CASE REPORT

Pontine haemorrhage mimicked by an olanzapine overdose

C Broyd, A McGuinness

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Olanzapine, an atypical antipsychotic of the thienobenzodiazepine class, has been on the market since 1996. Its popularity has increased over recent years because of excellent clinical results as well as a favourable side effect profile. Mirroring this increased olanzapine use has been a rise in the number of non-accidental overdoses. The clinical picture of olanzapine overdose can be surprisingly variable. In the case presented, the patient's low Glasgow Coma Score prevented an accurate history being taken. Examination revealed bilateral upgoing plantars, pinpoint pupils, increased tone, and brisk reflexes; however initial investigations, including an urgent CT head, were normal. The patient required 24 hours of intensive care before he regained consciousness and admitted to the overdose. Although there are several reports of olanzapine mimicking opiate intoxication in overdose, this is one of the first cases where overdose has mimicked an intracerebral event. The authors highlight some of the literature regarding clinical presentation and treatment options, and discuss the relation between olanzapine therapy and diabetes.

A 53 year old man presented to the emergency department with a Glasgow Coma Score (GCS) of 5. The patient was unresponsive to voice and the history was taken from the ambulance crew. He had been witnessed by his neighbours to be acting "strangely" and had then rapidly deteriorated in front of them, falling unconscious within about 60 seconds. When his wife arrived in the department we ascertained his past medical history included one TIA, a DVT plus PE, type II diabetes, and depression. His only medications were gliclazide and olanzapine.

On examination he was afebrile and his BM was 9.0. Although his GCS was 5 (E1, V1, M3), unusually, at several points during his initial assessment he sat up briefly, and threw out all four limbs wildly before becoming unresponsive again. He had no neck stiffness. His pupils were pinpoint and he had bilateral upgoing plantar reflexes, increased tone throughout, and brisk reflexes. He was tachycardic at 110 bpm and the rest of his examination was normal. The working diagnosis at this point was a pontine haemorrhage.

Initial investigations revealed a normal arterial blood gas, normal baseline bloods, and sinus tachycardia on electrocardiography. There was no response to IV naloxone and his finger prick test for salicylates and paracetamol was negative. He was intubated and ventilated in the emergency department. An urgent CT head performed within 60 minutes was normal. The possibility of a basilar artery infarct was raised but the decision was made not to thrombolysed the patient.

The patient spent the night on the intensive care unit during which his observations remained within normal parameters. He was successfully extubated the following morning. His neurology had now normalised and he had equally reactive pupils and downgoing plantars. It was at this point that the patient admitted to having taken an overdose of 260 mg of olanzapine on the day of presentation. He was discharged the following day after a psychiatric review.

DISCUSSION

Olanzapine is a second generation atypical antipsychotic drug which has shown encouraging results when used in the treatment of schizophrenia and bipolar affective disorder. The impressive safety profile of this drug at therapeutic doses compared to other antipsychotics is well known. Notably, there is a lower risk of extrapyramidal features, agranulocytosis, hyperprolactinaemia, and prolongation of the QT interval. For these reasons drug licence changes, introduced five years ago, shifted prescriptions in favour of the atypical antipsychotics. This has been mirrored by an increase in the number of searches on TOXBASE, telephone enquiries, and inpatient admissions relating to olanzapine overdose in Scotland and England.¹

Documented symptoms recognised in overdose include somnolence and central nervous system depression, mydriasis, blurred vision, respiratory depression, hypotension, extrapyramidal and anticholinergic effects, and hyperpyrexia.² Several deaths, attributed to probable cardiac toxicity, have been reported from olanzapine overdose.³

Olanzapine has also caused other problems in an emergency setting and there is a growing body of evidence linking therapeutic olanzapine use with the development of diabetes. There have been several reports of patients with no previous history of diabetes presenting in frank ketoacidosis after a course of olanzapine and 15 deaths have been reported from olanzapine induced hyperglycaemia.⁴ Deaths have also occurred with the development of olanzapine related pancreatitis and status epilepticus.⁵

There is no antidote to olanzapine and treatment is thus largely supportive. Early administration of activated charcoal may decrease its bioavailability by 50–60%.⁶ In 10% of cases of olanzapine overdose hypotension is a recognised feature.³ Because olanzapine exerts this effect through alpha-blockade the hypotension is dopamine resistant but has been shown to respond well to norepinephrine.⁷ Although the risk of QT prolongation, and consequent fatal arrhythmias, is lower compared with other antipsychotics, it is still an important consideration especially in patients with concomitant cardiovascular disease or risk factors. Cardiac monitoring is therefore appropriate in all but the most trivial cases.

Miosis is seen in about 35% of cases of all olanzapine overdoses and 82% of moderately severe overdoses. Additionally, it has also been noted that overdose can cause a fluctuating central nervous system picture from depression to agitation and aggression.⁸ These two features have been suggested as characteristic signs of olanzapine overdose, as is evidenced by our case report.

Although there are several reports of olanzapine overdose mimicking opiate intoxication there have been none demonstrating a striking similarity with an intracranial event.⁹ The key issues causing this deception were a rapid deterioration in conscious level, constricted pupils, upgoing plantars, and increased tone, which are all recognised features of a pontine haemorrhage.

This case highlights some of the challenges encountered in managing unconscious patients for whom an accurate history

Abbreviation: GCS, Glasgow Coma Score.

cannot be established in the emergency department. While the cause may be unknown, the assessment and treatment of patients with a GCS of less than 15 should follow a protocol or guideline that includes a drug history (when available) and initial blood glucose estimation. Finally, emergency practitioners should be aware of the clinical picture presented here, particularly the combination of upgoing plantars and pupillary constriction as clinical features of olanzapine overdose.

Authors' affiliations

C Broyd, Department of Gastroenterology, Queen Mary's Hospital, Kent, UK

A McGuinness, Department of Emergency Medicine, University College Hospital London, London, UK

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Correspondence to: Dr Christopher Broyd, c/o A+E Secretaries, University College Hospital London Accident and Emergency Department, 235 Euston Road, London NW1 2BU, UK; chrisbroyd@doctors.org.uk

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