Cardiopulmonary Medicine

Case Report

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Sudden cardiac death in a young male endurance athlete

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Abstract: Sudden cardiac death (SCD) is a rare yet devastating event that can occur in young athletes. Although hypertrophic obstructive cardiomyopathy is the most common cause of SCD, some other genetic abnormalities have been identified as proarrhythmic. However, there is not routine screening for these other genetic abnormalities. Furthermore, consumption of caffeine, stimulant medication, or prolonged exercise can potentiate the underlying arrhythmic potential. In the event of SCD, advanced cardiac life support (ACLS) should be performed immediately and exactly. The authors present a case of an otherwise healthy young male who collapsed during a marathon and could not be resuscitated despite aggressive measures. After aggressive resuscitative efforts, the patient ultimately expired. A postmortem autopsy revealed no cardiac structural abnormalities, and the cause of death was determined to be cardiac arrhythmia of undetermined etiology. Postmortem genetic testing revealed a heterozygous variation in calcium voltage-gated channel auxiliary subunit beta 2 (CACNB2), a gene associated with arrhythmia and calcium channelopathy. Toxicology showed therapeutic levels of amphetamine. This case highlights the eminent risk of cardiac death in young athletes with proarrhythmic genetic variations, especially in the setting of endurance sport.

Sudden cardiac death (SCD) is a rare but tragic event that can occur in endurance sport athletes [1]. It is usually caused by underlying cardiac structural or electrical abnormalities, which can sometimes be detected by preparticipation screening. However, in some cases, the underlying cause remains unknown. We present a case of an otherwise healthy young male runner who collapsed during a marathon and could not be resuscitated despite aggressive measures. This case highlights several principles important to emergency medicine and acute care, including: (1) the need for preparticipation screening in endurance sporting events, which commonly have little to no minimum required screening for entry; (2) the risk of genetic variants of undetermined significance (VUS) in young athletes with known family history; and (3) precautions for athletes who are prescribed stimulants for attention deficit disorder. This case is reported with the informed consent of next of kin.

Case description

A 22-year-old male presented to the emergency department via emergency medical services (EMS) after collapsing near the end of a marathon. Reportedly, just 2 min prior to his collapse, he had been running at his race pace and was alert and oriented. A police officer was posted nearby and observed the collapse. The officer began CPR, and EMS was summoned. EMS reported that the patient was pulseless upon their arrival, and CPR was continued. An intravenous (IV) catheter access was obtained, and one mg of epinephrine and a 200 cc fluid bolus were administered. Despite best efforts, intubation failed at the scene due to a significant amount of blood in the mouth and oropharynx due to dental fracture and facial abrasion from falling prone. As they were about to administer electricity, the patient regained weak return of spontaneous circulation (ROSC), and the patient was delivered to the emergency room, which was approximately 1.9 miles away. An intraosseous catheter was placed in transit.

On arrival at the hospital, the patient had a Glasgow Coma Scale (GCS) of 8. His vital signs included: heart rate 164; respiratory rate 40 breaths per minute; blood pressure 125/46 mmHg; and oxygen saturation 84 %. Venous blood gas revealed a pH of 7.1. Electrocardiogram (ECG) tracing upon arrival showed sinus tachycardia with a short PR interval and a complete right bundle branch block, as shown in Figure 1. He exhibited some respiratory effort, but it was very shallow and tachypneic. His gag reflex was moderate, but he was not protecting his airway well. Endotracheal intubation was performed utilizing the rapid-sequence intubation technique. Proper positioning of the tube was confirmed. iStat analysis

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showed hyperkalemia to be at 5.8 mmol/L. He received multiple doses of epinephrine, calcium gluconate, and lactated ringer solution. Multiple electrolyte derangements were identified via laboratory analysis (Table 1).

He seemed to stabilize initially enough for a computed tomography (CT) scan of the head, which did not show any acute abnormality either as a source of his symptoms or as a sequela from any traumatic injury. While the patient was being scanned, a brief interview with the family was conducted, which revealed that the patient's medical history was only significant for attention deficit hyperactivity disorder (ADHD) and he had no known cardiac conditions. At this time, there was no known family history of cardiac death or dysrhythmia. The patient had trained for at least 6 months for the marathon. They reported that the patient took an Adderall (amphetamine and dextroamphetamine) and a caffeinated "energy shot" before the race, which would have been approximately 3½ h before his collapse.

Over the next 30 min, the patient started to demonstrate softer blood pressures with a slowing heart rate. ECG showed a nonspecific intraventricular conduction block that seemingly replaced or overrode the right bundle branch block previously identified. The ST segment elevation was now present in limb leads II, III, aVF, V4, V5, and V6, indicating inferior and lateral infarction as shown in Figure 2. His pulse became thready, and a central line was placed to further resuscitate. Norepinephrine 0.1 mcg/kg/min was administered, which did not improve his pressures. Shortly thereafter, the patient's pulse flatlined, and cardiopulmonary resuscitation (CPR) was restarted. Multiple rounds of epinephrine and other code medications were administered without ROSC, and he remained in pulseless electrical activity. After all that could feasibly be done, the patient expired.

Table 1: The chemistry panel obtained upon admission to the emergency department with reference ranges.

Chemistries	Reference range
Sodium: 138 mmol/L	137–146 mmol/L
Potassium: 5.8 mmol/L	3.5–5.0 mmol/L
CO_2: 14 mmol/L	19–30 mmol/L
Glucose: 131 mg/dL	65–99 mg/dL
BUN: 28 mg/dL	8–20 mg/dL
Creatinine: 2.2 mg/dL	0.77–1.35 mg/dL
Lactic acid (plasma): 11.9 mmol/L	0.5–2.0 mmol/L
Creatinine kinase: 1,024 unit/L	56–356 unit/L
Troponin 0.24 ng/mL	0.00–0.04 ng/mL

BUN, blood urea nitrogen.

Postmortem analysis

Pertinent findings at postmortem examination were severely congested and edematous lungs, which is likely consistent with prolonged CPR. There was no evidence of trauma. Genetic testing for mutations that cause cardiac arrhythmias and cardiomyopathies revealed a variant in calcium voltage-gated channel auxiliary subunit beta 2 (CACNB2). This gene encodes a subunit of a voltage-dependent calcium channel protein that is a member of the voltage-gated calcium channel superfamily. Mutations in

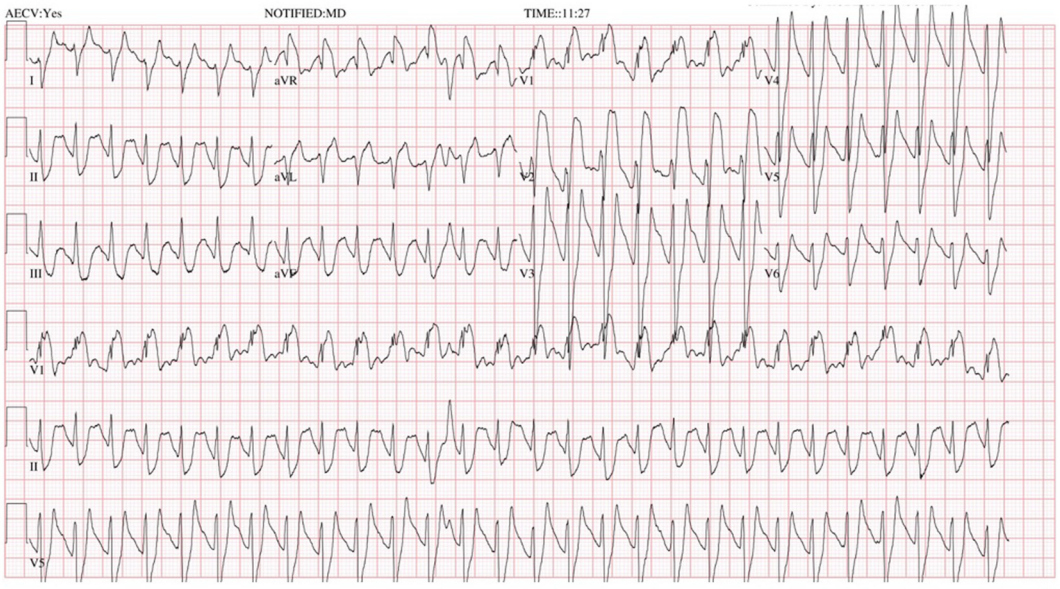

Figure 1: The 12-lead electrocardiogram (ECG) tracing upon admission to the emergency department demonstrating sinus tachycardia with a short PR interval and a complete right bundle branch block.

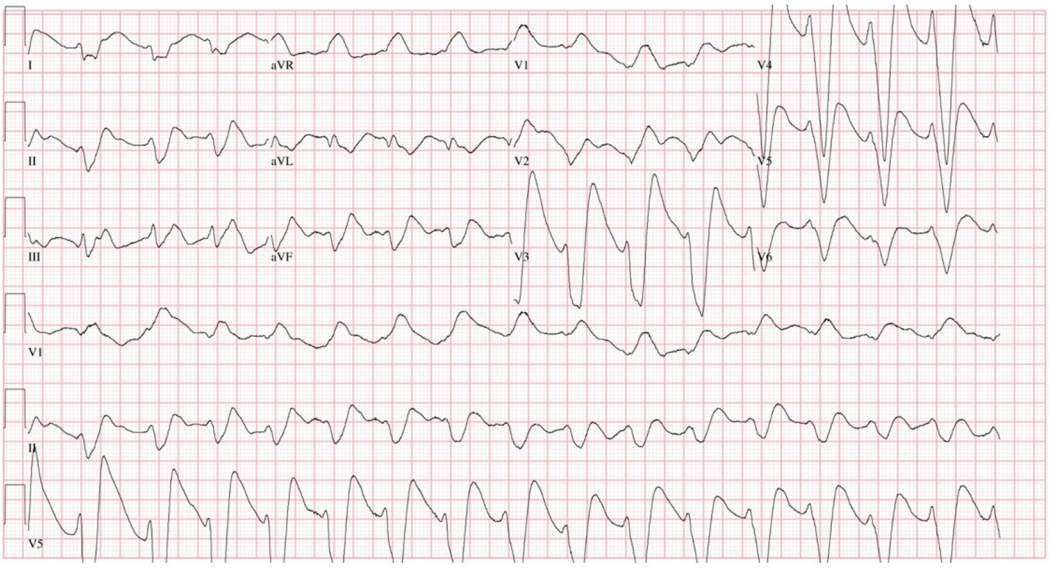

Figure 2: The 12-lead electrocardiogram (ECG) tracing 1 h after admission to the emergency department showing a nonspecific intraventricular conduction block that seemingly replaced or overrode the right bundle branch block previously identified. ST segment elevation was now present in limb leads II, III, aVF, V4, V5, and V6, indicating inferior and lateral infarction.

this gene are associated with Brugada syndrome and autosomal-dominant short QT syndrome (SQTS) [2–4].

Alternatively spliced variants encoding different isoforms have been described [5]. Toxicology on postmortem femoral blood was positive for therapeutic levels of amphetamine. Histologic examination of the organs revealed pulmonary hemorrhages, also thought to be from resuscitative efforts, and there was no evidence of significant natural disease that would cause death. The vitreous electrolyte abnormalities are mild and were thought to be consistent with someone participating in a marathon and normal postmortem changes. The conclusive cause of death was determined to be cardiac arrhythmia of undetermined etiology.

Family history included a brother with Wolf–Parkinson–White syndrome and a maternal grandmother with hypertrophic obstructive cardiomyopathy. However, both relatives' conditions were discovered after the patient's death. With this family history along with the patient's heterozygosity for a mutation in CACNB2, the patient's participation in prolonged exertional activity in combination with severe electrolyte derangements in the setting of caffeine and amphetamine stimulants likely culminated in sudden deadly arrhythmia.

Discussion

SCD of a young athlete is a devastating event that has far-reaching implications for the individual, their family, and the wider community [1]. SCD in young athletes is usually caused by underlying cardiac structural or electrical abnormalities, which can be detected by preparticipation screening. However, in some cases, the definite underlying cause remains unknown.

Endurance sports can place significant stress on the cardiovascular and respiratory systems, and underlying health issues such as hypertension, coronary artery disease, or asthma may increase the risk of sudden cardiac events or respiratory failure [6]. Therefore, preparticipation screening is an essential step in identifying athletes who may be at risk of developing a medical emergency during endurance sporting events [7]. Guidelines consistently agree that preparticipation screening for cardiovascular abnormalities in competitive athletes should include history and physical examination focused on assessing cardiac risk. Furthermore, the American Heart Association and American College of Cardiology (AHA/ACC) recommend use of the AHA/ACC 14-point screening guideline [8] in conjunction with history and physical examination to detect or raise suspicion of genetic/congenital cardiovascular abnormalities. Some studies have provided strong evidence in support of a preparticipation 12-lead ECG. Hypertrophic cardiomyopathy (HCM) is the leading cause of SCD in athletes. However, preparticipation ECG screening has been criticized for failing to meet cost-effectiveness thresholds, in part because of high false-positive rates [9]. In this case, the patient was not aware of a significant family history of heart conditions that could lead to dysrhythmia, nor did he complain of any symptoms.

Advanced Cardiac Life Support (ACLS) is a set of evidence-based guidelines designed to provide healthcare providers

with a structured approach to managing cardiac arrest and other life-threatening cardiovascular emergencies [10]. The principles of ACLS emphasize the importance of rapid recognition and intervention, including the use of immediate CPR and airway management in the setting of SCD. In retrospect, ACLS was followed in this case, including nearly immediate CPR by the police officer and early ROSC. Therefore, the ability to restore sustained cardiac activity in this patient was superseded by a combination of derangements in physiology and possibly structure, which was: 1) difficult to identify in the acute scenario with little to no history; 2) difficult to correct in a timely manner due to severe electrolyte derangement over the course of hours of rigorous exercise; and 3) cardiac infarction.

Genetic VUS are variations in DNA that have been identified but have not yet been linked to a specific disease. In young athletes with known family history of cardiac disorders and VUS, there is a potential risk of SCD during sports participation, even if there are no apparent symptoms or abnormal findings on physical examination [11]. As such, genetic testing and screening should be considered in young athletes with a family history of cardiac disorders, particularly in those with VUS, to identify those who may be at risk of SCD and require further evaluation or intervention before participating in sports. Further investigation is needed to evaluate the efficacy or necessity for genetic testing before sport participation. Preparticipation screening should be reemphasized as a requirement to identify high-risk individuals who require further evaluation or treatment before participating in such events, ultimately improving the safety and well-being of all participants.

Studies have identified eight different categories of a condition known as Brugada Syndrome (BS) (BS1 to BS8), which are associated with specific genetic mutations in the SCN5A, GPD1-L, CACNA1c, CACNB2b, SCN1B, KCNE3, SCN3B, and HCN4 genes. The majority of individuals with BS do not exhibit any symptoms. However, the primary clinical indication of this syndrome is the presence of polymorphic ventricular tachycardia, which can degenerate to ventricular fibrillation (VF) and SCD. Diagnosing this condition is challenging, and it involves analyzing not only the patient's ECG for abnormalities but also considering their clinical and demographic information. Molecular genetic testing has proven to be a useful method, as it can identify mutations in 20–38 % of patients with BS [12]. The ECG findings in BS are characterized by ST segment elevation in the right precordial leads (V1–V3). The ST segment elevation is typically coved in shape and is often associated with a negative T wave. The ECG changes can be transient and may be unmasked or augmented by pathophysiologic changes such as electrolyte derangement [13]. Patients with known risk for BS can undergo testing and if confirmed have an intracardiac defibrillator (ICD) implanted [14].

The patient also had therapeutic levels of amphetamine on postmortem toxicology screening. Amphetamine is a stimulant drug that can cause tachycardia, hypertension, and arrhythmias. Amphetamine is commonly utilized by athletes to improve performance and endurance; however, in this case, the patient was prescribed the medication for ADHD. There is an AHA/ACC recommendation for baseline ECG for patients with ADHD starting stimulants with a known cardiac risk factors [15]. This recommendation conflicts with the American Academy of Pediatrics recommendation [16]. However, in healthy persons, the present recommendation is limited to history and physical examination before starting stimulant medications, with an emphasis on the identification of risk factors for sudden death, but it does not routinely recommend electrocardiographic screening or cardiac subspecialist consultation unless indicated by history or physical examination findings. While it is unclear to what degree amphetamine use contributed to the patient's arrhythmia and subsequent cardiac arrest, it is important to consider the potential risks of drug use in young athletes, especially in combination with caffeine. Caffeine is thought to potentiate the effects of amphetamine and has been shown to increase amphetamine-induced death in murine studies [17]. Therefore, athletes with ADHD who are prescribed stimulant medication should undergo a thorough medical evaluation and cardiac screening before engaging in strenuous exercise or sports and avoid concomitant use of caffeine to prevent SCD or severe electrolyte imbalances [18]. Adequate hydration and electrolyte replacement are also essential to prevent electrolyte imbalances, which can be life-threatening. Ultimately, it is crucial for athletes with ADHD to be evaluated and cleared by a physician to ensure that they can safely participate in sports while managing their condition and medication.

Conclusions

SCD is a rare but devastating event that can occur in endurance sport athletes. The postmortem examination revealed a variant in CACNB2 that is thought to be associated with BS and could be a contributing factor to this patient's SCD. This case underscores the need for further research and enhanced preventive measures to decrease the incidence of SCD in athletes and draws attention to the variety of factors that must be considered. Additionally, precautions should be taken for athletes who are prescribed stimulants for ADHD. In evaluating young patients for sports participation, emphasis should be given to prevention, early recognition, and appropriate management of SCD.

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Conflicts of interests: None reported.

Ethical approval: The Rocky Vista University Institutional Review Board (IRB) approved this report (RVU IRB# 2022-172) and considered it exempt from full IRB investigation on the basis of its retrospective and anonymous nature.

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