CASE REPORT

Quetiapine-induced hypertriglyceridaemia causing acute pancreatitis

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SUMMARY

Second-generation antipsychotics have well-known metabolic side effects such as hyperlipidaemia and hyperglycaemia. A middle-aged man presented with epigastric and flank pain associated with nausea, and was noted to have elevated triglycerides (3590 mg/dL or 40.53 mmol/L), lipase and glucose. Haematological parameters revealed neutropenia with pancytopenia. The patient was started on conservative management for acute pancreatitis, and on intravenous insulin and oral gemfibrozil for lowering of his triglycerides. He gradually improved and was transitioned to oral atorvastatin and fenofibrate. His triglycerides, glucose and leucocyte counts normalised at discharge and he was transitioned to ziprasidone. The combination of hypertriglyceridaemia, worsening hyperglycaemia and neutropenia made us suspect quetiapine as the causative agent. Medications cause only 0.1–7% of acute pancreatitis cases, with quetiapine implicated in only five-reported cases. Hypertriglyceridaemia (>600 mg/dL or 6.77 mmol/L) is frequently reported with quetiapine use, but severe hypertriglyceridaemia (>1000 mg/dL or 11.29 mmol/L) has been reported in <10 patients.

BACKGROUND

Second-generation antipsychotics (SGAs) such as quetiapine, olanzapine and risperidone, have well-known metabolic side effects such as hyperlipidaemia and hyperglycaemia.^{1 2} Although rare, these side effects of SGAs can lead to serious complications, such as hypertriglyceridaemia-induced acute pancreatitis, of which there are limited reported cases.^{3 4} SGA-induced metabolic disturbances are often accompanied by depression of particular cell lines, such as neutropenia, though this is not diagnostic.⁵ We present a case of quetiapine-induced hypertriglyceridaemia causing acute pancreatitis, seen at our tertiary-care academic medical centre.

CASE PRESENTATION

A 50-year-old Caucasian veteran with a history of bipolar disorder, hyperlipidaemia, type-2 diabetes mellitus, morbid obesity, irritable bowel syndrome and generalised anxiety disorder, presented with progressive 10/10 epigastric pain radiating to the back and nausea of 6 days duration. Additionally, he reported fatigue, polyuria and polydipsia for the past 1 month. The previous day, during his scheduled primary care clinic visit, routine laboratory parameters revealed elevated triglycerides 3590 mg/dL (40.53 mmol/L), lipase 2079 IU/L, blood glucose 533 mg/dL (29.58 mmol/L) and glycated haemoglobin 10.4%. The patient was advised to return to the

emergency department for further evaluation and admission. Six months prior to this presentation, he was started on quetiapine for management of his bipolar disorder, and had tolerated it well without any side effects.

INVESTIGATIONS

Admission laboratory parameters were significant for pancytopenia with 3.9 leucocytes/mm³, haemoglobin of 12.4 g/dL and platelets of 129 cells/mm³. Differential leucocyte count revealed 40.8% neutrophils and 44% lymphocytes. Metabolic panel demonstrated normal electrolytes, hepatic and renal function. Abdominal ultrasound was unrevealing for gallbladder or bile duct pathology.

TREATMENT

The patient was managed conservatively for acute pancreatitis with bowel rest, intravenous hydration and adequate pain control. He was started on intravenous insulin for suspected hyperglycaemic hyperosmolar syndrome and hypertriglyceridemia. Additionally, he was started on oral gemfibrozil and within 24 h of initiating treatment, the patient's triglycerides decreased to 1334 mg/dL (15.06 mmol/L) and blood glucose levels were better controlled. The triglyceride levels continued to improve to 684 mg/dL (7.72 mmol/L) at 72 h. He started to tolerate an oral diet and was transitioned to his home medication of atorvastatin with the addition of fenofibrate.

OUTCOME AND FOLLOW-UP

The combination of hypertriglyceridaemia, worsening of diabetic control and pancytopenia with predominant neutrophil depression, made us suspect quetiapine as the cause of these abnormalities. In light of metabolic and haematological disturbances, likely caused by quetiapine, the patient was tapered off it over the subsequent 2 days and ziprasidone was initiated. The patient continued to improve and his insulin regimen was optimised after calculating his 24 h requirements. Additionally, extensive education on diabetes mellitus, substance abuse and healthcare maintenance was provided. He was subsequently discharged on hospital day 7 with triglyceride levels of 628 mg/dL (7.09 mmol/L) and serum glucose <200 mg/dL (<11.1 mmol/L) maintained over 24 h. His leucocyte count was 6.0/mm³ with additional normalisation of other cell lines. At 2-month posthospitalisation follow-up, the patient continued to improve with good medication compliance, and remained symptom free.

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DISCUSSION

Quetiapine is a SGA that is frequently prescribed for patients with major depressive and bipolar-type disorders, and has been shown to significantly reduce the number of psychiatric admissions ($p < 0.001$) and episodes of emergent suicidality compared to placebo (0.3% and 0.5%, respectively).^{6,7} Metabolic disturbances including hyperglycaemia and hypertriglyceridaemia are well-documented side effects of SGAs, and seen in up to 10% of patients treated with olanzapine or quetiapine.^{1,8–10} However, complications from these metabolic side-effects, such as acute pancreatitis and diabetic ketoacidosis, are exceedingly rare.³

Medications are attributed as the cause for only 0.1–7% of acute pancreatitis cases.^{4,11,12} Acute pancreatitis caused by hypertriglyceridaemia side effects of quetiapine use has only been reported in five published case reports.^{4,8} Hypertriglyceridaemia (>600 mg/dL or 6.77 mmol/L) is frequently reported with quetiapine use in asymptomatic patients, but severe hypertriglyceridaemia (>1000 mg/dL or 11.29 mmol/L) has been reported in fewer than 10 patients.^{8,11} In addition to acute pancreatitis, hyperlipidaemic states are associated with increased risk of cardiovascular disease, the leading cause of death in patients with severe mental illnesses.¹ Hypertriglyceridaemia-induced acute pancreatitis from quetiapine use does not appear to be related to medication dosing, but appears instead to be related to the duration since initiation of the drug. All cases have been reported within the first 8 months of an established dose, most frequently at 3 months of treatment, with one report of occurrence within 72 h.^{1,4,8,11} The mechanism by which quetiapine causes hyperlipidaemic disturbances is not entirely understood. Some hypothesise that the medication stimulates hepatic triglyceride production and secretion or alters lipase-mediated triglyceride hydrolysis.¹³ Alterations in triglyceride metabolism can cause a high free-radical state, potentially leading to consequences such as acute pancreatitis.¹¹

SGAs also possess a well-documented side effect of blood dyscrasias, such as agranulocytosis. While this side effect is documented most frequently with clozapine use, seen in up to 3% of patients taking this medication, quetiapine has also been shown to depress leucocyte cell lines.¹⁴ Leukopenia associated with quetiapine is most predominantly pronounced by selective absolute neutrophil depression, though the absolute incidence is not known.^{5,14,15}

Many reports argue for the recommendation of frequent laboratory follow-up for patients beginning or adjusting treatment with SGAs.^{4,8} Nearly 80% of the patients who develop hyperlipidaemia after initiation of SGA therapy do not have baseline hyperlipidaemia prior to treatment, suggesting that all patients initiating SGA therapy should be monitored regardless of their previous lipid profiles.¹ In addition, previously-diagnosed diabetes mellitus does not correlate with an increased risk of hyperglycaemia or hyperlipidaemia with initiation of therapy.¹ Early investigations suggest that patients with previously-diagnosed hypertension may be at slightly increased risk of emergent hyperlipidaemia with initiation of SGA treatment.¹ More recent literature has highlighted the role of quetiapine in the causation of insulin hypersecretion and insulin resistance.^{16,17} Quetiapine induces pancreatic β cells to produce more insulin, and yet, paradoxically, increases the insulin resistance. This is brought about by two mechanisms—slow weight gain, resulting in long-term insulin resistance, and acute action on the pancreatic β cells.¹⁷ Since risk factors for developing severe metabolic disturbances are not clearly defined, it is difficult to recommend laboratory follow-up guidelines based on

pre-existing conditions. Nevertheless, clearly defined guidelines for laboratory follow-up are needed to identify metabolic disturbances with SGA therapy.

We reported a case of hypertriglyceridaemic pancreatitis caused by quetiapine use. Further suspicion of an aetiological diagnosis was strengthened by laboratory identification of pancytopenia with predominant neutropaenia. This case also emphasises the importance of routine laboratory follow-up when initiating therapy with SGAs. We believe that this case study will aid clinicians identify, with confidence, a rarely published, albeit serious side effect of a common antipsychotic medication.

Learning points

- ▶ Second-generation antipsychotics (SGAs) are generally safe, but can occasionally cause serious metabolic and haematological complications.
- ▶ Severe hypertriglyceridaemia is a rare metabolic complication of SGAs, and has been reported only 10 times previously in the literature.
- ▶ Acute pancreatitis is rarely caused by medications, and quetiapine has been implicated only five times prior to this case report.
- ▶ Quetiapine also causes pancytopenia, specifically neutropenia, making this an additional diagnostic consideration.

Contributors JMF was involved in the evaluation of the patient, drafting of manuscript, literature review. SV was involved in the evaluation of the patient, literature review, critical analysis, finalising manuscript. TJG was involved in the evaluation of the patient, critical analysis, finalising manuscript.

Competing interests None declared.

Patient consent Obtained.

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