Is this a prolonged QT interval?

VIVIENNE MILLER
MB BS, FRACGP, DRACOG, DCH, MACPM, MWAME

ECG Education articles use real cases to illustrate the importance of knowledge about ECGs in relation to clinical situations in general practice. Management is not discussed.

Juana, aged 52 years, has been advised to find herself a GP. She presents to you with a discharge referral from a psychiatric unit stating she has longstanding schizophrenia and depression and is taking clozapine 400 mg/day and fluoxetine 20 mg/day. She has been otherwise medically well, except for a recurrent tooth abscess. An ECG has not been documented as being conducted in hospital, so you arrange one – see the ECG on this page.

Key points

- **The QT interval varies with heart rate.**
- **It lengthens with slower heart rates and shortens with faster heart rates.**
- **Prolonged QT intervals occur much more commonly in women than men.**
- **A QT interval of 500 ms is always long and 430 to 450 ms is often long.**
- **An ECG is the usual diagnostic investigation.**

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Dr Miller is a GP in Sydney, NSW. She is also an editor, author and medical journalist and is the Medical Editor of *Cardiology Today*.

Q1. Why should you arrange an ECG for this woman?

This patient is on two medications that can cause prolonged QT intervals (see the box on page 40). Prolonged QT intervals can lead to arrhythmias (especially ventricular tachycardia) and sudden death. Women are also at increased risk of arrhythmias from prolonged QT interval, compared with men. Co-existent cardiac disease (as occurs in older age groups) is also likely to increase this risk.

Q2. What is the QT interval?

This is the time measured from the beginning of the Q wave to the end of the T wave for each heart beat documented on an ECG. The QT interval normally decreases with increasing heart rate. There are a number of mathematical formulas that can be used to calculate the corrected QT interval at variable heart rates.

Q3. Does this patient's ECG show a prolonged QT interval?

Yes.

Q4. What is the prevalence of prolonged QT interval in the general population?

About 2.5% of the population will have a prolonged QT interval on their ECG. However, the prevalence of congenital long QT syndrome is about one in 2500 to 7000 people. Long QT syndrome is present in all racial groups.

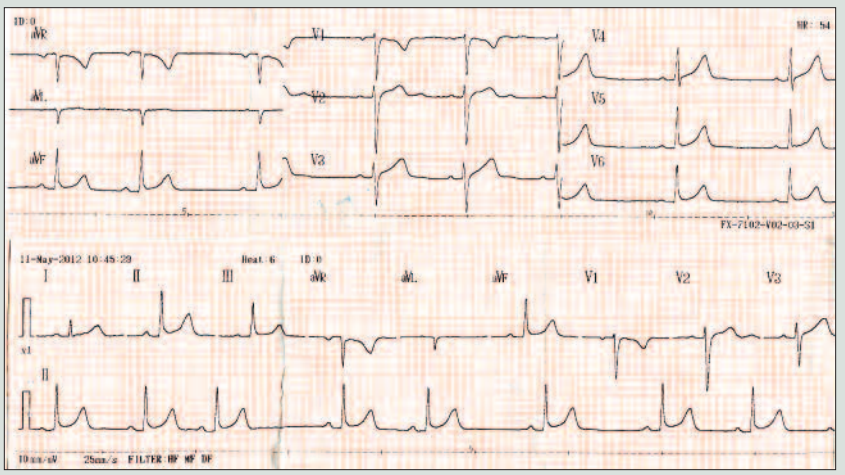
Q5. What is long QT syndrome?

Long QT syndrome consists of the occurrence of cardiac arrest or syncope due to ventricular fibrillation (VF) or torsades de pointes ventricular tachycardia (TdP) in a patient whose ECG shows a long QT interval in sinus rhythm (or in atrial fibrillation). Long QT intervals increase the risk of sudden death, due to TdP and VF.

There are many gene mutations associated with prolonged QT intervals that may appear de novo or be inherited. These abnormal genes prolong the action potential of the ventricle and thus the length of the QT interval. The abnormal repolarisation of the ventricle increases the risk of chaotic re-entry within the myocardium, producing TdP or VF. The trigger for these arrhythmias is sometimes adrenaline (from stress or exercise) and adrenergic medications (see the box on page 40), and sometimes other changes in autonomic nervous influence on the heart (from sleep, swimming or alarms).

Although the ECG is the simplest way of diagnosing this syndrome, about 15% of patients with the condition have a normal QT interval on their ECGs. There are approximately 10 genes responsible for long QT syndrome (LQT); some are autosomal dominant and some are recessive.

Of those patients with long QT syndrome, approximately 35% have LQT1, caused by an abnormality of the gene *KCNQ1* on chromosome 11p15.5, which affects one particular



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potassium channel. The next most common type of long QT syndrome is LQT2, found in about 30% of cases, caused by an abnormality of the *hERG* gene on chromosome 7 and which affects another potassium channel.

There are other associations with long QT syndrome. Jervell and Lange-Nielsen syndrome includes congenital deafness and sudden death (especially with sudden stress or fright) from ventricular arrhythmias. It appears to have autosomal recessive inheritance, and is now recognised as the more severe homozygous form of autosomal dominantly inherited long QT syndromes. The mortality rate is 50% by the mid-teenage years if untreated.

The gene responsible for Andersen-Tawil syndrome (LQT7) has autosomal dominant inheritance and is associated with skeletal deformities, low-set ears, clinodactyly, micrognathia and periodic paralysis, but there is much clinical variability.

Common medications associated with long QT syndrome*

- Amiodarone
- Antidepressants
- Antipsychotics
- Chloroquine
- Fluconazole and other azoles
- Fluoroquinolones
- Indapamide
- Lithium
- Macrolides
- Methadone
- Tamoxifen
- Tricyclic antidepressants
- Sotalol
- Sulfamethoxazole–trimethoprim
- Sumatriptan
- Quinine

*See www.qtdrugs.org for further information.

Medications that may trigger arrhythmias in patients with long QT syndrome

- Adrenaline
- Dopamine
- Methylphenidate
- Pseudoephedrine
- Salbutamol
- Terbutaline

Q6. What other conditions are related to prolonged QT intervals?

Bradycardias, hypothyroidism, hypocalcaemia (hypercalcaemia may be associated with a short QT interval), hypokalaemia, anorexia, myocarditis, cardiomyopathies and certain types of congenital cardiac diseases are related to prolonged QT intervals. Specific medication use is also related (see the box on this page).

Q7. What other investigations would be advisable in Juana if not already performed?

Juana's cardiovascular risk factors should be assessed because ventricular arrhythmias are more common in patients with prolonged QT intervals and cardiac disease. Metabolic syndrome is common in patients taking antipsychotics. Juana needs to have her fasting cholesterol, triglycerides, LDL-cholesterol, HDL-cholesterol and fasting blood glucose levels measured. If her fasting blood glucose level is in the upper range of normal, or she is very overweight or has a strong family history of diabetes, a two-hour glucose tolerance test is advisable. She also needs a thyroid function test, measurement of her vitamin D level and an adjusted calcium level, and liver function tests.

Clozapine has a side effect profile including myocarditis, QT prolongation and neutropenia. Guidelines state that Juana should have full blood counts routinely every four weeks for life while taking clozapine; she has been on clozapine for more than a year so the period of weekly then fortnightly testing for agranulocytosis has passed. If there is neutropenia caused by clozapine then this would be contributing to the recurrent tooth infection. Care must be taken to avoid use of sulfonamides, macrolides or fluoroquinolones when managing this condition, and the dentist needs to be made aware of Juana's long QT interval.

Myocarditis due to clozapine use typically occurs several weeks after commencing therapy and is initially diagnosed by serum troponin 1 and C-reactive protein levels, ECG and then echocardiography. Juana may need a cardiac echocardiogram because of the risk of undiagnosed heart disease that could increase her risks associated with the prolonged QT interval.

Outcome

Juana was referred to a cardiologist and her psychiatrist was consulted. The cardiologist thought the QT prolongation was mild and the risk of ventricular arrhythmias was not too great but would be increased further should she develop cardiac disease. If possible, she should have her medication changed, bearing in mind that Juana's psychiatric condition is clearly severe enough for her to require clozapine.

Unfortunately, all antidepressants and antipsychotic medications may cause a prolonged QT interval and so the risk of destabilising her mental health must be taken into account if medication is to be ceased or altered. At present, hospitalisation and changing to quetiapine is being contemplated, because this has a greater antidepressant effect and may allow the cessation of fluoxetine. She should be closely monitored for stability of her mental condition and whether there is a lesser effect on her QT interval. **CT**

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