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CME Article

Electrocardiographical case. Young woman with epilepsy

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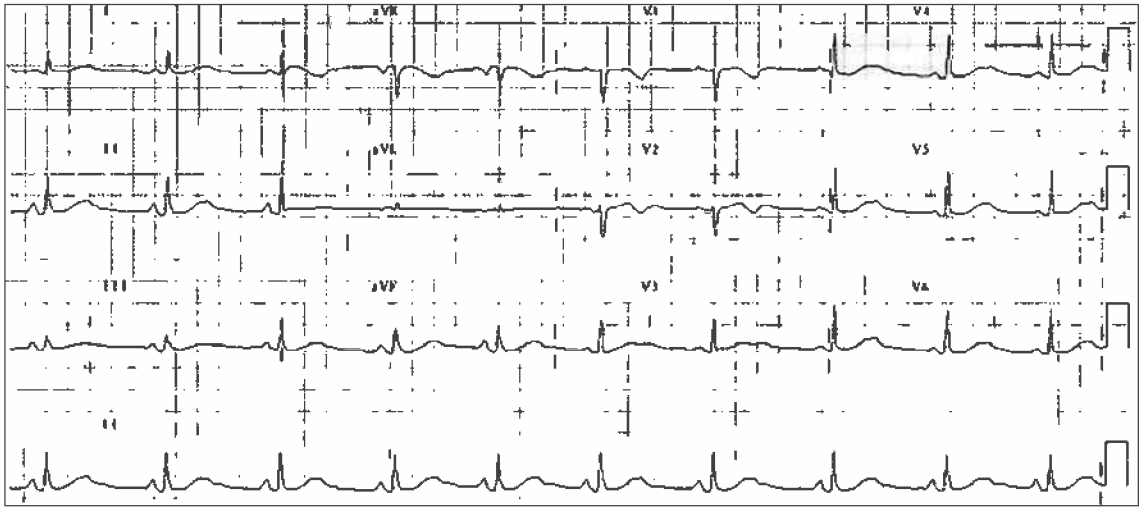

Fig. 1 ECG on presentation.

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CLINICAL PRESENTATION

A 24-year-old Chinese woman with a history of epilepsy was referred for evaluation of palpitations. She was diagnosed with epilepsy at the age of ten years, and had been taking carbamazepine since then. She had a younger sister who died in her sleep at the age of 17 years. The patient's cardiac examination was normal. What does the electrocardiogram (ECG) show (Fig. 1)? What is your diagnosis?

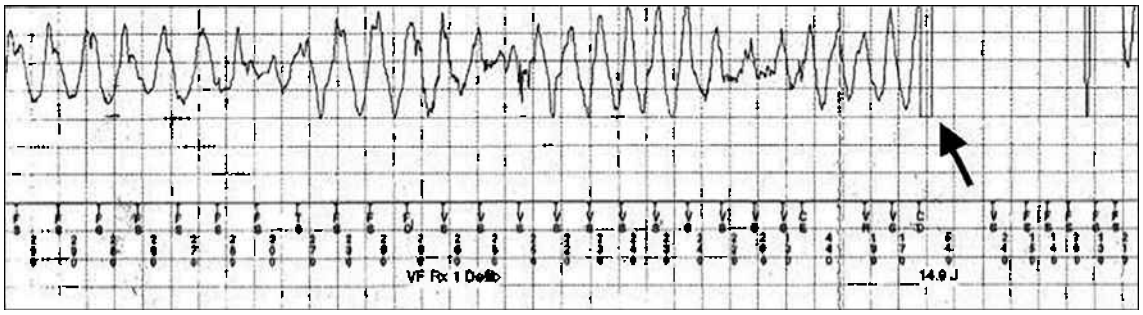

Fig. 2 An endocardial tracing obtained from the patient's ICD shows polymorphic VT, followed by a discharge (arrow) to terminate the arrhythmia and restore sinus rhythm.

ECG INTERPRETATION

The ECG (Fig. 1) shows normal sinus rhythm and normal axis with prolonged QT interval and a T-U complex. The rate-corrected QT interval (QTc) using the Bazett correction ($QTc = QT/\sqrt{RR}$ with all intervals in seconds) is 600 ms. In a young patient with no history of cardiac problems presenting with syncope and seizure and a family history of unexplained sudden death, the ECG findings strongly suggest congenital long QT syndrome (LQTS). ECGs were obtained in all her immediate family members. Prolonged QTc (470 ms) was identified in the patient's father.

DIAGNOSIS

Congenital long QT syndrome.

CLINICAL COURSE

The patient's ECG revealed normal ejection fraction and no structural abnormalities. Tilt testing could induce neither syncope nor arrhythmias. Exercise stress testing did not induce any ventricular arrhythmias. The patient was given atenolol 50 mg daily. In addition to beta-blockers, she agreed to an implantable cardioverter-defibrillator (ICD; Gem, Medtronic, Minneapolis, MN, USA) in view of recurrent episodes of syncope and a family history of presumed sudden cardiac death. 12 days after implantation, she reported an episode of near-syncope associated with a discharge from the ICD. Interrogation of the ICD revealed an episode of polymorphic ventricular tachycardia (VT), which was appropriately terminated by the ICD (Fig. 2).

Since then, she has had another episode of near-syncope caused by polymorphic VT and terminated by an ICD discharge. Consequently, her dosage of atenolol was increased to 75 mg daily, and carbamazepine ceased. She has remained asymptomatic since then. Despite having a prolonged QTc, her father was managed conservatively as he had remained asymptomatic.

DISCUSSION

Congenital LQTS is a familial disease with variable penetrance, characterised by abnormally prolonged ventricular repolarisation caused by one of several mutations in the genes coding for the transmembrane sodium or potassium ion-channel proteins. This diagnosis is made clinically, and supported by ECG findings. Diagnostic criteria[1] are available to provide a systematic approach to the diagnosis and degree of probability of the syndrome. In the last decade, seven genes (LQT1–LQT7) with over 180 variants had been identified. There are two well-described syndromes of the congenital LQTS. The Jervell-Lange-Nielsen syndrome, first described in 1957, is a rare cardio-auditory syndrome inherited in an autosomal recessive pattern (two affected alleles). The more common Romano-Ward syndrome, associated with normal hearing, is inherited in an autosomal dominant pattern (one affected allele). Mutations in LQT7, discovered in 2001, are responsible for Andersen syndrome, a rare neurological disorder characterised by periodic paralysis, skeletal developmental abnormalities, and QT prolongation.

The clinical presentation is the result of torsade de pointes (TdP). Presentation ranges from dizziness to more disabling symptoms such as syncope, seizures and even sudden death. An individual episode of TdP is generally short lived and usually terminates spontaneously. However, it has the tendency to recur and degenerate into ventricular fibrillation (VF), leading to sudden death. Management priority should include immediate cardioversion in situations where TdP does not terminate spontaneously, resulting in haemodynamic compromise. Physical activity and intense emotional stress tend to precipitate cardiac events in the LQT1 genotype, and loud auditory stimuli in the LQT2 group. Patients with the LQT3 genotype typically experience sudden death during sleep and at rest, while patients with variants of

the LQT6 genotype are at risk from certain medications and from exercise.[2]

The mortality rate of congenital LQTS in untreated patients ranges from 1%–2% per year, varying as a function of the genotype.[3] The high-risk predictors of sudden cardiac death include recurrent episodes of syncope, failure of medical therapy, survival from cardiac arrest, congenital deafness, female sex, QTc > 600 ms, relative bradycardia, symptomatic family member, and sudden cardiac death in a family member at an early age.[4] On the surface ECG, LQTS is characterised by a QTc > 450 ms in men or > 460 ms in women and children. Other defining features include increased QT interval variability due to labile repolarisation,[5] and T- and U-wave abnormalities. Of note, about 6%–12% of patients have a normal QTc interval.[3]

As sudden increases in sympathetic activity are the triggers for many episodes of life-threatening arrhythmias in congenital LQTS patients (especially those with the LQT1 genotype), long-term anti-adrenergic therapy can provide protection. Beta-blockers are the cornerstone of therapy, unless specific contraindications are present. According to Moss et al, long-term use of beta-blockers has been shown to result in a significant reduction in the rates of cardiac events in probands (0.97 ± 1.42 events per year before versus 0.31 ± 0.86 events per year after initiation of beta-blockers, $p < 0.001$) and in affected family members (0.26 ± 0.84 events per year before versus 0.15 ± 0.69 events per year after initiation of beta-blockers, $p < 0.001$).[6] High left thoracic sympathectomy is another effective method of anti-adrenergic therapy though it has been largely superseded by the use of adjuvants such as the implantation of a permanent pacemaker or ICD.

A permanent pacemaker should be considered as an adjuvant in patients who are symptomatic despite full doses of beta-blockers and in those with bradycardia as a prominent feature of the syndrome. The ICD is an appropriate alternative, in addition to anti-adrenergic therapy, in patients with documented TdP/VF requiring cardioversion or resuscitation. However, drawing the line between candidates for medical therapy versus ICD can be difficult; pros and cons of either therapy must be carefully considered. This case illustrates the typical clinical presentation of congenital LQTS. The ability of clinicians to recognise and treat the disease is extremely effective in preventing sudden cardiac death in young patients.

ABSTRACT

A 24-year-old Chinese woman was referred for evaluation of palpitations. She had a background history of epilepsy. A 12-lead electrocardiogram (ECG) showed prolonged rate-corrected QT of 600 ms and a T-U complex. The ECG findings with her typical history suggest a diagnosis of congenital long QT syndrome. Diagnosis and treatment options are discussed.

Keywords: arrhythmia, long QT syndrome, sudden cardiac death

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SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME
Multiple Choice Questions (Code SMJ 200702B)

	True	False
Question 1. The following statement(s) is/are true of ECG characteristics of long QT syndrome:		
(a) A normal QTc excludes the diagnosis of long QT syndrome.	☐	☐
(b) Increased QT interval variability may be seen.	☐	☐
(c) T waves may be notched, bifid, or biphasic in appearance.	☐	☐
(d) ST changes are commonly confused with ischaemic changes.	☐	☐
Question 2. Which of the following is/are high-risk predictors of sudden cardiac death in long QT syndrome?		
(a) Female gender.	☐	☐
(b) Age > 50 years old.	☐	☐
(c) QTc of 520 ms on a surface electrocardiogram.	☐	☐
(d) History of sudden cardiac death in the family.	☐	☐
Question 3. Investigations for long QT syndrome should include:		
(a) A good history and physical examination.	☐	☐
(b) A surface electrocardiogram.	☐	☐
(c) An electrophysiology study.	☐	☐
(d) Electrolytes (K, Ca, Mg).	☐	☐
Question 4. The following therapies have been shown to be effective in managing long QT syndrome:		
(a) Beta blockers.	☐	☐
(b) Permanent pacemaker.	☐	☐
(c) Implantable cardioverter-defibrillator.	☐	☐
(d) Amiodarone.	☐	☐
Question 5. Which of the following is/are associated with cardiac events in long QT syndrome?		
(a) Intense exercise and emotional stress.	☐	☐
(b) Strobe lights.	☐	☐
(c) Loud noise from alarm clock.	☐	☐
(d) At rest or during sleep.	☐	☐

Doctor's particulars:

Name in full: _____

MCR number: _____ Specialty: _____

Email address: _____

SUBMISSION INSTRUCTIONS:
(1) Log on at the SMJ website: **www.sma.org.sg/cme/smj** and select the appropriate set of questions. (2) Select your answers and provide your name, email address and MCR number. Click on "Submit answers" to submit.

RESULTS:
(1) Answers will be published in the SMJ April 2007 issue. (2) The MCR numbers of successful candidates will be posted online at **www.sma.org.sg/cme/smj** by 15 April 2007. (3) All online submissions will receive an automatic email acknowledgment. (4) Passing mark is 60%. No mark will be deducted for incorrect answers. (5) The SMJ editorial office will submit the list of successful candidates to the Singapore Medical Council.

Deadline for submission: (February 2007 SMJ 3B CME programme): 12 noon, 25 March 2007