30-Year-Old Man With Outside-of-Hospital Cardiac Arrest

Georgios Christopoulos, MD; Christopher V. DeSimone, MD, PhD; and Nandan S. Anavekar, MB, BCh

A 30-year-old man was admitted to the cardiac intensive care unit after experiencing an out-of-hospital cardiac arrest. He was found unresponsive in bed and underwent 30 minutes of cardiopulmonary resuscitation, including 5 shocks for ventricular fibrillation before return of spontaneous circulation.

His medical history was notable for bipolar disorder, past suicidal ideation during adolescence, tobacco and alcohol abuse, and motor vehicle accidents resulting in cervical and thoracic spinal injuries. He had no prior cardiovascular history or symptoms before the cardiac arrest. There was no family history of premature coronary artery disease, cardiomyopathy, or sudden cardiac death. His medications included supplements used to enhance athletic performance in bodybuilding, including anabolic steroids, creatine monohydrate, clenbuterol (a β2-agonist not approved by the US Food and Drug Administration [FDA]), taurine, saw palmetto, and amino acid supplements. He had used lithium in the past, but the last documented use was 3 years prior to presentation.

Physical examination revealed an unresponsive man with a body mass index of 35 kg/m². His initial blood pressure was 197/93 mm Hg, with a regular pulse of 91 beats/min; he was afebrile, and his oxygen saturation was 73%. He had no cardiac murmur, jugular venous pressure was not elevated, and his extremities were cool and clammy but without evidence of edema or trauma. A prehospital airway device was in place, but the patient continued to be hypoxic in the emergency department and there were concerns about upper airway obstruction due to blood in the oropharynx. Therefore, surgical access was established and mechanical ventilation was initiated through a tracheostomy.

Laboratory evaluation was remarkable for an initial troponin T level of 0.6 ng/mL, which peaked at 2.1 ng/mL at 3 hours; hemoglobin level of 19 g/dL (hematocrit, 62%), white blood cell count of 18.9 × 10³/mL, platelet count of 247 × 10³/mL, serum potassium value of 5.3 mEq/L, serum bicarbonate level of 28 mEq/L, serum lactate concentration of 1.0 mmol/L, and arterial pH of 6.99. Electrocardiography (ECG) revealed peaked T waves with 3-mm J point elevation in the anterior leads with upsloping T waves, a rightward axis, and a corrected QT interval of 385 milliseconds. Chest radiography revealed mild enlargement of the cardiac silhouette, bilateral perihilar patchy airspace opacities, and no pneumothorax or pleural effusions. Computed tomographic angiography of the chest was negative for pulmonary embolism and aortic dissection.

The patient underwent urgent coronary angiography, which revealed normal coronary arteries without evidence of anomalous origin.

1. Which one of the following is the most likely etiology of the patient’s cardiac arrest?
   a. Hypertensive cardiomyopathy
   b. Myocarditis
   c. Brugada syndrome
   d. Hypertrophic obstructive cardiomyopathy
   e. Long QT syndrome

Hypertensive cardiomyopathy tends to occur in older adults who have long-standing essential hypertension but would be a less likely etiology in this young man with no history of hypertension. Myocarditis is a possibility but is not a common cause of cardiac arrest and would be typically associated with subacute onset of symptoms, such as chest pain, dyspnea, or fever. Furthermore, myocarditis is not a common cause of cardiac arrest. The patient’s ECG results were not consistent with a Brugada pattern, and his QT segment was not prolonged. Hypertrophic obstructive cardiomyopathy would be the most likely etiology for such a presentation in a young patient.
patient who has no evidence of atherosclerotic coronary disease. In an autopsy-based analysis of 298 cases of unanticipated sudden cardiac death in adults younger than 35 years, sudden cardiac death occurred secondary to an unidentified cause in 41.3% of the cases, followed by coronary atherosclerosis in 23.2% and hypertrophic obstructive cardiomyopathy in 12.8% (myocarditis [5.7%], idiopathic dilated cardiomyopathy [4.7%] and hypertensive cardiomyopathy [3.7%] were discovered less frequently). Finally, congenital channelopathies (such as long QT syndrome) are rare, and patients typically have a family history of the disorder and long QT segment on the ECG.

Transthoracic echocardiography revealed an ejection fraction of 22% and severe global dysfunction with the best-preserved function in the anterior and anteroseptal walls, eccentric left ventricular hypertrophy (increased left ventricle size and thickness), and moderate right ventricular enlargement with a moderate decrease in right ventricular function (normal right ventricular wall thickness).

2. Which one of the following tests would be the most appropriate next step in the evaluation of the patient’s echocardiographic findings?
   a. Hemodynamic cardiac catheterization
   b. Cardiac computed tomography (CT)
   c. Cardiac magnetic resonance imaging (MRI)
   d. Electrophysiologic study
   e. Repeated echocardiography in 3 months

   This patient has evidence of structural heart disease on echocardiography. As a next step, he requires higher-resolution imaging in an attempt to define the presence of scarring, inflammation, arrhythmogenic right ventricular dysplasia (ARVD), or an infiltrative process that could serve as a substrate for his arrhythmia. Hemodynamic cardiac catheterization would identify the intracardiac and pulmonary pressures but would not clarify the anatomic abnormality responsible for the arrhythmia. Multidetector cardiac CT would be a reasonable alternative in the evaluation for ARVD because it is able to distinguish fatty infiltration from normal myocardium. However, MRI is usually preferred given its lack of radiation associated with multidetector CT and its ability to characterize inflammatory changes and scar. Cardiac MRI would be the best next option because it would further characterize the myocardial tissue and further specify the anatomic abnormality. An electrophysiologic study would not be recommended at this point because the work-up for structural heart disease is still incomplete. Finally, observation with repeated echocardiography in 3 months would not be reasonable given the risk of a recurrent event without proper risk stratification and therapy.

   Cardiac MRI revealed mild diffuse hypokinesis, most conspicuous in the left ventricular apex and in the inferior segment of the right ventricle. The left ventricle had borderline chamber enlargement and normal wall thickness. The right ventricle had normal size and normal wall thickness. There was no myocardial edema, no perfusion defects on resting first-pass perfusion imaging, and no myocardial delayed enhancement to suggest infarction, inflammation, fatty infiltration, or fibrosis. The MRI did not show evidence of hypertrophic obstructive cardiomyopathy (no evidence of dynamic left ventricular outflow tract obstruction).

3. Given the findings of the imaging study and the original presentation, which one of the following is the most likely cause of the patient’s right and left ventricular hypertrophy?
   a. Chemical substances to enhance athletic performance
   b. ARVD
   c. Catecholaminergic polymorphic ventricular tachycardia
   d. Severe pulmonary hypertension
   e. Athletic heart syndrome

   The cardiac MRI findings are nonspecific in terms of revealing an underlying structural etiology. This young patient has no MRI demonstration of a congenital anatomic abnormality, and therefore acquired etiologies should be investigated. The fact that this patient had been self-administering non–FDA-approved medications to improve athletic performance and increase muscle mass was of particular concern. Therefore, emphasis was placed on eliminating offending medications that are the most likely culprits in this case—anabolic steroid use and supplementation. Arrhythmogenic right
ventricular dysplasia can be excluded based on lack of fatty infiltration of the right ventricle on imaging studies, regional right ventricular focal akinesia, dyskinesia, aneurysm, or dyssynchronous right ventricle contraction. Catecholaminergic polymorphic ventricular tachycardia is a genetic disorder caused by mutation of proteins that regulate calcium release from the sarcoplasmic reticulum. It is not associated with right or left ventricular hypertrophy. Furthermore, it typically occurs in patients during activity, rather than rest which was the case with this patient. It is one of the rare causes of bidirectional ventricular tachycardia. Severe pulmonary hypertension can be seen in patients with left and right ventricular hypertrophy, but in our patient, echocardiography revealed no tricuspid regurgitation, and based on secondary measures, the degree of pulmonary hypertension was only mild. Athlete’s heart can present with the symmetric left ventricular hypertrophy that was seen on this patient’s echocardiography and MRI. However, athlete’s heart has not been linked to serious ventricular arrhythmias and sudden cardiac death.

Chemical-induced cardiomyopathy was diagnosed on the basis of clinical presentation and lack of alternative diagnoses that would be suggested from the cardiac MRI. The patient was successfully extubated on day 3 of hospitalization and was able to attest that he was using a multitude of chemical substances to enhance his performance before the cardiac arrest. His hospital course was complicated by delirium, which was treated with sedative agents. An investigation was initiated to determine the chemical agent most likely responsible for the patient’s findings.

4. Which one of the following supplements mentioned in the patient’s history is most likely to have caused ventricular hypertrophy?
   a. Amino acids, including taurine
   b. Clenbuterol (β2-agonist not approved by the FDA)
   c. Anabolic steroids
   d. Lithium
   e. Saw palmetto

   Amino acids (including taurine) are supplements commonly used to boost athletic activity, but their association with cardiac arrest is not established. Clenbuterol is a β2-adrenergic agonist that is commonly used to enhance performance and accelerate fatty tissue metabolism. It has been used to treat asthma in horses and in adults outside the United States. It has been associated with development of ventricular arrhythmias and sudden cardiac arrest. Although clenbuterol may have synergy with other substances responsible for cardiac hypertrophy, its β2-agonist action is more likely to have contributed to proarrhythmia rather than hypertrophy itself. Anabolic steroids (such as testosterone) have been associated with cardiac hypertrophy in otherwise healthy individuals without known heart disease. Anabolic steroids have been found to cause increased left ventricular wall thickness, decrease in systolic and diastolic function, and endomyocardial apoptosis and fibrosis. Lithium overdose has been reported to unmask Brugada syndrome and precipitate sudden cardiac death. However, this patient’s lithium level was undetectable on admission. Lithium has a half-life of 24 hours and would be expected to be present in the blood if the cardiac arrest was caused by recent overdose. Saw Palmetto is an over-the-counter extract used to treat benign prostatic hyperplasia. Most common adverse effects are gastrointestinal or related to bleeding and sexual function. Beta-sitosterol, a chemical present in saw palmetto, was reported to increase the risk for heart attack in one trial. However, a meta-analysis of 17 trials found no connection between serum sitosterol status and cardiovascular disease.

   Anabolic steroid–induced cardiomyopathy was diagnosed. The patient did not sustain neurologic damage from the cardiac arrest. His tracheostomy was removed, and he was discharged from the hospital on day 7 with scheduled outpatient cardiology follow-up.

5. In addition to discontinuing possible offending agents, which one of the following is the most appropriate next step in the prevention of future cardiac arrest in this patient?
   a. Wireless pulmonary artery pressure monitoring
   b. Implantable cardioverter-defibrillator (ICD)
   c. Flecainide
   d. Electrophysiologic study with anatomy-based ablation
   e. No additional measures are required
A wireless pulmonary artery pressure monitor is a pulmonary artery pressure sensor that is invasively placed during right-sided heart catheterization. The device senses increased intracardiac pressures as an early sign of volume overload. It was found to significantly decrease the frequency of hospital admissions in patients with heart failure in a randomized control trial.  It has no role in predicting or treating ventricular arrhythmias. The patient has a class I indication for secondary-prevention ICD due to survived ventricular fibrillation arrest. Flecainide is a class IC antiarrhythmic agent that can be used to restore sinus rhythm in atrial fibrillation but is not indicated for prevention of sudden death or ventricular arrhythmias. Antiarhythmic medications (mexiletine, amiodarone, or sotalol) can be used in patients with an ICD to decrease the frequency of defibrillations. However, class IC agents are not used in this setting because they have been reported to increase the risk of proarrhythmia and nonarrhythmic cardiac death. Electrophysiologic studies with substrate-based ablation can be a treatment choice in patients who experience recurrent ICD shocks in spite of medical therapy. It is not a primary treatment after ventricular fibrillation. Finally, no additional measures would be inappropriate; the patient’s anatomic cardiomyopathy and recent cardiac arrest would qualify him for secondary prevention with ICD.

The patient was dismissed with the recommendation to receive an ICD. Given his recent tracheostomy, the infectious diseases service recommended that ICD placement be delayed for 1 week, and therefore he was discharged with a defibrillator vest and had ICD implantation 1 week following dismissal. On follow-up at 2 months, he had no ICD discharges. Holter monitoring revealed sinus rhythm without malignant arrhythmias. Repeated echocardiography revealed improvement of ejection fraction to 48%, similar left ventricle size and thickness, and no diastolic dysfunction.

**DISCUSSION**

Anabolic steroid-induced cardiomyopathy is a well-established entity in the literature. A number of case reports have linked anabolic steroids to ventricular hypertrophy, dilated cardiomyopathy, hypertension, atrial and ventricular arrhythmias, atherosclerotic disease, and myocardial infarction and sudden cardiac death. Our case demonstrates that cardiomyopathy induced by anabolic steroids and performance-enhancing drugs should be considered in the differential diagnosis of ventricular arrhythmias in young patients without a personal or family history of organic heart disease. In addition, an elevated hemoglobin level of 19 g/dL, as seen in our patient, is not normal in a young, healthy man and should alert the clinician to further investigate for the driving etiology.

Anabolic steroids mimic endogenous steroids, such as testosterone and dihydrotestosterone, and act on the androgen receptors, which are expressed in the nuclei of skeletal muscle and cardiac myocytes. Anabolic steroids initiate a cascade of events that result in focal myocarditis, apoptosis, and alterations in heart structure, including ventricular dilatation and hypertrophy. Athlete’s heart can often times mimic steroid-induced cardiomyopathy.

Studies performed in weightlifters revealed increased left ventricular end-diastolic volume dimension and posterior wall thickness when compared with normally active matched control subjects. However, resistance training by itself does not cause systolic or diastolic dysfunction and has not been proven to cause malignant arrhythmias. Based on a recent survey, anabolic steroids are used by approximately two-thirds of professional bodybuilders. Since the discovery of testosterone in 1932 and its first use by Olympic athletes in the mid 20th century, the use of anabolic steroid derivatives has been expanding.

Several case reports and descriptive studies have described the clinical, echocardiographic, and ECG characteristics of anabolic steroid-induced cardiomyopathy. A recently published cross-sectional cohort study described the effects of anabolic steroid use in recreational male weightlifters 34 to 54 years of age. The study compared 86 men reporting 2 or more years of cumulative lifetime anabolic steroid use and 54 nonusing men and found reduced left systolic and diastolic function in the anabolic steroid use group (left ventricular ejection fraction, 52%±11% vs 63%±8%, P < .001; and early relaxation velocity, 9.3±2.4 cm/s vs 11.1±2.0 cm/s, P < .001). Interestingly, in this study users were found to have higher coronary

February 2018;93(2):e69-e73
artery plaque volume than nonusers, and plaque burden on coronary CT angiography was positively associated with duration of anabolic steroid use. In spite of the observational design, one of the study’s strengths was the demonstration of the effects of anabolic steroid use in nonelite weightlifters enrolled from gymnasiums, underscoring that anabolic steroid toxicity may be a generalized and unrecognized public health concern.

Most of the studies of the effect of anabolic steroid use on the heart have been performed in weightlifters, raising the question of whether exercise represents a confounder in this population. Indeed, one study found whether exercise is not well documented; with the exception of left ventricular mass, the other values were not statistically significant when corrected for the total body mass in the aforementioned study. In contradistinction, other studies on the same subject have reported no difference in left ventricular morphology, including left ventricular mass, posterior wall thickness, ventricular septal wall thickness, and diastolic cavity dimension.17,18

We conclude that chemical toxicity is an important part of the evaluation of ventricular fibrillation and hypertrophic obstructive cardiomyopathy in young adults. Clinical clues that may point to anabolic steroid-induced cardiomyopathy include increased muscle mass, polycythemia, young age, and asymmetric left ventricular cardiomyopathy. Implantation of an ICD is indicated for secondary prevention in survivors of cardiac arrest due to ventricular arrhythmias without an easily reversible trigger, as in this case of anabolic steroid-associated cardiomyopathy.

Potential Competing Interests: The authors report no competing interests.

Correspondence: Address to Nandan S. Anavekar, MB, BCh, Department of Cardiovascular Medicine, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (anavekar.nandan@mayo.edu).

REFERENCES


CORRECT ANSWERS: 1. d. 2. c. 3. a. 4. c. 5. b