Syncope in a Woman With a History of Myocardial Infarction

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56-year-old woman presents for evaluation of several syncopal episodes that occurred during the past 2 weeks. These episodes were associated with various activities--eating while seated, walking slowly, and standing upright--and rendered her briefly unconscious.

A 56-year-old woman presents for evaluation of several syncopal episodes that occurred during the past 2 weeks. These episodes were associated with various activities--eating while seated, walking slowly, and standing upright--and rendered her briefly unconscious. However, she experienced no other symptoms before, during, or after the episodes.

The patient has a history of myocardial infarction (MI), which was managed with intracoronary stent placement; the MI caused no significant left ventricular dysfunction. Since the MI, her drug regimen has included metoprolol and aspirin. About 1 month ago, furosemide was prescribed for dependent lower extremity edema.

The patient is alert and oriented. Vital signs and physical findings are normal. A 12-lead ECG reveals significant T-wave inversion in the inferior, anterior, and lateral leads; this ECG was similar to an earlier tracing with respect to the T-wave inversion in the inferior, anterior, and lateral distributions.

She is referred to the emergency department (ED) for further evaluation. Before she is transferred, however, she experiences a syncopal episode that renders her unresponsive and without palpable pulse or respiratory effort. While appropriate cardiopulmonary resuscitation is started, an ECG monitor is placed, which reveals the rhythm strip shown at top (A). Immediately before defibrillation, the rhythm suddenly changes (B); the patient regains consciousness; and blood pressure, heart rate, and respiratory rate return to normal and stabilize.

On arrival in the ED, the patient is alert and has no complaints. The 12-lead ECG (C) is unchanged.
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from that obtained in the office.

**What do these ECG tracings reveal about the cause of this patient's recurrent syncope?**

**WHAT THE ECGs SHOW**

This patient has long QT syndrome (LQTS); in this electrophysiologic syndrome, the ventricular repolarization phase is lengthened.\(^1\) This lengthening of ventricular repolarization is demonstrated on the ECG by a prolongation of the QT interval (Figures 1 and 2).

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**WHAT THE ECGs SHOW**

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**Figure 1** – This ECG rhythm strip, which was obtained immediately after the patient experienced a spontaneous return of pulse, blood pressure, and respiration, following a syncopal episode, shows normal sinus rhythm.

**Figure 2** – This ECG, obtained when the patient presented to the emergency department, showed no change from an ECG obtained earlier in her physician’s office just before a syncopal episode. Note the prolonged QT interval. T-wave inversions, a result of her past myocardial infarction, are also present. However, these findings play no role in the current dysrhythmic presentation; earlier ECGs, obtained remotely, show that these diffuse T-wave abnormalities represent no significant change.

**Figure 3** – This ECG rhythm strip was obtained while the patient had no pulse or respiration. It shows torsade de pointes.

Although LQTS is defined by the lengthening of the QT interval on a 12-lead ECG, the name of the syndrome is a misnomer of sorts. The QT interval reflects not only repolarization but also depolarization of the ventricle. Thus, "long JT syndrome" would be a more accurate name; the J point is the juncture of the QRS complex, and it is the lengthening of the JT interval that specifically reflects prolongation of the ventricular repolarization phase. Patients with LQTS are at risk for sudden cardiac death, usually as a result of polymorphic ventricular tachycardia (PVT).\(^2\) While this woman’s 12-lead ECG shows lengthening of the QT interval, the rhythm strips obtained during her syncopal episode reveal PVT (Figure 3). The type of PVT she experienced—torsade de pointes—is characterized by the presence of abnormal ventricular repolarization, as demonstrated by QT-interval prolongation.

**PATHOPHYSIOLOGY**

The electrical activity of the heart is regulated by the flow of ions in and out of cardiac cells; disruption of this flow alters the depolarization/repolarization of the heart. In a normal cardiac cycle, the inflow of positively charged ions results in depolarization of the myocardium. When the outflow of positively charged ions exceeds the inflow, myocardial repolarization occurs. In LQTS, an excess of positively charged intracellular ions—which can result from either excessive inflow or inadequate outflow—extends ventricular repolarization and causes prolongation of the QT interval.\(^3\)

**ETIOLOGY**

LQTS can be either congenital or acquired. Congenital LQTS is attributed to gene mutations that result in abnormalities in the transmembrane channels that regulate the sodium and potassium currents.\(^1\) Both autosomal dominant and autosomal recessive forms of inheritable LQTS have been
identified. The various forms of congenital LQTS have different presentations. The best-described congenital forms are Jervell and Lange-Nielsen syndrome (a rare autosomal recessive disorder associated with marked QT prolongation and congenital deafness) and Romano-Ward syndrome (a more common autosomal dominant disorder with less potential for dysrhythmia). Prolongation of the QT interval can also be an acquired condition. Causes include medications, electrolyte imbalance, toxins, ischemic heart disease, severe bradycardia (as in sick sinus syndrome), and various systemic events and illnesses.

Medications are the most common cause of acquired QT-interval prolongation. Cardioactive agents that prolong the QT interval are often implicated: these include class IA antidyssrhythmics (procainamide, quinidine, and disopyramide) and class III antidyssrhythmics (ibutilide, sotalol, and amiodarone). Other drugs that prolong the QT interval are antibiotics (eg, erythromycin, trimethoprim-sulfamethoxazole, and sparfloxacin), antifungal agents (eg, ketoconazole and itraconazole), psychopharmacologic agents (eg, tricyclic antidepressants and haloperidol), antihistamines (eg, astemizole and terfenadine), and tacrolimus. Because QT-interval prolongation develops in only a minority of patients who use these medications, it is believed that those in whom drug-induced prolongation does occur probably have a mild form of congenital LQTS.

Electrolyte disorders are the second most frequently seen cause of acquired QT-interval prolongation. Hypokalemia, hypomagnesemia, and hypocalcemia are common causes of acquired LQTS. Numerous toxins, including cocaine and insecticides that contain organophosphates, can also lengthen the QT interval. Acute systemic events that affect other organ systems, such as subarachnoid hemorrhage and hypothyroidism, have also been known to prolong the QT interval.

Finally, cardiac abnormalities, such as myocardial ischemia and severe bradycardia (as in sick sinus syndrome), can sometimes precipitate torsade de pointes, secondary to QT-interval prolongation.

**DIAGNOSIS**

**Clinical features.** Patients with LQTS may present with a variety of symptoms, ranging from mild dizziness to syncope or, in the extreme, sudden cardiac death. Alternatively, a prolonged QT interval may first be noted as an incidental finding on evaluation of another unrelated complaint. Congenital LQTS usually first becomes apparent in childhood and early adolescence. In patients with congenital LQTS, symptoms—including sudden death—are most likely to occur after an adrenergic surge, such as that caused by physical exercise, emotional stress, sleep deprivation, or auditory stimuli. The risk of sudden death is also greater in the early morning when the QT interval is at its peak.

**ECG features.** The QT interval varies inversely with heart rate. The QTc interval, or "corrected QT interval," takes into account the effect of heart rate. It can be calculated with the Bazett formula, or when the heart rate is between 60 and 100 beats per minute and the patient is in sinus rhythm, it can be evaluated by comparing the length of the RR and QT intervals. These techniques are explained in the Box. In the majority of patients with LQTS, the QTc interval is more than 440 milliseconds. The risk of sudden death in patients whose QTc interval is more than 440 milliseconds is 2 to 3 times greater than that in patients whose QTc interval is less than 440 milliseconds. The QT interval typically lengthens with age and is longer in women than in men; different cutoff values for LQTS are thus used in men and women and in the elderly.

In about 10% of patients with LQTS, the QTc interval is normal. In such patients, the diagnosis is difficult to establish and is dependent on other findings, including T-wave and U-wave abnormalities. The QT interval may be more variable, and T waves may be larger, prolonged, or bizarre-looking and may have a bifid, biphasic, or notched appearance. T wave alternans is rare but is highly suggestive of LQTS. It is characterized by beat-to-beat variability in the T-wave amplitude and is caused by the increased electrical instability during repolarization. The U-wave abnormalities that are sometimes seen include bizarre-looking and pronounced U waves; U wave alternans may also occur.

The most troublesome ECG manifestation of LQTS is torsade de pointes. PVT (of which torsade de pointes is one type) is diagnosed when the QRS-complex configuration is not stable when viewed in a single ECG lead (eg, the QRS-complex electrical axis or amplitude demonstrates episodic changes, or more than 2 QRS-complex morphologies are present in any single lead [see Figure 3]). Syncope and sudden cardiac death can result from rapidly recurring or sustained episodes of torsade de pointes, which ultimately degenerate into ventricular fibrillation.

**Diagnostic criteria.** Ultimately, the diagnosis is based on a combination of factors, including both ECG and clinical features. Schwartz and colleagues developed a set of diagnostic criteria with assigned point values. This quantitative approach allows the clinician to determine the probability of LQTS objectively—as low, intermediate, or high (Table).
### Table — Criteria for the diagnosis of long QT syndrome

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Point Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG findings</td>
<td></td>
</tr>
<tr>
<td>QTc &gt; 480 ms</td>
<td>3</td>
</tr>
<tr>
<td>QTc = 460 - 470 ms</td>
<td>2</td>
</tr>
<tr>
<td>QTc = 450 ms (in males)</td>
<td>1</td>
</tr>
<tr>
<td>Polymorphic ventricular tachycardia</td>
<td>2</td>
</tr>
<tr>
<td>T wave alternans</td>
<td>1</td>
</tr>
<tr>
<td>Notched T waves (in at least 3 leads)</td>
<td>1</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>.05</td>
</tr>
<tr>
<td>Clinical history</td>
<td></td>
</tr>
<tr>
<td>Syncope with stress</td>
<td>3</td>
</tr>
<tr>
<td>Syncope without stress</td>
<td>1</td>
</tr>
<tr>
<td>Congenital deafness</td>
<td>.05</td>
</tr>
<tr>
<td>Family history of long QT syndrome</td>
<td>1</td>
</tr>
<tr>
<td>Family history of sudden death before 30 y (immediate family)</td>
<td>.05</td>
</tr>
</tbody>
</table>

*Scoring: ≤ 1 point = low probability; 2 - 3 points = intermediate probability; ≥ 4 points = high probability.

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

‡ Polymorphic ventricular tachycardia and syncope cannot both be counted in the same patient.

§ The same family member cannot be counted twice.


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**MANAGEMENT**

Stabilization of the heart rhythm is a primary focus in the management of prolonged QT interval-related dysrhythmia. For patients in sustained PVT, emergent treatment involves stabilization via standard electrical defibrillation, together with strategies to prevent PVT recurrence. These strategies include correction of any electrolyte abnormality, removal of any potentially offending agent, and institution of temporary transvenous overdrive cardiac pacing if needed.
Evaluating the QTc Interval: Bazett Formula—and a Simple Bedside Technique

The Bazett formula can be used to calculate the QTc interval in any patient:

$$\text{QTc} = \frac{\text{QT}}{(\text{RR})^{0.5}}$$

Divide the measured QT interval (in seconds) by the square root of the RR interval (in seconds). A QTc interval greater than .440 second, or 440 milliseconds, is seen in most patients with long QT syndrome.

When a patient is in sinus rhythm and the heart rate is between 60 and 100 beats per minute, the QTc interval can be evaluated at the bedside simply by comparing the length of the RR interval with that of the QT interval. The QTc interval is not prolonged if it is less than half the length of the accompanying RR interval. In the Figure below, for example, the QT interval is significantly longer than half the length of the RR interval; thus, the QTc interval is clearly prolonged. (Application of the Bazett formula confirms this result. The QT interval measures 0.420 s, and the RR interval, 0.780 s. Thus, the QTc interval = 0.420 ÷ [0.780]^{0.5} = 0.480.)

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Figure – In this ECG complex, the QT interval is more than half the length of the RR interval. This is evidence that the patient’s QTc interval is prolonged.
Intravenous electrolyte replacement is a vital part of early management. Intravenous magnesium is highly effective at terminating torsade de pointes as well as suppressing future recurrences in both the congenital and acquired forms of LQTS, regardless of the serum magnesium level. Intravenous administration of potassium is also important for the short-term management of torsade de pointes. Given along with intravenous magnesium, it can help prevent recurrences as well. Temporary cardiac pacing, via either a transcutaneous or transvenous route, is another effective short-term means of preventing recurrences of torsade de pointes. Initiate pacing at a rate of 90 to 110 beats per minute when intravenous magnesium fails to prevent recurrences. The acquired form of LQTS generally does not require any long-term treatment. Attention to the offending event (eg, cessation of a medication, correction of an electrolyte imbalance, or restoration of an adequate heart rate) is often curative. However, long-term treatment of congenital LQTS is essential to prevent recurrences of torsade de pointes. The most commonly used agents in this setting are b-adrenergic blocking agents. These agents prevent the development of dysrhythmia by blocking the adrenergic surge that usually precipitates torsade de pointes in congenital LQTS. For patients who do not respond to b-adrenergic blocking agents, a permanent pacemaker that shortens the long QT interval is often implanted. Implantation of a cardioverter-defibrillator is used as a third-line strategy when the combination of b-adrenergic blocking agents and a pacemaker fails. However, most electrophysiologists prefer to use this device as a first-line strategy in patients with symptomatic congenital LQTS. It is important to continue b-blocker therapy indefinitely, regardless of the implantation of any electrical device. There is some debate about whether asymptomatic patients with congenital LQTS require treatment. Because sudden death is the first symptomatic event in 30% to 40% of patients with congenital LQTS, most cardiologists treat asymptomatic patients who are younger than 40 years with b-adrenergic blocking agents. In addition, the screening of family members can potentially reduce the number of future sudden deaths.

OUTCOME OF THIS CASE

Results of the physical examination were unremarkable. Laboratory studies revealed low serum magnesium and potassium levels (0.4 mEq/dL and 2.3 mEq/dL, respectively). Replacement therapy was initiated in the ED and was continued in the inpatient unit. Furosemide therapy was discontinued while serum electrolytes were closely monitored. With electrolyte replacement, the QTc interval normalized. Acquired LQTS was diagnosed, probably the result of electrolyte abnormalities caused by diuretic therapy. The patient's ED and hospital course was uneventful; no further syncope or dysrhythmia was noted.

References: REFERENCES:
3. Al-Khatib SM, LaPointe NM, Kramer JM, Califf RM. What clinicians should know about the QT interval. JAMA. 2003;289:2120-2127.


Links:
[1] [http://www.physicianspractice.com/authors/richard-harrigan-md](http://www.physicianspractice.com/authors/richard-harrigan-md)
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