Quetiapine-associated cardiomyopathy

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Congestive heart failure due to dilated cardiomyopathy is an unusual cause of shortness of breath in young patients. Causes of dilated cardiomyopathy include myocarditis, familial cardiomyopathies, coronary artery disease, alcohol, pregnancy, and drugs, although it is most common not to find a specific aetiology.

Psychoactive medications, in particular clozapine, have been linked with the development of cardiomyopathy, possibly through the development of a preceding Type 1 hypersensitivity reaction leading to eosinophilic myocarditis.¹

We report here two cases of cardiomyopathy associated with quetiapine. The study was approved by the Lower South Ethics Committee.

Case reports

Patient 1—The first patient, a 33-year-old male diagnosed with catatonic schizophrenia, had been treated with quetiapine for 4 years. He had been stabilised on a dose of 1000 mg daily for 2 years. Eight weeks prior to presentation he had an influenza-like illness. He presented with a 2-week history of shortness of breath, ankle swelling and orthopnoea. On examination he was tachycardic with a heart rate of 126 beats per minute, jugular venous pressure 10 cm above the sternal angle, crepitations on lung auscultation, and hepatomegaly.

An echocardiogram showed globally severely impaired left and right ventricular systolic function, with a left ventricular (LV) end diastolic dimension of 6.5 cm and an ejection fraction of 14%. Coronary angiography showed no obstructive epicardial coronary artery disease. A previous echocardiogram performed 10 years previously had shown normal ventricular function. Despite extensive investigation for infectious and metabolic causes, no underlying cause for his cardiomyopathy was able to be determined.

A diagnosis of dilated cardiomyopathy due to quetiapine was made, and his quetiapine withdrawn. He symptomatically improved after treatment with cilazapril, carvedilol, furosemide, digoxin and spironolactone, and was discharged 9 days after admission. However his mental status deteriorated rapidly, leading to admission 10 days later to an acute psychiatric unit.

Ziprasidone therapy was started but had to be withdrawn after QT interval prolongation. Amisulpride therapy was then commenced. Four days later, 36 days after his initial presentation, he was found dead in the morning, with no external cause of death found. The cause of death was thought to be a malignant arrhythmia related to his underlying cardiomyopathy.
Patient 2—The second patient, a 28-year-old woman, presented with rapid onset of shortness of breath starting 2 days previously. She had been taking quetiapine 800 mg daily and venlafaxine 150 mg daily for 2 years as treatment for depression and possible borderline personality disorder. On examination she was obese and tachycardic but without clinical signs of congestive heart failure. She was initially investigated for a pulmonary embolus, and was anticoagulated after a CT pulmonary angiogram was possibly consistent with pulmonary emboli.

However her dyspnoea continued to progress and a subsequent echocardiogram showed globally severely impaired LV systolic function, with a LV end diastolic dimension of 6.5 cm and an ejection fraction of 15%. Pharmacological stress myocardial perfusion scanning showed no inducible ischaemia and the results were interpreted as being consistent with a non-ischaemic dilated cardiomyopathy.

Detailed testing failed to show any infectious nor metabolic cause for her cardiomyopathy. A diagnosis of quetiapine induced cardiomyopathy was made, and the quetiapine was stopped. She responded well to initial treatment with quinapril, carvedilol, furosemide and spironolactone, with subsequent echocardiograms showing an improvement in ejection fraction to 35%.

Discussion

The first case described highlights the difficulty in managing the mental health of patients with severe cardiomyopathy where there are concerns about chronic therapy being related to presentation with heart failure. Withdrawal of the psychoactive medication led to a rapid decline in the patient’s mental status.

A common alternative for patients who have failed therapy with quetiapine is clozapine, which is contraindicated in the setting of a pre-existing cardiomyopathy. Many alternative agents are associated with QT interval prolongation, as we found in this case, complicating suitable therapeutic options.

These two case reports add to the small worldwide literature on quetiapine-induced heart disease. There has been one case report previously describing quetiapine-associated myocarditis and one describing quetiapine-associated cardiomyopathy. Another case report described a fatal dilated cardiomyopathy thought to be due to methylphenidate, but may also have been due to quetiapine.

As quetiapine and clozapine are both benzazepine derivatives with similar chemical structures, given the cardiac toxicity associated with clozapine, there is a clear possibility that quetiapine could have a similar effect. Clozapine is usually viewed as leading to myocarditis in the initial stages of treatment, but a recent New Zealand case series showed that 20% were diagnosed after a month of treatment and 12% diagnosed after a year.

Dilated cardiomyopathy would necessarily present later than a causative myocarditis. There were cases of cardiomyopathy associated with clozapine occurring after 3 years of treatment, with a mean duration of treatment of 12 months.

In conclusion, we have presented two cases of quetiapine-associated cardiomyopathy, one of whom died. Along with the five previously reported cases, this may indicate an adverse drug reaction signal that warrants further evaluation.
Although quetiapine was not implicated in a data mining study examining cardiotoxicity associated with antipsychotic drugs, the study relied on adverse drug reactions being reported to a pharmacovigilance centre. It is accepted that adverse reactions are widely underreported. We hope that this paper will prompt such reports to facilitate further analysis.

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References: