Fatal Case of Delayed Repolarization Due to Cocaine Abuse and Global Ischemia

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When a previously healthy, middle-aged patient presents with apparent seizures, what should alert the physician to the possibility of underlying cardiac disease? This report describes a case of long QT syndrome, initially presenting as seizures, which expressed itself at an atypically advanced age as a result of cocaine use, global myocardial ischemia, and ventricular tachycardia. [Rev Cardiovasc Med. *2003;4(1):47–53*]

Key words: Syncope • Seizure • Long QT syndrome • Torsade de Pointes • Electrocardiogram

Syncope affects 30%–50% of adults at some point in their lives and is responsible for up to 6% of emergency room visits and up to 1% of hospital admissions each year.[1,2] It is a common manifestation of various noncardiac diseases and can be mistaken for seizures,[3] which are also prevalent in the adult population.[4,5] The literature is also replete with reports of cardiac syncope in young individuals, especially due to arrhythmias, presenting and misdiagnosed as seizures.[6-11] The history and physical examination are the guideposts to clinicians in diagnosing cardiac syncope and ruling out seizures,[6] thus enabling identification of the correct cause of syncope.[12] Many consider resting and ambulatory electrocardiography useful in the evaluation of syncope.[13-15] In addition, assessment of left ventricular function is essential in determining the probability of a serious ventricular arrhythmia as an underlying cause. We describe an interesting patient who presented with seizures as an initial symptom of life-threatening cardiac arrhythmia due to a common underlying cardiac disease.

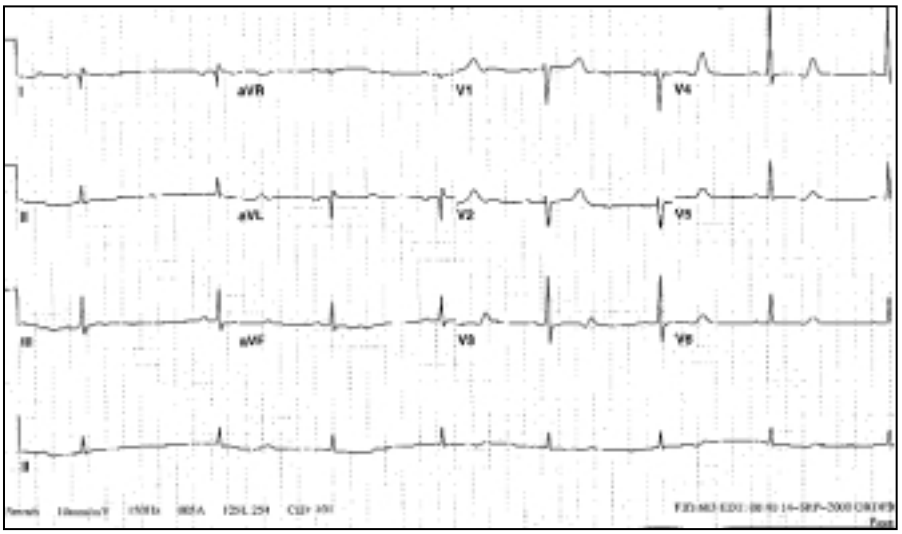
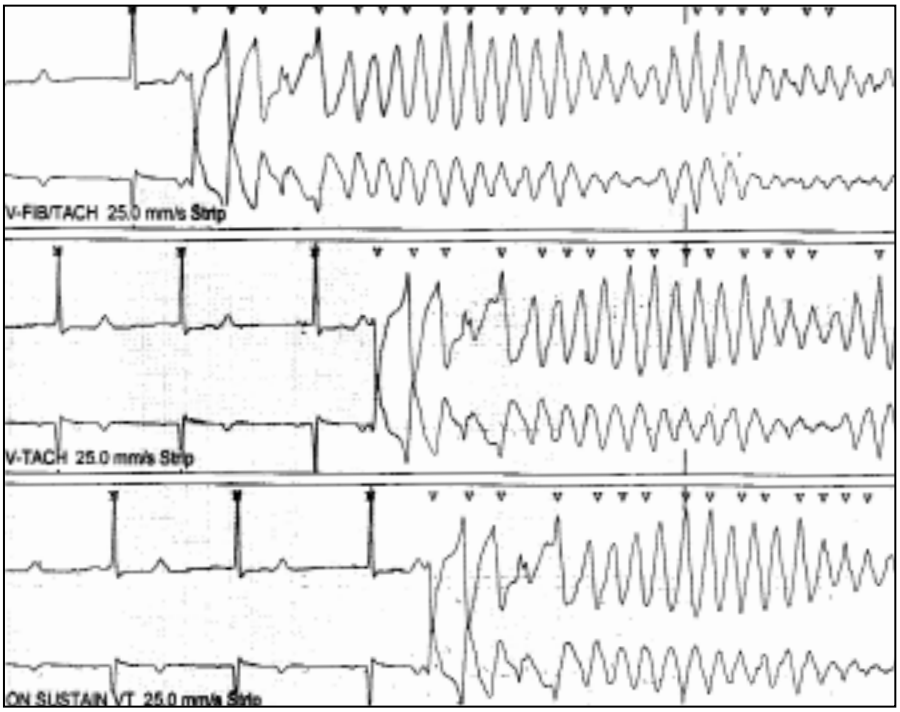


Figure 1. *Admission electrocardiogram at initial presentation showing prolonged QT/QTc interval.*

A previously healthy 61-year-old African-American male was brought to the emergency department with "seizures" after his spouse found him "thrashing around in the bed." The patient had no recollection of the events and denied any symptoms on presentation. He was not taking any medications and denied any drug allergies. The family history was unremarkable. The patient admitted past and current cigarette smoking for several years. Although he did not immediately disclose the fact, the patient was found to have used crack cocaine within 3 days prior to admission. Physical examination revealed a well-nourished, well-built male in a mildly anxious state, with pulse 54 beats/min and regular, blood pressure 140/78 mm Hg, respiratory rate 16 breaths/min, and no fever. Head examination revealed normal facies. Neck examination revealed normal carotid upstrokes without bruits, normal thyroid, and no elevation in jugular venous pressure. Heart examination revealed a normally placed point of maximal impulse and soft heart tones, without any murmurs or gallops. The lungs were clear to auscultation. The abdomen and extremities were normal, as were the results of neurological examinations.

Initial laboratory results were as follows: sodium 139 mmol/L, potassium 3.8 mmol/L, chloride 107 mmol/L, bicarbonate 21 mmol/L, creatinine 0.9 mg/dL, blood urea nitrogen 12 mg/dL, magnesium 2.7 mmol/L, and glucose 158 mg/dL. Serial troponin and creatine kinase tests were negative. The baseline lipid profile was as follows: total cholesterol 165 mg/dL, high density lipoprotein cholesterol 56 mg/dL, low density lipoprotein cholesterol 77 mg/dL, and triglycerides 167 mg/dL. The complete blood count, prothrombin time, partial thromboplastin time, and thyroid stimulating hormone levels were within normal limits. The urine drug screen was positive for cocaine metabolites. The chest x-ray revealed mild cardiomegaly and clear lung fields. The initial electrocardiogram (ECG) showed sinus bradycardia and prolonged QT and QTc intervals at 540 ms and 516 ms, respectively (Figure 1). A computed tomography head scan was normal. Echocardiography revealed an estimated ejection fraction of 45%. The patient was admitted to the hospital

Figure 2. *Single-lead tracings of Torsade de Pointes while in hospital.*



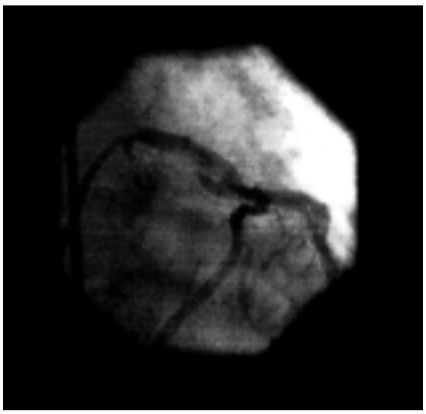


Figure 3. *Catheterization films showing high-grade left main disease.*

with a diagnosis of new-onset seizure disorder.

While in the intensive care unit, the patient had what appeared to be a seizure, with generalized stiffness of the body and some myoclonic jerking, lasting for less than a minute. At the time of the apparent seizure, the cardiac monitor displayed the rhythm shown in Figure 2, which then spontaneously reverted to sinus rhythm. A diagnosis of Torsade de Pointes (TdP) was made and the patient was treated with a 100-mg bolus of lidocaine followed by a 2-mg/min intravenous infusion. Over the next 12 hours the patient had two more episodes of TdP and syncope despite treatment with lidocaine and three intermittent boluses of magnesium (total of 6 grams) intravenously. Frequent sustained symptomatic TdP occurred, requiring cardioversion once. The storm of TdP was ultimately controlled with insertion of a temporary transvenous pacemaker, and pacing induced suppression at a rate of 80 beats/min. An amiodarone infusion was started with a 150-mg bolus over 10 minutes, and then 1 mg/min for 6 hours, followed by 0.5 mg/min for 48 hours. Metoprolol 25 mg twice daily was also started. Over the course of the next 3 days the underlying rhythm remained sinus bradycardia, and the QT interval remained prolonged.

Coronary angiography revealed a calcified 80% very proximal left main (LM) coronary artery lesion as shown in Figure 3, along with significant obtuse marginal (OM) and posterior descending artery (PDA) lesions. The patient underwent coronary artery bypass surgery at a neighboring institution with left internal mammary artery graft to left anterior descending (LAD) artery, sequential saphenous vein grafts (SVG) to first OM and left circumflex artery (LCX), and SVG to PDA branch of right coronary artery (RCA).

Postoperatively the patient required pacing for approximately 12 hours. His postoperative ECG showed normalization of the QTc of 435 ms, as displayed in Figure 4. The epicardial pacing wires were removed and the patient was discharged on the fifth postoperative day on aspirin 325 mg per day and metoprolol 25 mg twice a day. The patient was seen in follow-up 4 weeks after bypass surgery and was asymptomatic and recovering satisfactorily. A 12-lead ECG obtained at the time revealed normal QT/QTc, as shown in Figure 5. Three months later the patient presented to the emergency room with another episode of syncope. Baseline ECG revealed prolonged QTc of 510 ms and abnormal "T" waves in limb leads, as displayed in Figure 6. Electrolytes were within normal range with magnesium of 1.6 mmol/L and potassium of 4.5 mmol/L. Acute myocardial infarction was ruled out and a cardiac catheterization revealed sluggish flow in distal LAD and an occluded graft to LCX, whereas the grafts to OM branch of LCX and RCA were patent. Sluggish LAD flow was thought to be secondary to competitive flow. After a surgical consultation, the patient underwent percutaneous transluminal coronary angioplasty/stenting of LM, with excellent results. The patient also underwent placement of a pacemaker with atrial and ventricular leads for carotid sinus hypersensitivity. An electrophysiology study at the time failed to induce sustained ventricular arrhythmias. The patient's ECG at discharge showed a normal QTc interval of 428 ms, as shown in Figure 7. Attempts were being made to obtain DNA analysis to pinpoint any known genetic polymorphism for long QT syndrome (LQTS) when 6 weeks later he was readmitted with severe diarrhea, dehydration, and acute renal failure. The patient was volume resuscitated with improvement in his renal function. A 12-lead ECG obtained at the time of admission revealed normal QT/QTc. While being monitored in the coronary care unit, the patient developed polymorphic ventricular tachycardia, as shown in Figure 8, and attempts to resuscitate him were unsuccessful. The patient's family declined the request for an autopsy and genetic work-up.

Syncope can be a manifestation of long QT syndrome and Torsade de Pointes, which at times are misdiagnosed as a seizure disorder.

Discussion

Syncope can be a manifestation of LQTS and TdP, which at times are misdiagnosed as a seizure disorder.[6-11,16–18] We believe our patient had a subclinical form of LQTS that manifested itself in the form of syncope and

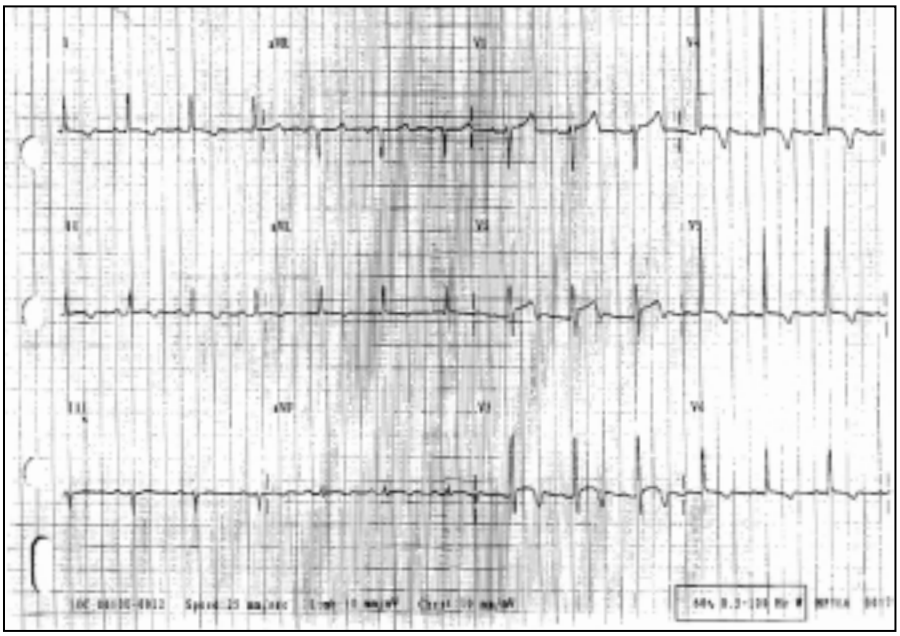


Figure 4. *Twelve-lead electrocardiogram after coronary artery bypass surgery showing normalization of QT/QTc interval.*

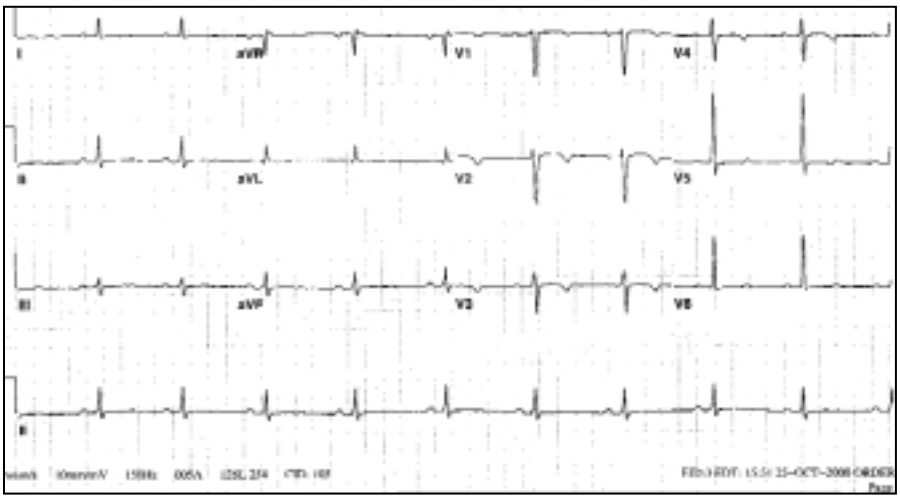


Figure 5. *Twelve-lead electrocardiogram 4 weeks after coronary artery bypass surgery.*

"seizures" brought on by cocaine ingestion and global myocardial ischemia and ventricular tachycardia. Despite the elimination of cocaine from the system at the initial hospital admission and abstinence from that point forward, continued ischemia without infarction precipitated a TdP storm, initially requiring multiple clinical responses and probably leading to the terminal events.

The causes of LQTS are broadly divided into two categories, congenital and acquired. Drugs, cardiac or noncardiac, are the main cause of acquired LQTS. Other causes include electrolyte disturbances, bradycardia, cerebrovascular accidents, and some special diets (Table 1).[19] Although usually not considered as a common or a definite cause of LQTS or TdP by itself, cardiac ischemia has appeared in case reports as a cause of prolonged QT interval and TdP.[20-23] Attempts have also been made to correlate the severity of coronary artery disease (CAD) and QT-interval prolongation.[24,25] Polymorphic ventricular tachycardia in patients with CAD is typically not pause dependent and there is usually no increase in the QT interval in the ECG complex preceding the initiation of the tachyarrhythmia.[26] Cocaine abuse has also been reported occasionally as a cause of syncope secondary to TdP due to congenital or cocaine-induced LQTS without cardiac ischemia.[27,28] Our case demonstrates that the presence of cocaine and severe ischemia in an individual with the genetic substrate of LQTS can be fatal.

Congenital LQTS typically presents with unexplained syncope in the second or third decade of life; it rarely presents later in life. There is usually a history of an event precipitating syncope. Family history of sudden cardiac death, LQTS, or unexplained syncope is frequently present. In addition, the patient may have sensorineural deafness, depending upon the genotype. The tachyarrhythmia associated with congenital LQTS is typically pause dependent (long-short cycle phenomenon) and there is frequently prolongation of the QT interval in the ECG complex preceding the TdP.[26] Electrophysiological studies are not very helpful in the diagnosis or work-up of LQTS, as TdP is not inducible by programmed electrical stimulation.[26] Various mutations (LQT1, 2, 3, 4, and 5) have been identified in the cardiac ion channel genes effecting rapid (I_{KR}) or slow (I_{KS}) component of the delayed rectifier potassium (K^+) current and sodium (Na^+) current (I_{Na+}) responsible for the LQTS. The genotype also influences the electrocardiographic

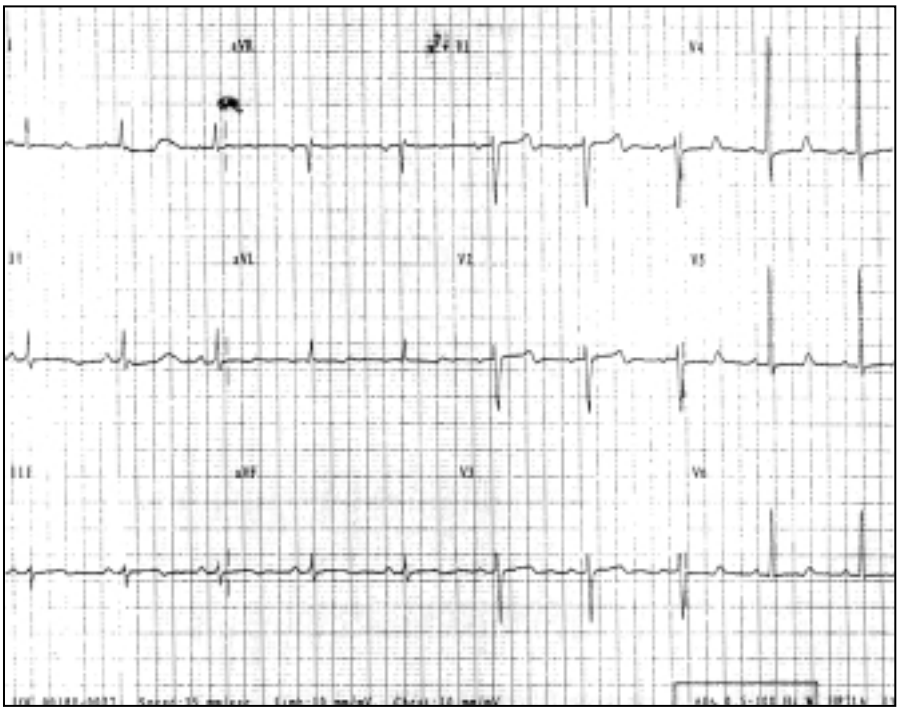


Figure 6. *Twelve-lead electrocardiogram on readmission 3 months later with syncope showing prolonged QT/QTc interval.*

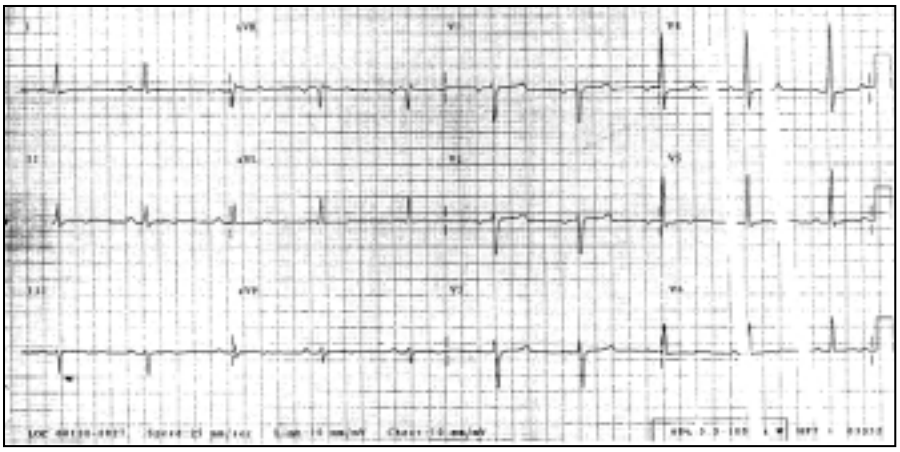


Figure 7. *Twelve-lead electrocardiogram after successful percutaneous transluminal coronary angioplasty/stenting of left main coronary artery, showing normal QT/QTc interval.*

manifestations and the clinical course of the disease.[29,30] Genetic mapping is currently not widely available and is used only to identify the members of the patient's family who are at risk.

According to the diagnostic criteria for congenital LQTS,[31] our patient scored 6.5 points, putting him in the high-probability group for idiopathic LQTS. Our patient had prolonged QTc interval (3 points), TdP (2 points), syncope (without stress, 1 point) and lower heart rate for age (0.5 points). There were no definite "T" wave abnormalities, congenital deafness, or previous history of any near or total syncope or seizures, and no family history of these events. Analysis of the rhythm strips revealed that at times the TdP was pause dependent and there was some prolongation of the QT interval in the preceding beat (typical of congenital LQTS). However, at other times both these phenomena were absent prior to the initiation of the arrhythmia (suggesting CAD-related polymorphic ventricular tachycardia). Whether the diagnostic criteria described here can be used in the presence of underlying ischemia is debatable. In addition, ideally, this patient should have had an exercise treadmill test to document the classic 50% reduction in the QT interval with exercise. However, he did not recover adequately between hospital admissions to allow us to administer the test. Furthermore, the QT/QTc corrected itself after each admission with intervention for CAD and abstinence from cocaine.

We believe that the prolonged repolarization and subsequent TdP in this patient were the initial manifestations of congenital LQTS, probably due to a low-penetrance gene polymorphism. The condition expressed itself at this later age with the development of significant CAD and perhaps the superimposed cocaine use.

Conclusion

We reported a case of prolonged repolarization as a result of cocaine use and global myocardial ischemia. The repolarization abnormality initially resolved after revascularization and abstinence from cocaine, only to recur with the occlusion of the grafts. Given the modern-day epidemics of coronary disease and cocaine use in American society, it is likely that this "face" of LQTS will be seen more frequently. This eventuality highlights the importance

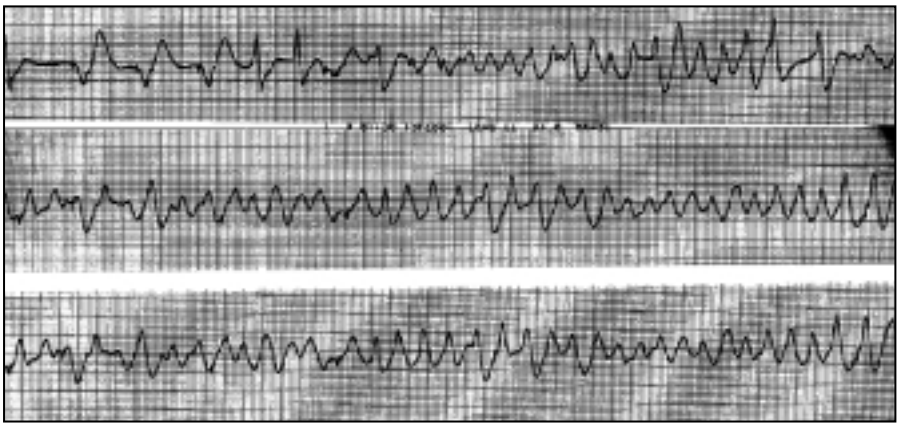


Figure 8. *Single-lead electrocardiogram during cardiac arrest showing polymorphic ventricular tachycardia.*

of future genetic epidemiological investigations into LTQS and its environmental precipitants. ■

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Table 1
Selected Causes of Acquired Long QT Syndrome

Exposure	Examples
Antiarrhythmic agents	Quinidine, procainamide, ibutilide disopyramide sotalol, amiodarone
Lipid-lowering agents	Probucol
Antibiotics	Trimethoprim-sulfamethoxazole, erythromycin, pentamidine
Antihistamines	Terfinadine,* astemizole
Antifungals	Ketoconazole, fluconazole, itroconazole
Gastrointestinal agents	Cisapride*
Antidepressants	Amitriptyline, imipramine, doxepin
Phenothiazines	Chlorpromazine, thioridazine
Antipsychotic agents	Haloperidol, risperidone
Bradycardia	Sinus bradycardia, atrioventricular block
Electrolyte and metabolic disturbances	Hypokalemia, hypomagnesemia, hypocalcemia
Central nervous system diseases	Stroke, intracranial hemorrhage
Special diet	Liquid protein diets, anorexia nervosa

* Withdrawn from U.S. market.

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Main Points

- Syncope affects 30%–50% of adults at some point in their lives.
- Syncope is a common manifestation of various noncardiac diseases and can be mistaken for seizures.
- Syncope/seizures can be initial symptoms of long QT syndrome (LQTS) and Torsade de Pointes (TdP).
- Causes of acquired LQTS include drugs, electrolyte disturbances, bradycardia, and some special diets.
- Congenital LQTS typically presents with unexplained syncope between the ages of 10 and 30, and family history of sudden cardiac death, LQTS, or unexplained syncope is usually present.
- The tachyarrhythmia associated with congenital LQTS is typically pause dependent and there is frequently prolongation of the QT interval in the electrocardiogram complex preceding the TdP.
- The presence of cocaine and severe ischemia in an individual with the genetic substrate of long QT syndrome can be fatal.