



## Şizofrenik Bir Erişkinde Olanzapine Bağlı Rabdomiyoliz: Olgu Sunumu Olanzapine Induced Rhabdomyolysis in A Schizophrenic Adult: Case Report

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### Öz

Rabdomiyoliz iskelet kasının akut nekrozu ve hücre içeriğinin dolaşıma geçmesi ile karakterize bir sendromdur. Travma, egzersiz, enfeksiyonlar ve bazı metabolik hastalıklara bağlı ortaya çıkabildiği gibi çeşitli ilaç kullanımlarına sekonder de görülebilen bir durumdur. Bilinen 2 aydır şizofreni tanısı olan 34 yaşındaki erkek hasta acil servisimize intihar amaçlı toplamda 35 tane 10 mg Olanzapin alımı nedeniyle yakınları tarafından getirilmiş. Yapılan değerlendirilmesinde ekstrapiramidal sistemde patolojik bulguları olan ve laboratuvar tetkiklerinde kreatin kinaz (CK) düzeyi 42670 U/L (referans aralığı 30-200 U/L) saptanan hasta olanzapin kullanımına sekonder rabdomiyoliz nedeniyle servisimize interne edildi. Yattığı süre içerisinde sadece medikal tedaviyle CK düzeyi normale dönen ve böbrek ve karaciğer fonksiyon bozukluğu gelişmeyen hasta psikiyatri poliklinik kontrolü önerilerek taburcu edildi. Rabdomiyoliz antipsikotik ilaçlara karşı nadir ve potansiyel olarak ciddi bir advers ilaç reaksiyonudur. Vakamızda olduğu gibi yüksek doz atipik antipsikotik ilaç alımından sonra hastalar mutlaka rabdomiyoliz ve buna bağlı akut böbrek hasarı gibi ciddi komplikasyonlar açısından takip edilmelidir.

**Anahtar Kelimeler:** Olanzapin, Rabdomiyoliz, İntihar

### Abstract

Rhabdomyolysis is a syndrome characterized by acute necrosis of skeletal muscle and subsequent release of its cellular contents into the circulation. It can occur due to trauma, exercise, infections and some metabolic diseases, as well as secondary to the use of various drugs. A 34-year-old male patient with a diagnosis of schizophrenia for 2 months was brought to our emergency department by his relatives because of the intake of 10 mg of olanzapine (35 pieces) for suicide. The patient whose pathological findings in the extrapyramidal system were present and whose creatine kinase (CK) was found to be 42670 U / L (reference range 30-200 U/L) in laboratory tests was hospitalized to our service because of the secondary rhabdomyolysis for the use of olanzapine. During the hospitalization period, only the medical treatment returned normalcy to the CK level, and the kidney and liver dysfunction did not develop, and the patient was discharged by psychiatric outpatient clinic control. Rhabdomyolysis is a rare and potentially serious adverse drug reaction to antipsychotic drugs. The patients should be evaluated for side effects and in terms of rhabdomyolysis facilitating factors. Especially in high doses, patients should be monitored for rhabdomyolysis, which is a serious complication, such as acute renal damage.

**Keywords:** Olanzapine, Rhabdomyolysis, Suicide

### INTRODUCTION

Rhabdomyolysis is a syndrome characterized by acute necrosis of the skeletal muscle and ingress of cell contents into the circulation. The etiology of rhabdomyolysis includes trauma, exercise, infections, some metabolic and genetic diseases, and various medications (1). There is the triad of myalgia, weakness, and dark-colored urine in most patients (1). Diagnosis is made by elevated creatine kinase (CK) level and urine and serum myoglobin level (1). While rhabdomyolysis may

be asymptomatic in many patients, it may cause serious problems such as severe kidney failure in some cases (2). The new generation of olanzapine, used in the treatment of schizophrenia, in the thienobenzodiazepine group is a broad-spectrum antipsychotic with minimal side effects (3). In our case, we presented the patient who used olanzapine for suicide and developed rhabdomyolysis afterwards.

### CASE REPORT

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A 34-year-old male patient with known schizophrenia for 2 months presented to the emergency yard due to the intake of 10 mg of olanzapine (35 pieces) for suicide purposes. On physical examination, the patient's general condition was good and conscious. There was no pathology in head and neck examination. There was no scleral icterus, conjunctiva appears normal; there was no lymphadenopathy; thyroid gland neither was palpable with nor had sign of nodularity; there was not pretibial edema. No pathological sound was heard in the lung examination and there was not blunting of costophrenic angle; S1-S2 were rhythmic and no pathological sound was on cardiovascular system examination. There was mild tenderness on abdominal examination. Extrapyramidal system findings were present in the neurological examination. Arterial blood pressure was 116/68 mmHg, pulse rate was 86bpm, and body temperature was 36.3 C. Electrocardiography was normal sinus rhythm and there was no ischemia sign. There was not trauma, fever, confusion, heavy exercise, surgery, immobilization, electric shock, heat stroke, and alcohol consumption in his medical history. There was only a recent known diagnosis of schizophrenia and use of olanzapine 10 mg. He was married with one child and he was an artisan. He had an 8 packs/year smoking history. CK: 42670 U / L (reference range 30-200 U/l), creatine kinase myocardial band: 12,5 ng / ml, pH: 7,28, partial pressure of oxygen: 70 mmHg, partial pressure of carbon dioxide: 30,7 mmHg, saturation: 95%, 4, lactate: 1,60 mmol / L, lactate dehydrogenase: 592 IU / L were detected in the laboratory tests, and other parameters were within normal limits. The patient was consulted with the clinic of psychiatric. No active suicidal ideation was detected in the patient. The patient was hospitalized in our internal medicine service with rhabdomyolysis associated with olanzapine. Intensive hydration and urinary alkalization therapy were started. The levels of enzyme and CK of the patient are summarized in Table 1. The

patient was discharged on the 9th day of hospitalization after his general condition has improved and muscle enzymes, liver and kidney function tests have returned to normal with only medical treatment. The patient was advised to attend control visits at psychiatric and internal medicine outpatient clinics.

## DISCUSSION

Rhabdomyolysis is a skeletal injury to the sarcophagus, resulting in the deterioration of sarcophagi integrity. Rhabdomyolysis, first described by Fleisher in 1881 as intense exercise after hemodilution, can be explained by traumatic or non-traumatic causes leading to clinical and laboratory findings of systemic circulation of intracellular components after injury of striated muscle cells (1). It may develop due to trauma, alcoholism, intoxications, coma, long term immobilization, excessive physical activity, epileptic seizures, hyperthermia, hypothermia, drug use, electrolyte imbalances, infections, some metabolic and genetic diseases (1,2,4). The frequency of etiologic causes varies among countries. Drug abuse comes first in developed countries, traumatic causes are more important in developing countries (4). For the diagnosis of rhabdomyolysis, the upper limit of the normal level of CK must be increased 10-fold and muscle findings should be present (4). In our case, CK level was measured to be 42670 IU / L, which accompanied intense muscle pain and weakness. This value was 213-fold higher than the upper limit.

Atypical antipsychotics used in the treatment of schizophrenia have less neurological side effects such as extrapyramidal symptoms, tardive dyskinesia, akathisia, acute dystonia, neuroleptic malignant syndrome, and tardive dyskinesia than typical antipsychotic drugs. For this reason, it has become the main treatment for schizophrenia treatment. However, several metabolic complications of atypical antipsychotics have been reported in recent years (5). Olanzapine is

an atypical antipsychotic having a different blocking mechanism for D2, 5-HT2 and muscarinic receptors (6). Metabolic side effects of olanzapine and clozapine from atypical antipsychotics have been reported to be greater than others (5,6). Rhabdomyolysis is a very rare and potentially serious adverse drug reaction to antipsychotic drugs (7). Psychiatric drugs likely to cause rhabdomyolysis include clozapine, loxapine, melperone, risperidone, olanzapine, and haloperidol. However, reports on metabolic complications are extremely rare for aripiprazole, amisulpride, risperidone and ziprasidone (5). It is not known exactly what mechanism rhabdomyolysis of olanzapine is caused, but it is thought that it may lead to this situation because it causes muscle hypermetabolism (6,7). The most feared complication of drug-induced rhabdomyolysis is acute renal failure. It is estimated that 10% to 40% of all rhabdomyolysis cases develop acute renal failure (2,8). Despite the high CK level in the present case, early diagnosis and treatment prevented the onset of acute renal failure in our patient. The rhabdomyolysis in our case was dramatically improved with the discontinuation of olanzapine treatment and the beginning of intensive hydration and supportive treatment. Literature suggests that most cases of secondary rhabdomyolysis for drug use are due to the chronic use of drugs (9). Interestingly, however, in our case, rhabdomyolysis developed at an early stage due to drug use. The treatment of rhabdomyolysis varies according to the patient's condition. In asymptomatic patients, withdrawal of the drug may be enough, but hospitalization and dialysis may be necessary in patients with severe enzyme elevation and metabolic disorders (10).

## CONCLUSION

In conclusion, the use of atypical antipsychotics such as olanzapine is common and caution should be exercised against potential side effects of olanzapine, which, although rare, can be fatal.

The patients should be evaluated for side effects and should be evaluated in terms of rhabdomyolysis facilitating factors. Patients receiving high doses of olanzapine should be followed up for rhabdomyolysis, a serious complication such as acute kidney injury.

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**Table 1.** The patient's enzyme and creatine kinase levels

|                     | CK<br>(RR: 30-200 U/l) | CKMB<br>(RR: 5-25 ng/ml) | Creatinine<br>(RR: 0.7- 1.4 mg/dl) | ALT<br>(RR: <31 IU/L) | AST<br>(RR: 5-34<br>IU/L)) | LDH (RR:125-220<br>IU/L) |
|---------------------|------------------------|--------------------------|------------------------------------|-----------------------|----------------------------|--------------------------|
| 1 <sup>st</sup> day | 42670                  | 12,5                     | 0,83                               | 14                    | 26                         | 592                      |
| 2 <sup>nd</sup> day | 38935                  | 2,2                      | 0,86                               | 12                    | 21                         | 332                      |
| 3 <sup>rd</sup> day | 17268                  | 2,1                      | 0,7                                | 25                    | 31                         | 295                      |
| 4 <sup>th</sup> day | 8378                   | 1,9                      | 0,68                               | 20                    | 24                         | 297                      |
| 5 <sup>th</sup> day | 4267                   | 1,1                      | 0,71                               | 19                    | 24                         | 297                      |
| 6 <sup>th</sup> day | 1992                   | 1,2                      | 0,68                               | 19                    | 23                         | 185                      |
| 7 <sup>th</sup> day | 1274                   | 1,4                      | 0,73                               | 16                    | 18                         | 176                      |
| 8 <sup>th</sup> day | 970                    | 1,5                      | 0,73                               | 29                    | 28                         | 96                       |
| 9 <sup>th</sup> day | 134                    | 1,2                      | 0,7                                | 22                    | 20                         | 75                       |

CK: Creatine Kinase; RR: Reference Range; CKMB: Creatine Kinase Myocardial Band; ALT: Alanineamino transferase; AST: Aspartateamino transaminase; LDH:Lactate dehydrogenase