Rhabdomyolysis from ziprasidone after attempted suicide

Ziprasidone, an atypical neuroleptic drug, has been repeatedly implicated in the pathogenesis of rhabdomyolysis (1,2,3). The following example suggests that high doses of ziprasidone may be myotoxic.

A 26-year-old HIV-negative caucasian male with a history of chronic paranoid schizophrenia was admitted to the intensive care unit after an attempted suicide by ingestion of stones and cutting the left-sided ankle arteries and a suspected generalised tonic-clonic seizure. He had been on long-term therapy with ziprasidone (160 mg/d) and lorazepam (3 mg/d) for 8 months, and chlorprothixen (50 mg/d) for 2 days. Seven weeks earlier he had been admitted after ingestion of 250 mg chlorprothixen in addition to ziprasidone, lorazepam and chlorprothixen (150 mg/d, altogether 400 mg/d), and a suspected generalised tonic-clonic seizure with severe lactacidosis of 39 mmol/l (*n*, <2.0 mmol/l), hypernatremia of 154 mmol/l (*n*, 136–145 mmol/l), and creatine-kinase (CK) elevation up to 617 U/l (*n*, <170 U/l). Since this event chlorprothixen had been discontinued until 2 days before admission.

On admission he was soporous, and presented with a conjugated bulbar deviation to the right and a negative oculo-cephalic reflex. There was a marked hyponatremia, slight hypokalemia, and a lactate of 3.8 mmol/l. Hyponatremia normalised within 1 day under forced correction. He had a slight normochromic and normocytic anaemia. Liver function parameters were normal on admission but increased slightly to maximal values 3 days later and then continuously decrease thereafter. CK was slightly elevated on admission and subsequently increased to a maximum of 29 733 U/l 3 days later. X-ray examination of the abdomen, carried out after emesis of three stones, revealed multiple foreign bodies with a diameter of 3–4 cm in the projection of the stomach (Fig. 1). On endoscopy, the foreign bodies turned out to be stones and were successfully removed from the stomach and larynx (Fig. 2). A CT scan of the brain showed a hypodense lesion in the right fronto-parietal region. Magnetic resonance imaging (MRI) of the cerebrum revealed various T2-hyperintense subcortical white matter lesions. Electroencephalography was normal. Shortly after admission, the patient required mechanical ventilation but could be successfully extubated 24 h later and then remained in good condition. Ziprasidone and chlorprothixen were discontinued. After transfer to the department of psychiatry 5 days later ziprasidone, chlorprothixen were restarted in the same dosage as before. CK normalised under ziprasidone and chlorprothixen 19 days after the attempted suicide.

While taking high-dose ziprasidone for paranoid schizophrenia, the patient had attempted suicide, experienced a questionable seizure, and sequentially developed severe hyponatremia and rhabdomyolysis. The cause of rhabdomyolysis remains speculative. Rhabdomyolysis could have been due to hyponatremia (4), the forced correction of hyponatremia (2), due to a toxic effect of ziprasidone, the combination of ziprasidone with chlorprothixen, psychosis (5), a tonic-clonic seizure triggered by ziprasidone-induced hyponatremia, from immobilisation during sleep, or an undetected neuromuscular disorder. An argument against hyponatremia is that there was a slight hyper-CK-emia also on his admission 7 weeks earlier, at that time associated with hypernatremia. Arguments against the seizure are that there was no urinary incontinence or tongue biting, that he did not complain about sore muscles, muscle

https://doi.org/10.1111/j.1601-5215.2009.00381.x Published online by Cambridge University Press

aching or myalgia after awaking from sleep, that the individual and family history was negative for epilepsy, that the encephalogram was normal, and that the maximal muscle enzyme elevation occurred not earlier than 4 days after the event. A psychiatric stupor was excluded by the history and the intact personality constitution after awaking and since his treating psychiatrist described him as stable and without productive symptomatology at the last follow-up 2 days prior to admission. An argument against forced normalisation is that serum CK-levels during such a procedure usually reach values lower than those observed in the presented patient (2). A primary myopathy was largely excluded upon the negative family history, normal clinical neurologic examination at follow-up, normal electromyography and normal muscle enzymes. There was also no evidence for muscle trauma, infection, immunological disorder, stiffness, swelling or signs of a malignant neuroleptic syndrome.

Rhabdomyolysis and hyponatremia in the described patient were most likely due to the high dosage of ziprasidone or the combination of both neuroleptics. The pathogenesis could have started with ziprasidone-induced hyponatremia, which resulted in hyper-CK-emia and a seizure. The seizure could have enhanced hyper-CK-emia, induced by the direct muscle toxic effect of one or both neuroleptics. In fact, well-known side-effects of ziprasidone, which could explain the findings, are tonic-clonic seizures and elevated liver function parameters. Only in single cases ziprasidone triggered the development of a malignant neuroleptic syndrome (3). Also other neuroleptics have been reported to cause rhabdomyolysis. Whether elevated liver function parameters were due to the neuroleptics or due to a primary hepatopathy remains speculative.

This case shows that ziprasidone may induce hyponatremia and rhabdomyolysis. Although a causative role of ziprasidone remains speculative, it should not be underestimated and assessed thoroughly. Hyponatremia and rhabdomyolysis can resolve promptly upon immediate withdrawal of the drug.

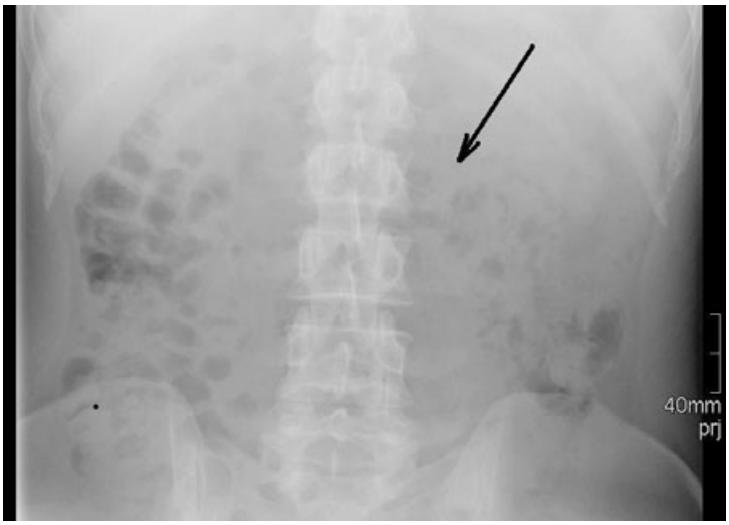

Fig. 1. X-ray of the abdomen prior to endoscopy shows a number of foreign bodies within the stomach, representing stones ingested during an attempted.

Fig. 2. Stones endoscopically removed from the stomach and the larynx in the described patient.

https://doi.org/10.1111/j.1601-5215.2009.00381.x Published online by Cambridge University Press

Josef Finsterer[1], Thomas Pulgram[2], Barbara Enzelsberger[3], Günther Mölzer[4]

[1]Krankenanstalt Rudolfstiftung, Vienna, Austria; [2]4th Medical Department, Krankenanstalt Rudolfstiftung, Vienna, Austria; [3]Second Medical Department, Krankenanstalt Rudolfstiftung, Vienna, Austria; and [4]Department of Radiology, Krankenanstalt Rudolfstiftung, Vienna, Austria

Dr Josef Finsterer
Postfach 20 1180 Vienna, Austria, Europe
Tel: +43-1-71165;
Fax: +43-1-4781711;
E-mail: fifigs1@yahoo.de

Acta Neuropsychiatrica 2009: 3:152–155

References

1. Akkaya C, Sarandol A, Sivrioglu EY, Kotan Z, Kirli S. A patient using ziprasidone with polydipsia, seizure, hyponatremia and rhabdomyolysis. Prog Neuropsychopharmacol Biol Psychiatry 2006;**30**:1535–1538.
2. Zaidi AN. Rhabdomyolysis after correction of hyponatremia in psychogenic polydipsia possibly complicated by ziprasidone. Ann Pharmacother 2005;**39**:1726–1731.
3. Yang SH, McNeely MJ. Rhabdomyolysis, pancreatitis, and hyperglycemia with ziprasidone. Am J Psychiatry 2002;**159**: 1435.
4. Strachan P, Prisco D, Multz AS. Recurrent rhabdomyolysis associated with polydipsia-induced hyponatremia — a case report and review of the literature. Gen Hosp Psychiatry 2007;**29**: 172–174.
5. Sivakumar K, Okocha CI. Neurosyphilis and schizophrenia. Br J Psychiatry 1992;**161**:251–254.

https://doi.org/10.1111/j.1601-5215.2009.00381.x Published online by Cambridge University Press