Faint of heart
Syncope and familial long QT syndrome

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Articles in this section use cases to illustrate the emergency management of patients presenting in general practice with cardiac problems. They are inspired by, but not based on, real patient situations.

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CARDIOLOGY TODAY 2017; 7(1): 35-37

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Hayden is a 13-year-old boy who, accompanied by his concerned mother, presents to your practice after collapsing unconscious while playing soccer. He recovered quickly and felt fine, so his coach had not called an ambulance. Hayden remembers drinking plenty of water before the game. Hayden has no known medical problems and is fully immunised. He denies any episodes of feeling dizzy, but has felt his heart beat forcefully at times. As Hayden is unsure of the duration of these episodes, you ask him to tap on your desk to provide an example. He taps at a rate of well over 100 beats per minute for a period of 15 to 20 seconds. Importantly, Hayden does not consume any caffeine or energy drinks. You ask about any sudden deaths in the family, and his mother reports that her brother died unexpectedly at 34 years of age. She recalls the autopsy was 'normal', however you acknowledge that routine genetic testing was not yet available at that time.

What does the clinical examination show?

Hayden looks comfortable at rest. He is 156 cm tall, weighs 52.5 kg and has a body mass index of 21.3 kg/m^2, which is within the normal range. His heart rate is 67 beats per minute and regular, and his blood pressure is 110/70 mmHg. He is afebrile with a temperature of 36.8˚C.

Hayden's peripheries are warm and pulses are equal at radial and femoral arteries. He has no conjunctival pallor. His carotid arteries have no bruits, his heart sounds are dual with subtle splitting of the second heart sound on inspiration, which resolves with expiration. This is a normal finding in a young person. His lung fields are clear to auscultation. His abdomen is soft and non-tender, and there is no organomegaly. His blood sugar level is normal.

You perform an ECG, which shows a normal sinus rhythm at 65 beats per minute, with a normal narrow QRS interval, and a prolonged corrected QT interval (QTc) of 485 milliseconds (reference QTc, <440 milliseconds). Because of the importance of this finding in a child with syncope you manually measure the QT interval, from the beginning of the QRS complex to the end of the T wave, and use one of the online calculators that corrects for heart rate. This confirms a prolonged QT interval, similar to that on the ECG shown in Figure 1.

What are the potential causes for this presentation?

The causes of syncope in children are listed in Table 1.[1,2] Hayden has exertional syncope in the setting of a family history of probable sudden cardiac death in a second-degree relative. This, along with Hayden's description of palpitations and the prolonged QT interval on ECG, suggests a cardiogenic cause of syncope. Although further cardiac investigations are indicated, you suspect that he has congenital long QT syndrome (LQTS). Secondary causes for a prolonged QT interval among the general population include electrolyte disturbances, hypothermia, myocardial ischaemia and many medications, including antipsychotics, antiarrhythmics, tricyclic antidepressants and antihistamines. It is unlikely that children will have been prescribed these drugs, but this may be ruled out before investigating further.

Should Hayden go to hospital?

Features that would require immediate referral to hospital include presyncope or syncope at rest or on minimal exertion,

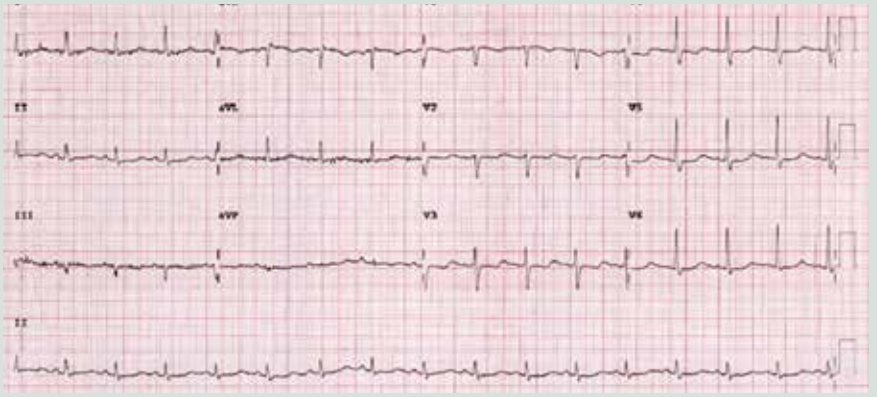

Figure 1. ECG of an adult patient with congenital long QT syndrome. Prolonged QT segment is seen best in lead II.

head injury, heart rate or blood pressure outside normal limits and ECG evidence of a ventricular arrhythmia.

You arrange for Hayden to see a paediatric cardiologist, who orders echocardiography and genetic testing. Holter monitors are of limited value for people with LQTS. In the meantime, the cardiologist advises that it is not safe for Hayden to exercise, and he cannot play soccer until further notice. You check his electrolyte levels and full blood count results, both of which are normal.

How is long QT syndrome diagnosed?

Congenital LQTS is a cardiac channelopathy causing delayed repolarisation of myocardium in a structurally normal heart and carries an increased risk for syncope and sudden cardiac death. The incidence of LQTS is up to one in 2500, and it is most commonly inherited in an autosomal dominant pattern, and very rarely in an autosomal recessive pattern.[3] The Schwartz Score (Table 2) provides a scoring system to predict probability of LQTS in patients of all ages, and is based almost completely on the patient's phenotype.[4] The patient's genotype is also analysed, as LQTS mutations in at least 15 genes have been identified.[3] However, the main benefit of genotyping is in the cascade testing of family members once a pathological genotype has been identified. As for any medical procedure, informed consent for genetic testing is given by the individual who is being tested, or their legal guardian. The cost of genetic testing is sometimes covered by clinical genetics and cardiology services, however commercial laboratory testing is not covered by Medicare and may cost in the hundreds to thousands of dollars. Electrophysiological studies are not usually helpful in making the diagnosis.

Hayden scores five points using the Schwartz scoring system, based on a prolonged QT interval and syncope after physiological stress. This classifies him with a high probability of having LQTS. The second percentile range for heart rate in his age group is 49 to 101 beats per minute at rest.

The Schwartz criteria include congenital deafness due to a rare familial syndrome (Jarvell and Lange-Nielson syndrome) that includes severe sensorineural deafness and LQTS, along with low gastric acid secretion and iron deficiency anaemia.[3] The inclusion of family members with confirmed LQTS includes those having received a clinical diagnosis, given not all genes are identified and some diagnoses may predate genetic screening.

How is LQTS managed?

Beta blocker therapy should be initiated in patients with LQTS who have had symptoms, or those with a QTc of >470 milliseconds, particularly in preadolescent boys such as Hayden.[3] Metoprolol should not be used. Propranolol is preferred.[4,5] In males at high risk due to having the LQT1 genetic subtype, the reduction in fatal arrhythmias by using appropriate beta blockers is 67%.[6]

In addition, cardiac sympathectomy is a treatment option for patients who have

Table 1. Causes of syncope in children[1,2]

Cause	Proportion of syncope presentations to the ED
Cardiogenic causes	
Hypotension (e.g. hypovolaemia, hypoaldosteronism, anaphylaxis)	2 to 5%
Structural heart disease (e.g. hypertrophic cardiomyopathy, congenital heart disease, arrhythmogenic right ventricular cardiomyopathy)	
Arrhythmia (e.g. pre-excitation syndrome, Brugada syndrome, long QT syndrome, catecholaminergic polymorphic ventricular tachycardia)	
Neurocardiogenic causes	
Vasovagal	70 to 90%
Conditions that mimic syncope	
Seizure disorder	5 to 9%
Hyperventilation	1%
Hypoglycaemia	2%
Narcolepsy	–

Abbreviation: ED = Emergency Department.

symptoms despite beta-blockade. This involves surgical removal of the first three or four thoracic sympathetic ganglia and results in significant reduction of fibrillation and cardiac events.[4]

Implantable cardioverter defibrillator (ICD) placement is considered by the cardiologist, based on risk factors and clinical scoring tools. ICDs are recommended in patients who have experienced resuscitated cardiac arrest (strong recommendation), or recurrent arrhythmic syncope while taking beta blockers (moderate recommendation).[3] Ultimately, the risk of life-threatening arrhythmia is balanced against the risk of inappropriate shocks, periprocedural or late complications of device and lead placement and the burden of activity limitations that accompany ICD implantation. Subcutaneous ICD systems are preferred in young patients who do not require pacing, as they reduce the complications that arise from transvenous ICD access.[3]

Triggers for life-threatening arrhythmias can be reduced if patients follow lifestyle guidelines specific to the genetic subtypes of LQTS. In people with the LQT1 subtype, arrhythmias are frequently triggered by exercise or emotional upheaval, and swimming and diving are generally contraindicated. People with the LQT2 subtype are at high risk of arrhythmias if they have derangements of serum potassium levels or experience sudden loud noise, and are advised to avoid loud alarm clocks and telephones. People with the LQT3 subtype can develop arrhythmias at rest or in their sleep, and are advised not to sleep alone or to have an intercom system to detect changes in breathing.[5] LQT1, LQT2 and LQT3 together account for up to 85% of cases of familial LQTS.

An adult patient with a similar presentation to Hayden would be investigated and managed in the same manner, and warrants referral to cardiology and genetic services. Overall, LQTS is the most common of the cardiac channelopathies. Others include Brugada syndrome, short QT syndrome and catecholaminergic polymorphic ventricular tachycardia.[7] All can result in sudden cardiac death, and if suspected the patient should be referred urgently for further investigation.

Outcome: Hayden was found to have a KCNQ1 gene mutation, correlating to the LQT1 subtype. He was instructed not to swim until further notice. Hayden was started on propranolol, which was uptitrated over several weeks. He had no further symptoms and the decision for ICD implantation was safely deferred. Hayden's family underwent genetic testing. Hayden's father and brother were negative for the mutation. Hayden's mother, who was asymptomatic and 43 years of age, was found to have a positive genotype despite a negative phenotype and a normal QTc on stress ECG. This highlights the incomplete penetrance of genetic mutations that is one of the clinical hallmarks of LQTS. Not all people with the mutation will have clinical signs or be at risk. Hayden's extended maternal family were referred for genetic testing. The Australian Genetic Heart Disease Registry has a wealth of resources for families like Hayden's, with a list of services and referral centres in Australia and New Zealand for genetic cardiology disorders.[8] CT

Table 2. The Schwartz criteria for diagnosis of LQTS[3]

Criteria		Points
*ECG findings**		
A	QTc† in males or females of:	
	≥480 milliseconds	3
	460–479 milliseconds	2
	450–459 milliseconds (in males only)	1
B	QTc at fourth minute of recovery from exercise stress test ≥480 milliseconds	1
C	Torsade de pointes‡	2
D	T wave alternans	1
E	Notched T wave in three leads	1
F	Low heart rate for age§	1
Clinical history		
A	Syncope‡	
	With stress	2
	Without stress	1
B	Congenital deafness	0.5
Family history‖		
A	Family members with confirmed LQTS	1
B	Unexplained sudden cardiac death in first degree family members who were <30 years of age	0.5

Abbreviations: LQTS = long QT syndrome; QTc = corrected QT interval.

Total score: ≤1, low probability of LQTS; 2–3, intermediate probability of LQTS; ≥3.5, high probability of LQTS.

* In the absence of medications or disorders known to affect these ECG features.

† Calculated by Bazett's formula: QTc = QT interval/√RR interval (milliseconds).

‡ Mutually exclusive.

§ Resting heart rate below the second percentile for age.

‖ The same family member cannot be counted for A and B.

References

A list of references is included in the online version of this article (www.cardiologytoday.com.au).

COMPETING INTERESTS: None

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