A CASE FOR EDUCATION

The approach to pediatric syncope with exercise

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Introduction

Syncope is defined as a temporary loss of consciousness and postural tone resulting from an abrupt transient decrease in cerebral blood flow.[1] It is a relatively frequent symptom in children, peaking around the age of 15 years.[2] Whereas the vast majority of episodes of syncope are benign, a minority of events can be more serious or even life threatening.

The group of patients who may be considered high risk and thus require additional cardiac workup include those with syncope during peak exercise or immediately after exercise, family history of unexplained death (cardiac arrest), convulsive or traumatic syncope, chest pain preceding syncope, syncope with structural heart disease, syncope with an abnormal cardiovascular examination, or syncope with focal neurologic defects.[1] Exercise-related syncope can occur either during or immediately after a period of exercise. Syncope that occurs during exercise tends to raise more concerns than that occurring in the postexertional state. Although the great majority of cases of syncope are benign and have a favorable outcome, young and otherwise healthy patients who present with exertional (rather than nonexertional) syncope have a greater probability of an organic etiology.[3,4] Evaluation and workup for these patients should be done very carefully and thoroughly.

For educational purposes, we will review 2 case reports demonstrating the evaluation for very different but important clinical presentations.

Case report

Case 1

A 14-year-old athletic male subject presented to clinic after a syncopal event with peak exertion. He reported he was running in a short-distance race. He got to the finish line and felt lightheaded and dizzy, nauseated, clammy, and weak. His vision went black and he lost consciousness. He recovered after about a minute. He had a relatively weak pulse and he was spontaneously breathing during this time, per his teammate's report. His past medical history was negative. He had a family history significant for his father having a history of supraventricular tachycardia that was ablated when he was a teenager. He did not report taking any medications. An electrocardiogram (ECG) (Figure 1) was obtained in clinic and showed normal sinus rhythm with an RSR′ pattern in V_1–V_2. An echocardiogram was obtained and was normal for age. A cardiac magnetic resonance image was done for further coronary artery anatomy evaluation and was normal. An exercise test was obtained that demonstrated normal ECG, blood pressure, oxygen saturation, and functional capacity with no ectopy or ST-segment changes from baseline, with a normal chronotropic response. It was noted during testing that his blood pressure and heart rate response were consistent with relative intravascular volume depletion, defined by an increase in heart rate with standing >30 beats per minute, a drop in systolic blood pressure during immediate recovery followed by a rebound, and/or delayed heart rate recovery.

Case 2

A 12-year-old female subject presented to the emergency room after collapsing while running during gym class. The teacher reported seeing her running and collapsing suddenly. The patient did tell her friend that she felt "funny" prior to the event. She was unconscious for about a minute and seemed confused after the event, returning to baseline about 30 minutes later. Per report she had a small amount of emesis and her arms looked stiff, associated with a tremor. She did not have bladder incontinence. Her past medical and family history were benign. An ECG was obtained (Figure 2), which demonstrated a normal sinus rhythm and marked QTc prolongation with a very abnormal morphology (bifid T waves in inferior and precordial leads). An echocardiogram was done and was normal for age. She did have a head computed tomography and electroencephalogram that were negative. An

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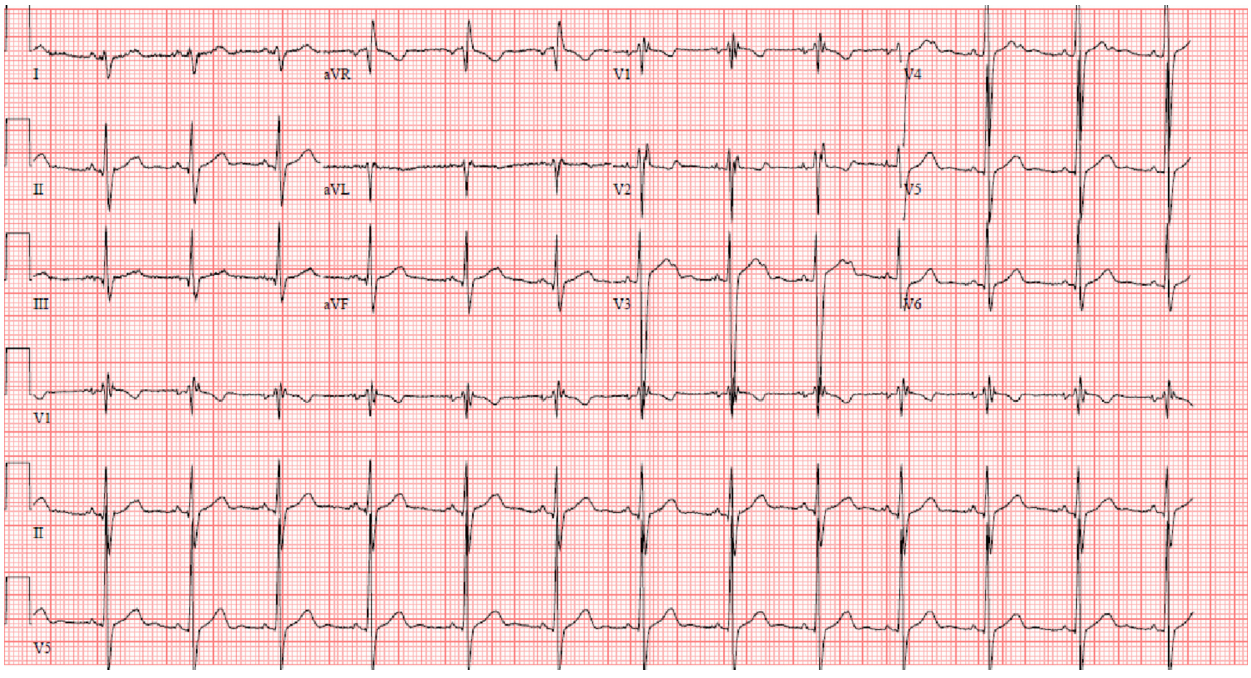

Figure 1 Baseline electrocardiogram (rate 79 beats/minute, PR 138 ms, QRS 90 ms, QTc 456 ms).

exercise test was done that demonstrated a prolonged QTc at baseline that shortened with exercise and prolonged in late recovery (Figure 3A–D). Genetic testing was done that revealed a de novo pathogenic *KCNH2* variant, which confirmed a diagnosis of long QT syndrome (LQTS) type 2.

Discussion

The clinical presentation associated with a syncopal event with exercise is very important. In most cases, exercise-related syncope is not an indicator of serious underlying cardiac disease. A prodrome consisting of vision changes, nausea, epigastric discomfort, a clammy and cold sweat, pallor, dizziness,

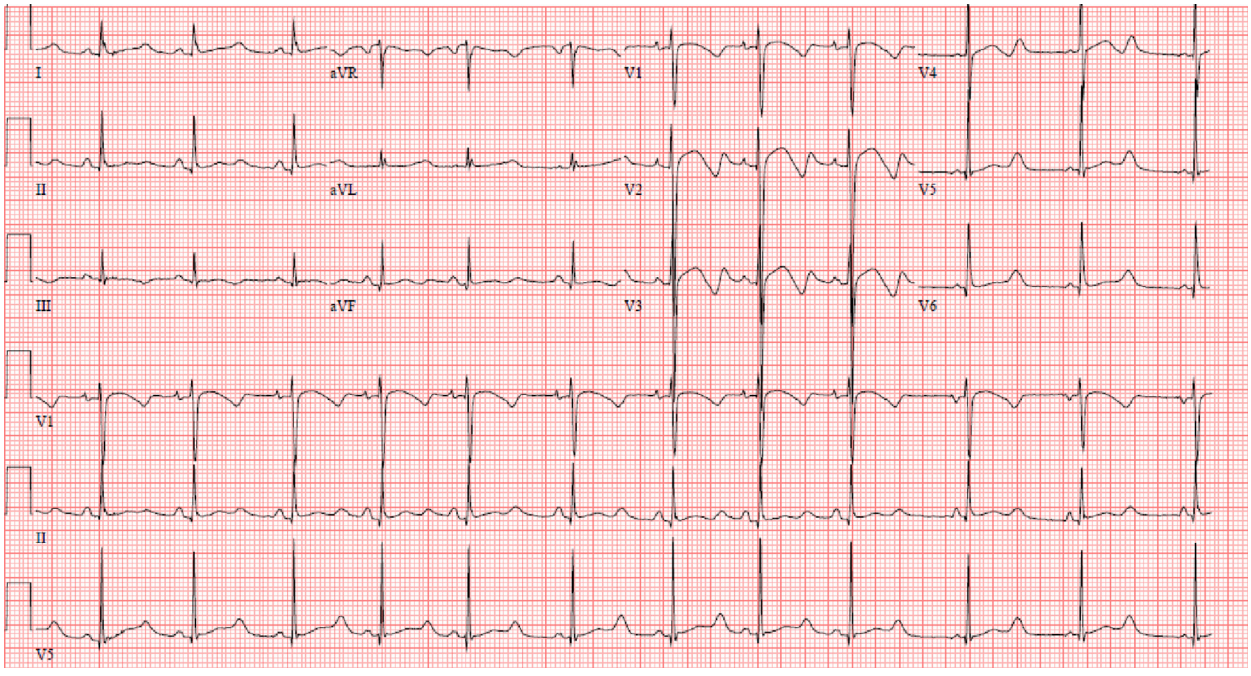

Figure 2 Baseline electrocardiogram (rate 71 beats/minute, PR 140 ms, QRS 86 ms, QTc 586 ms).

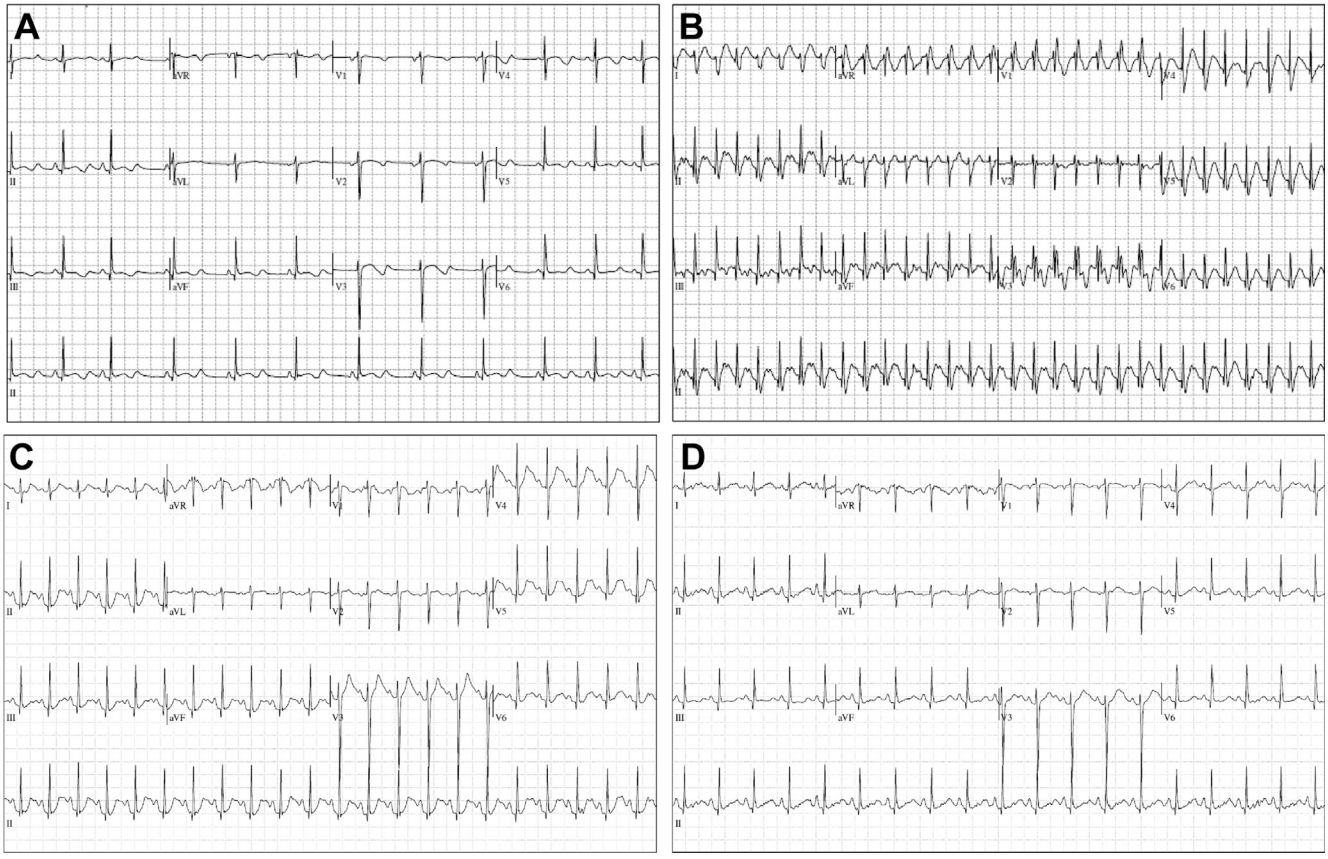

Figure 3 **A:** Baseline exercise test electrocardiogram (ECG) (QTc 510 ms). **B:** ECG with exertion during exercise test, heart rate (HR) 181 beats per minute (bpm), stage 6 of exercise (QTc 412 ms). **C:** ECG 2 minutes post exertion, HR 136 bpm (QTc 472–491 ms). **D:** ECG 4 minutes post exertion, HR 111 bpm (QTc 531 ms).

lightheadedness, tunnel vision, headache, and weakness suggests neurocardiogenic syncope or hypotension due to intravascular volume depletion, as in case 1. More characteristically, these patients start having prodromal symptoms during exercise, but do not faint until immediately after stopping exercise, owing to the withdrawal of sympathetic tone in the context of dehydration, or alternatively owing to a Bezold-Jarisch reflex triggered by catecholamine-induced increased ventricular contractility, subsequently leading to enhanced parasympathetic tone.[5] On the other hand, palpitations, chest discomfort, and a sudden loss of consciousness with minimal or no prodrome is more compatible with a cardiac etiology, as with case 2, warranting further evaluation. Studies have shown that children with mid-exertional syncope are at risk for cardiac disease and warrant evaluation. Reported symptoms may not differentiate benign causes from life-threatening disease.[6]

In addition to the clinical history, physical examination and the family history are vital in the evaluation of syncope. During the physical examination, orthostatic vital signs should be obtained, with close attention to the cardiac assessment. It is not uncommon to obtain a history of multiple family members who experienced syncope during adolescence, as there is a familial tendency toward vasovagal syncope. However, it is important to seek further clarification for the cause of these episodes, considering specific familial cardiac disorders. A sudden, unexplained history of cardiac arrest/death in children or young adults, seizures, or familial deafness should raise suspicion. These findings will help to dictate further testing and management.

The recent 2017 ACC/AHA/HRS guidelines for patients with syncope state that for the initial evaluation of patients with syncope, a resting 12-lead ECG is useful and indicated (class I recommendation). Routine and comprehensive laboratory testing is not useful in the evaluation of patients with syncope (class III recommendation: No Benefit). In addition, routine cardiac imaging is not useful in the evaluation of patients with syncope unless cardiac etiology is suspected based on an initial evaluation including history, physical examination, and ECG (class III recommendation: No Benefit).[7] Particularly in patients who experience syncope with exercise, exercise testing to reproduce symptoms can be helpful, in addition to Holter and long-term event monitoring. Understanding that the diagnostic evaluation can be quite involved and expensive is important in a careful and thoughtful approach to these patients.

Case 2 revealed the diagnosis of LQTS type 2. LQTS can be congenital or acquired, with mutations in at least 17 genes

identified thus far. This case, although clearly demonstrating a pathologic syncope, does not show a classic presentation for LQTS type 2. This further emphasizes the need for a detailed synthesis of information before premature conclusion of the diagnosis. The diagnostic approach should begin with a comprehensive clinical and family history in addition to a physical examination and review of the ECG. The diagnosis of LQTS should be suspected in the presence of a risk score $\geq$3.5 on the modified Schwartz scale[8] in the absence of an acquired cause for QT prolongation and/or in the presence of an unequivocally pathogenic mutation in 1 of the known LQTS-related genes or in the presence of a QTc $\geq$500 ms in repeated 12-lead ECGs and in the absence of acquired causes for QT prolongation. Of note, LQTS can be diagnosed in the presence of a QTc between 480 and 499 ms in repeated 12-lead ECGs in a patient with unexplained syncope in the absence of an acquired cause for QT prolongation and in the absence of a pathogenic mutation. Making the diagnosis and risk-stratifying these patients can be challenging, as patients may or may not show QTc prolongation or a life-threatening arrhythmia event. Holter monitoring and exercise testing are helpful to look for arrhythmias, dynamic T-wave changes, and also the presence of a maladaptive QT response during the recovery phase of exercise predominately for type I and type 2 LQTS patients. Genetic testing is reserved for patients with high clinical suspicion based on the presenting and family history, ECG findings, results of additional testing, and a high Schwartz score. Regardless of genotype, all patients with congenital LQTS should be advised to avoid medications that prolong the QTc, and replace electrolytes during vomiting or diarrheal illnesses.

The prognosis for vasovagal or neurocardiogenic syncope is favorable. Most patients show spontaneous resolution of their events in 6–12 months following the onset of the episodes.[5] Driving restrictions do apply to patients, and the length of time depends on state laws. Exercise restrictions are recommended in patients presenting with syncope suspected to be of an arrhythmic etiology. Participation in competitive sports is not recommended for athletes with syncope and phenotype-positive hypertrophic cardiomyopathy, catecholaminergic polymorphic ventricular tachycardia, LQTS1, or arrhythmogenic right ventricular cardiomyopathy before evaluation by a certified electrophysiologist (class III recommendation: Harm).[7] There is a recent tendency for an individualized approach specific to the patient and family, which requires a very clear understanding of the implications of participation in sports and specific emergency planning agreed between the physician, the patient/caretakers, and the school or team officials.[9]

Conclusion

Syncope in children is common. The vast majority of these events are due to neurocardiogenic syncope. Patients who present with syncope during exercise should be carefully evaluated. An organized, detailed approach to the diagnosis, with particular attention to the details of the clinical presentation, will result in a timely and cost-effective evaluation. Although syncope with exercise is rare, further evaluation needs to be performed to rule out a more serious underlying cardiac structural or functional cause, including arrhythmias and genetic arrhythmias. Patient-specific diagnosis is important to optimally define treatment, restrictions, and prognosis.

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