day.¹³ Our patient experienced olanzapine-induced unconsciousness for

more than 30 hours after taking a dose of nearly 700 mg. On admission, the patient's CK and MYO levels were 18,279 IU/L and 3413 ng/mL, respectively, and she was diagnosed with rhabdomyolysis. In addition to drug-induced muscle damage, akinesia was another pathogenic effect of rhabdomyolysis in this case. The patient's weight and duration of compression are crucial factors for muscle damage and rhabdomyolysis.

A Naranjo score of 6 suggests that the probable cause of rhabdomyolysis is olanzapine overdose.¹⁴ In our patient, NMS appeared to be one possible diagnosis. NMS is an unpredictable iatrogenic neurologic emergency condition that can arise following the administration of potent psychotropic agents,¹⁵ resulting in increased CK and MYO levels. The predominant clinical manifestations that our patient presented with on admission were drowsiness, excessive fatigue, fever, tachycardia, tachypnea, and elevated blood pressure. Laboratory tests on admission showed the main abnormalities to be significantly elevated CK and MYO levels and a mildly elevated WBC count. We determined that NMS was an additional factor contributing to the patient's rhabdomyolysis.

As the condition progressed, the patient's CK level again increased significantly, her hips and thighs became swollen, and severe gluteal muscle damage was found on ultrasound and CT examinations. The patient was not overweight, and her position was changed every 2 hours to prevent compression. However, muscle damage occurred in the hips. Previously, Panagiotopoulos et al.¹⁶ reported a case of drug-induced gluteal compartment syndrome and sustained immobilization because of unconsciousness induced by a drug overdose. In the present case, we deduced that the muscles were more prone to compression-related damage caused by olanzapine overdose.

Olanzapine may also induce rare adverse events, such as leukopenia⁵ and acute pancreatitis. Ustohal et al.¹⁷ reported a young female patient with severely high serum amylase and lipase levels after olanzapine treatment; she did not present with clinical symptoms of pancreatitis. In our case, we also found elevated serum amylase and lipase levels, but the patient was asymptomatic, and a diagnosis of pancreatitis was excluded. The cholinergic, serotonergic, and 5-HT₃ gastrointestinal receptors were inhibited by olanzapine, which promoted gastrointestinal hypomotility, and this may be the main mechanism of olanzapine-induced paralytic ileus.^{18,19} Paralytic ileus includes the classical symptoms of alimentary tract hemorrhage and causes anemia in the early phase. Initially, we considered anemia to be related to olanzapine poisoning until the patient's bowel sounds became hyperactive and melena was passed.

Hemodialysis is an effective treatment approach for rhabdomyolysis. Jarczak et al.²⁰ found that the systemic MYO and CK levels were decreased by 32% during continuous veno-venous hemodiafiltration. In this patient, the initial hemoperfusion reduced the MYO and CK levels from 3413 IU/L to 1847 IU/L and 18,279 IU/L to 13,027 IU/L, respectively, after 2 hours of treatment. Hemoperfusion could have also eliminated the drug from the body. The alimentary tract hemorrhage could potentially be associated with the use of heparin for hemoperfusion.

In conclusion, the main side effects of olanzapine overdose are sedative and anticholinergic effects. Sedation-induced coma causes long-term compression of muscle tissues, which results in a high risk of muscle tissue injury and the occurrence of rhabdomyolysis. Hemoperfusion may be the preferred treatment option for early-stage toxin-induced rhabdomyolysis.

Ethics statement

The reporting of this study conforms to the CARE guidelines.²¹ Ethics approval was obtained from the Qilu Hospital Ethics Committee for Human Research. Written informed consent was obtained from the patient for publication of the case details and accompanying images.


Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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