

# Successful Switch to Olanzapine after Rhabdomyolysis Caused by Water Intoxication and Clozapine Use

## A Case Report

T. Tényi, V. Vörös

We report on a case of rhabdomyolysis induced by the correction of hyponatremia after psychogenic polydipsia and clozapine use, where the switch to a high dose of olanzapine resulted in the non-recurrence of rhabdomyolysis. The 46-year-old patient with the diagnosis of schizophrenia paranoid type, who had been on clozapine treatment for the previous 4 years, was admitted with the symptoms of generalized seizure and vomiting, and as severe hyponatremia was proved, its correction with the parallel use of clozapine treatment was done. CK concentrations increased to 48 120 U/L without any symptom of neuroleptic malignant syndrome. To prevent acute renal insufficiency, high-volume alkaline diuresis was initiated and clozapine was tapered and stopped. On the day 12 of treatment, olanzapine was started and was elevated to 30 mg/day. CK concentration began to fall returning to the normal concentration on day 20. Six months after the switch to olanzapine no recurrence of rhabdomyolysis was detected; clinical and laboratory findings were normal. We suggest that after a benzodiazepine-type antipsychotic-induced rhabdomyolysis, a switch to another atypical antipsychotic can be a cautious clinical strategy.

## Introduction

Rhabdomyolysis is a common and potentially lethal clinical syndrome that results from acute muscle fiber necrosis with leakage of muscle constituents into blood. Myoglobinuria is the most significant consequence leading to acute renal failure in 15–33% of patients with rhabdomyolysis [3]. Exogenous toxins were reported as the most common cause of rhabdomyolysis with illicit drugs, alcohol and prescribed drugs. Among medical drugs antipsychotics, statins, zidovudine, colchicine, selective serotonin reuptake inhibitors and lithium were the most frequently involved [3]. In a retrospective evaluation of 475 hospitalized patients, rhabdomyolysis was recurrent in 11% of all cases [3]. Although rhabdomyolysis is a part of neuroleptic malignant syndrome (NMS) which also includes pyrexia, muscle rigidity and mental disturbances, antipsychotic drugs may cause rhabdomyolysis, myoglobinuria and renal failure without overt signs of NMS [5]. A special clinical form was reported by Wicki and his colleagues in 1998, where rhabdomyolysis was related to rapid correction of hyponatremia attributable to compulsive drinking of water, pos-

sibly complicated by clozapine use [10]. Most recently a similar report was published in connection with ziprasidone use [11]. As CK (creatinine kinase) elevation [4] and rhabdomyolysis induced by olanzapine [1] were also published, we see it as important to report on a case of rhabdomyolysis induced by the correction of hyponatremia after psychogenic polydipsia and clozapine use, where the switch to a high dose of olanzapine resulted in the non-recurrence of rhabdomyolysis.

## Case Report

The 46-year-old patient with the diagnosis of schizophrenia paranoid type, who had been on clozapine treatment for the previous 4 years, was admitted to our department with symptoms of generalized seizure and vomiting. The patient was admitted from a hospital for chronic patients and his medication was 400 mg/day clozapine. Nurses reported that several days before admission the patient showed compulsive drinking. The physical examination revealed normal vital signs and no fever or skin lesions. He was oriented but had amnesia for the time of the convulsion, CT and EEG were negative, no epileptic activity was registered. Results of neurologic examination were normal. Initial laboratory investigations revealed severe hyponatremia (113 mEq/L), a moderately elevated creatinine kinase (CK) concentration of 1726 U/L with 3.1% MB fraction. Mild anemia (hemoglobin 11.1 g/dL) was observed. Hyperosmolar sodium solution was administered to the patient to compensate for the sodium deficit, the next day his sodium level was 140 mEq/L and the CK 1051 U/L. Clozapine treatment was continued and at the fifth day of his treatment he reported mild muscle pain and asthenia, the CK serum concentration increased to 48 120 U/L with 0.7% MB fraction. He had no fever, no evidence of dystonia, rigidity, or disturbance of sensorium, so NMS was excluded. Routine urinary tests were normal or negative. To prevent acute renal insufficiency, high-volume alkaline diuresis was initiated and sodium and potassium were given at normal concentrations. The CK concentration began to fall returning to a normal concentration of 191 U/L on day 20. CK was 23 510 U/L on day 6, 8107 U/L on day 7, and 1921 U/L on day 10. Clozapine was tapered and stopped on day 11. On day 12 olanzapine 10 mg/day was started and on day 13, it was elevated to 30 mg/day. On day 12 CK concentration was 909 U/L. Oliguria, renal failure or compartment syndrome did not complicate the clinical picture. The patient was discharged on day 35 with the CK concentration 105 U/L, the only abnormal laboratory value recorded at discharge was mild anaemia (11.6 g/dL). Six months after the switch to olanzapine no recurrence of rhabdomyolysis was detected, clinical and laboratory findings were normal (CK 108 U/L).

## Discussion

A number of atypical antipsychotics (clozapine, risperidone, olanzapine, sulpiride, quetiapine and ziprasidone) can cause rhabdomyolysis with an elevated CK concentration and with mild or severe clinical symptoms [1, 3, 5, 7–11]. Earlier with clozapine, a special clinical form of rhabdomyolysis was reported, where CK elevation was related to the correction of hyponatremia and to clozapine [10]. Most recently in connection with zi-

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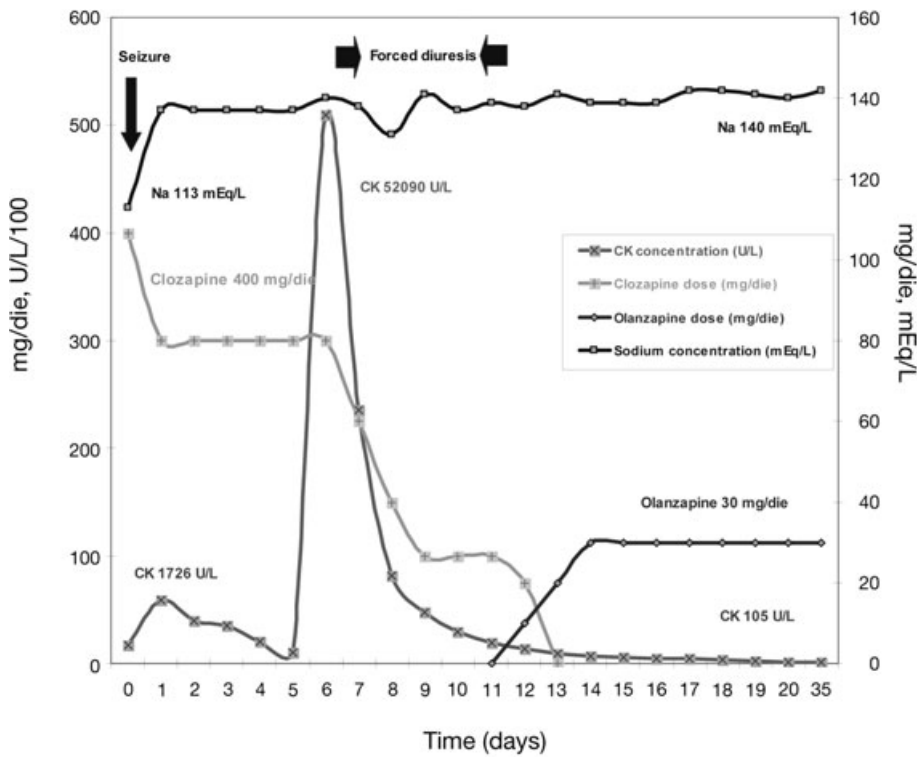


Fig. 1 The changes of the major laboratory values (plasma CK and sodium levels) and the therapeutic efforts (antipsychotic medication, forced diuresis) during hospitalisation.

prasadone, hyponatremia was found attributable to compulsive drinking of water [11]. The prevalence of psychogenic polydipsia is between 6.2 and 20% in the severely psychiatrically disabled population; severe hyponatremia develops in one-fourth of such patients [2,3]. With rapid correction of hyponatremia, severe neurologic complications including central pontine myelinolysis, cranial nerve palsies, coma and death may occur, but non-neurologic complications such as rhabdomyolysis have also been reported [6]. A possible explanation of cases complicated by clozapine and ziprasidone use, is that by increasing muscle cell permeability, clozapine and possibly other atypical antipsychotics may enhance the destruction of muscle cells [10,11]. It has been shown in rodents that 5-HT can be toxic to skeletal muscles [4] and that drugs with a relatively potent 5HT<sub>2A</sub> antagonism can cause muscle damage and rhabdomyolysis in some patients [1,5,11]. In our case the switch to olanzapine after a clozapine-induced rhabdomyolysis complicated by the rapid correction of hyponatremia resulted in the non-recurrence of rhabdomyolysis in a 6 months long follow-up. We point at the importance of CK monitoring beside benzodiazepine-type of atypical antipsychotic therapy when patients complain about muscular symptoms and we suggest that switch to an other atypical antipsychotic after an atypical antipsychotic-induced rhabdomyolysis can be a cautious clinical strategy.

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