CASE REPORT

Fatal hypertriglyceridaemia, acute pancreatitis and diabetic ketoacidosis possibly induced by quetiapine

Kristian Roerbaek Madsen

Multidisciplinary Intensive Care,
Odense University Hospital,
Odense, Denmark

Correspondence to

Dr Kristian Roerbaek Madsen,
kristian.roerbaek.madsen@
rsyd.dk,
krmaden1975@gmail.com

SUMMARY

A 27-year-old man treated with quetiapine for anxiety disorder developed hypertriglyceridaemia-induced acute pancreatitis and diabetic ketoacidosis. He was otherwise physically healthy with no family history of hyperlipidaemia. Despite aggressive intensive therapy he died of multiorgan failure within 36 h from initial presentation. While second-generation antipsychotics are well known to be causally linked to diabetes and hyperlipidaemia, this is to my knowledge the first-described case of a fatal triad of extreme hypertriglyceridaemia, acute pancreatitis and diabetic ketoacidosis possibly induced by quetiapine. Clinicians should be aware of this rare clinical presentation since rapid progression to multiorgan failure can occur. Early supportive therapy should be initiated. Lactescent serum and ketoacidosis in severe acute pancreatitis should not be overlooked—initiate insulin therapy and possibly plasmapheresis in case of extreme hypertriglyceridaemia.

BACKGROUND

Second-generation antipsychotics—including quetiapine—are associated with hypertriglyceridaemia and diabetes and occasionally even diabetic ketoacidosis. To my knowledge, however, this is the first-described case of a fatal triad of extreme hypertriglyceridaemia, acute pancreatitis and diabetic ketoacidosis possibly induced by quetiapine.

CASE PRESENTATION

A 27-year-old man presented at the emergency room of a local hospital reporting of excessive thirst, vomiting and upper abdominal pain for 2 days. He had a history of anxiety disorder with social phobia and occasional psychotic features, treated by a practising psychiatrist with quetiapine during the last year recently in increasing doses of up to 400 mg/day due to worsening anxiety. He received no other medication. His lipid profile had never been measured. Previously, his fasting blood glucose was normal. He was known to be physically healthy except for a body mass index of 34 kg/m² with a weight of 125 kg for a height of 192 cm. He was a non-drinker and had no history of alcohol or drug misuse, which was confirmed by his close relatives who saw him several times each day. Also he had no family history of hyperlipidaemia or diabetes mellitus. At admission the patient was alert and oriented with a Glasgow Coma Scale score of 15. He had a temperature of 37.6°C, a pulse of 114/min, a blood pressure of 129/95 mm Hg, a respiratory frequency of 14/min and a haemoglobin saturation of 97% with no supplemental oxygen.

Physical examination revealed a discrete acetone breath and epigastric tenderness without abdominal guarding, but was otherwise unremarkable.

INVESTIGATIONS

Initial laboratory work-up showed a pancreatic amylase of 1207 U/L (reference interval 10–65 U/L). Blood glucose was 28 mmol/L (504 mg/dL) with a urine test strip 4/4 positive for glucose and ketones. Arterial blood gas showed fully compensated metabolic acidosis with pH 7.35, a lactate of 1.5 mmol/L, bicarbonate 17 mmol/L and a carbondioxide tension of 3.6 kPa (27 mm Hg). Blood ketones were not measured. Lipaemic serum was noted, but a lipid profile was not measured at the local hospital. C reactive protein was 63 mg/L (<6 mg/L) and white blood cell count was 14.8×10⁹/L with 89% neutrophils. Plasma-creatinine, potassium, sodium, chloride, albumin, ionised calcium, aminotransferases, bilirubin, alkaline phosphatase and international normalised ratio were all within normal ranges at admission. An ultrasound examination of the upper abdomen was scheduled later the same day, and the patient was admitted to the surgical ward.

DIFFERENTIAL DIAGNOSIS

Owing to acute abdominal pain and markedly raised pancreatic amylase, the patient was correctly diagnosed with acute pancreatitis. However, an immediate CT scan of the abdomen was not made to confirm the diagnosis and reveal possible causes such as gallstones, though a subacute ultrasound examination was ordered. Alcohol-induced pancreatitis was ruled out, since the patient had no recent alcohol consumption as witnessed by close relatives, and drug-induced pancreatitis was not explicitly considered at this time. In fact the patient presented with the triad of acute pancreatitis, hypertriglyceridaemia and diabetic ketoacidosis. A diagnosis of diabetic ketoacidosis was unfortunately not immediately made at the local hospital, since initial arterial blood gas was without frank metabolic acidosis, the pH being 7.35 due to respiratory compensation and the patient did not yet seem in distress. Thus the hyperglycaemia was considered of minor importance and explained by previously undiagnosed type 2 diabetes mellitus or perhaps a mild diabetic manifestation of the acute pancreatitis. However, the urine test strip was positive (4/4) for ketones and the patient was hyperventilating as demonstrated in his initial arterial blood gas. Ketonaemia may well have aggravated his clinical course. Furthermore, the patient had documented

CrossMark

To cite: Madsen KR. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-202039

lactescent serum suggesting severe hypertriglyceridaemia, the significance of which was overlooked at this stage.

At this time, a quetiapine-induced triad of hypertriglyceridaemia, pancreatitis and diabetic ketoacidosis was not suspected.

A suspicion of malignant neuroleptical syndrome was also made at the local hospital, but was later ruled out at the university hospital since the patient had shown no muscular rigidity, and myoglobin and creatine kinase levels were only slightly elevated.

TREATMENT

At the local hospital the patient was admitted to the surgical ward and prescribed low-dose morphine and 3 L of normal saline as a slow continuous drip. It was considered safe to withhold insulin therapy for some hours since the hyperglycaemia was deemed of minor importance. However, in the following hours, he rapidly deteriorated developing a delirium, pallor, diaphoresis, cool extremities and a fever of 41.8°C. An acute CT scan of the abdomen confirmed a severe acute exudative pancreatitis with collateral oedema of the duodenal wall (figures 1 and 2). Gastric paresis was also noted. No signs of gallstones, stasis or inflammation of the biliary tract were found. Respiratory and circulatory compromise ensued. He was admitted to the intensive care at the local hospital 12 h after his presentation at the emergency room. At this time he was obtunded, hypoxaemic, metabolically acidotic with a pH of 7.18, in circulatory shock with a lactate of 4.5 mmol/L, oliguric with P-creatinine more than doubled, and a rise in C reactive protein to 323 mg/L and in P-amylase to 2202 U/L. He was sedated, intubated and mechanically ventilated, actively cooled for his hyperpyrexia and was treated with volume resuscitation with more than 5 L of crystalloid and human albumin. He was put on insulin and norepinephrine infusions, corticosteroids and empirical antibiotic treatment with cefuroxime. Due to progressive multiorgan failure, the patient was transferred to a university hospital. On arrival, echocardiography showed a hyperdynamic left ventricle with kissing walls, suggesting sustained hypovolaemia. The treatment was intensified with aggressive volume resuscitation (>10 L in 12 h)

Figure 1 Abdominal CT scan 12 h after admission showing diffuse pancreatitis (thin arrows), thickening of the duodenal wall (thick arrow), and gastric paresis (triangle).

Figure 2 Abdominal CT scan 12 h after admission showing diffuse pancreatitis (thin arrows), thickening of the duodenal wall (thick arrow) and gastric paresis (triangle).

guided by invasive cardiac output (combined transpulmonary dilution and pulse contour analysis). Already on arrival, lung ultrasound and chest X-ray were suggestive of adult respiratory distress syndrome (ARDS) which was treated with low tidal volume ventilation, inverse I : E ratio, permissive hypercapnia, deep sedation, neuromuscular blocking agents, 100% oxygen and 20 cm H₂O of positive end expiratory pressure. Volume restriction or prone position was not considered an ARDS treatment option due to extreme circulatory instability. In addition, the patient was treated with high-dose infusions of bicarbonate, insulin, norepinephrine and epinephrine, boluses of calcium chloride and continuous renal replacement therapy. Antibiotic treatment was empirically broadened to meropenem, ciprofloxacin and metronidazole. Lactescent serum was refound in all blood samples. P-triglycerides were measured to >55 mmol/L (>4867 mg/dL, Ref. <2 mmol/L) and total P-cholesterol >17.5 mmol/L (>677 mg/dL). Apart from insulin infusion, preparations were made to treat the hypertriglyceridaemia with therapeutic plasma exchange. However, the patient deteriorated in progressive lactate acidosis, hypoxaemia and catecholamine-resistant shock. Vasopressin was called for but was not available in time to be tested for effectiveness. Intra-abdominal pressure was 18–22 mm Hg. An abdominal surgeon was consulted regarding decompressive laparotomy as an ultimum refugium, but this was not considered of beneficence for the patient.

OUTCOME AND FOLLOW-UP

The patient died of multiorgan failure only 12 h after arrival at the referral hospital and 36 h after presentation at the local hospital. The patient's biological parents and siblings had normal or near-normal lipid profiles. The case was reported to the Danish Health and Medicine Authorities as a suspected quetiapine-related death.

DISCUSSION

In this case, a young man died from acute pancreatitis presumably caused by extreme hypertriglyceridaemia induced by quetiapine. He had no pre-existing physical comorbidity, received no other medication and no alternative explanation was found.

Extreme hypertriglyceridaemia is causally linked to acute pancreatitis, though mild to moderate hypertriglyceridaemia was observed as a secondary non-causal phenomenon during acute pancreatitis. Clinical trials with quetiapine have reported increased levels of triglycerides, low-density lipoprotein and

total cholesterol, and decreases in the high-density lipoprotein cholesterol as common adverse effects of quetiapine treatment (more than 10%).¹ Second-generation antipsychotics—including quetiapine—are thus known to be associated with hypertriglyceridaemia and diabetes and occasionally even with diabetic ketoacidosis.

Recently, Ely *et al*² reported 17 deaths due to diabetic ketoacidosis in psychiatric patients treated with second-generation antipsychotics. Quetiapine was the most frequently suspected agent.

However, quetiapine-associated *pancreatitis* has rarely been described. Only four cases are found in the literature: Gropper and Jackson reported three possible cases.³ All the three patients had comorbidities and received more than two medications obscuring the causal relationship. Thus two of the three patients were on valproic acid which is known to induce pancreatitis, though the temporal relationship did in fact suggest quetiapine as the responsible agent. Also Rashid *et al*⁴ described a young woman with the combination of pancreatitis and life-threatening diabetic ketoacidosis, possibly induced by quetiapine though the patient was also on ziprasidone.

However, no quetiapine-associated cases exhibiting the triad of extreme hypertriglyceridaemia, acute pancreatitis and diabetic ketoacidosis as in this case were found.

Apart from the general supportive care, insulin is the mainstay in the specific treatment of extreme hypertriglyceridaemia, also mitigating the diabetic ketoacidosis. Plasmapheresis is reported to be successful in severe cases.⁵

Learning points

- ▶ Quetiapine and other atypical antipsychotics can possibly induce extreme hypertriglyceridaemia, acute pancreatitis and diabetic ketoacidosis.
- ▶ Beware of rapid progression to multiorgan failure.
- ▶ Initiate early supportive therapy.
- ▶ Do not overlook lactescent serum in severe acute pancreatitis—initiate insulin therapy and possibly plasmapheresis in case of extreme hypertriglyceridaemia.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Quetiapine. Summary of Product Characteristics. The European Medicines Agency (Cited 13-09-13) <http://www.ema.europa.eu>
- 2 Ely SF, Neitzel AR, Gill JR. Fatal diabetic ketoacidosis and antipsychotic medication. *J Forensic Sci* 2013;58:398–03.
- 3 Gropper D, Jackson CW. Pancreatitis associated with quetiapine use. *J Clin Psychopharmacol* 2004;24:343–5.
- 4 Rashid J, Starer PJ, Javadi S. Pancreatitis and diabetic ketoacidosis with quetiapine use. *Psychiatry (Edgmont)* 2009;6:34–7.
- 5 Kyriakidis AV, Raitsiou B, Sakagianni A, *et al*. Management of acute severe hyperlipidemic pancreatitis. *Digestion* 2006;73:259.

Copyright 2014 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow