Title

Defying the Odds of Sudden Cardiac Death in Hypertrophic Cardiomyopathy.

Journal

JACC: Case Reports, 2(6)

Authors

Rostomian, Ara
Tang, Maxine
Shamsa, Kamran

Publication Date

2020-06-01

DOI

10.1016/j.jaccas.2020.04.046

JACC: CASE REPORTS VOL. 2, NO. 6, 2020

MINI-FOCUS ISSUE: CARDIOMYOPATHIES

ADVANCED

CASE REPORT: CLINICAL CASE

Defying the Odds of Sudden Cardiac Death in Hypertrophic Cardiomyopathy

Ara H. Rostomian, MD, MPH, MBA,[a] Maxine C. Tang, MD, MS,[b] Kamran Shamsa, MD[c]

ABSTRACT

We report an unusual case of a patient with hypertrophic obstructive cardiomyopathy, anomalous aortic origin of a coronary artery, obesity hypoventilation syndrome, and acquired long QT syndrome who was able to defy the odds of sudden cardiac death in the rarest of circumstances. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2020;2:930–4)

HISTORY OF PRESENTATION

A 48-year-old woman was admitted to the cardiac care unit for 1 year of worsening exertional dyspnea, chest pain, palpitations, light-headedness, and multiple episodes of syncope. A year prior, she had presented to the emergency department multiple times for persistent symptoms of dyspnea and chest discomfort, and was diagnosed with hypertrophic cardiomyopathy on echocardiogram.

Physical exam showed blood pressure of 132/82 mm Hg, pulse of 74 beats/min, respiratory rate of 12 breaths/min, temperature of 36.8°C, and oxygen saturation of 98% on room air. The patient was obese with a large neck and had a holosystolic murmur (grade III/VI) throughout the whole chest. Other systemic findings were unremarkable.

LEARNING OBJECTIVES

- To recognize risk factors for sudden cardiac death.
- To acknowledge that early screening and close follow-up are essential to ensure favorable outcomes in patients with hypertrophic cardiomyopathy.

MEDICAL HISTORY

Medical history included asthma, hyperlipidemia, hypertension, obesity, diabetes, obstructive sleep apnea and obesity hypoventilation syndrome (OHS), and family history of coronary artery disease.

INVESTIGATIONS

Her initial outpatient echocardiogram showed interventricular septal thickness at end diastole of 1.8 cm, posterior wall thickness of 1.7 cm, left ventricular outflow tract (LVOT) gradient of 70 mm Hg at rest and 76 mm Hg with Valsalva maneuver.

DIFFERENTIAL DIAGNOSIS

The differential diagnoses were worsening obstructive hypertrophic cardiomyopathy, coronary artery disease, or heart failure.

From the [a]Division of Cardiology, Kaiser Permanente-Los Angeles Medical Center, Los Angeles, California; [b]Department of Medicine, Olive View-UCLA Medical Center, Sylmar, California; and the [c]Division of Cardiology, Ronald Reagan UCLA Medical Center, Los Angeles, California. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC: Case Reports* author instructions page.

Manuscript received February 5, 2020; revised manuscript received March 27, 2020, accepted April 14, 2020.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2020.04.046

MANAGEMENT

Table 1 provides a timeline of the patient's clinical course. Before admission, the patient underwent left heart catheterization, which showed anomalous origin of the right coronary artery (RCA) and no obstructive coronary artery disease. She was started on diltiazem/disopyramide as an outpatient with some symptomatic improvement. She subsequently underwent an exercise stress echocardiogram (treadmill, Modified Bruce Protocol). She tolerated <4 min of exercise and achieved 2.8 METS. Echocardiogram showed a resting LVOT peak gradient of 71 mm Hg, which increased to 261 mm Hg post-exercise with evidence of septal anterior motion (**Figures 1A to 1D**). Diastolic function was normal.

Despite initial improvement on medical therapy, her symptoms worsened over several months as evidenced by 8 syncopal episodes. She had progressed from New York Heart Association functional class II at time of diagnosis to functional class III. She was admitted to the cardiac care unit for management of worsening hypertrophic obstructive cardiomyopathy (HOCM).

Further workup included computed tomography coronary angiography revealing the RCA arising from the left coronary cusp with an inter-arterial course (**Figure 2**), cardiac magnetic resonance imaging showing left ventricular hypertrophy with ejection fraction of 84%, and Holter monitor with 17 runs of nonsustained ventricular tachycardia (NSVT). Her inpatient electrocardiograms (ECGs) showed progressive QTc prolongation with a maximum QTc of 582 ms (**Figure 3**).

The patient underwent surgical left ventricular myomectomy with resection of the subaortic obstruction, which involved unroofing of the intramural right coronary artery, further assessment of the ascending aorta with epicardial echocardiography, and tricuspid valve annuloplasty due to moderate tricuspid regurgitation with a dilated annulus found intraoperatively.

She then underwent a dual chamber (single coil) implantable cardioverter-defibrillator (ICD) implantation for primary prevention of sudden cardiac death (SCD) in HOCM due to a calculated SCD risk of >6% based on echocardiographic measurements, history of NSVT, and unexplained syncope (1). She was counseled on the importance of using her continuous positive airway pressure machine given her long-standing OHS and counseled by a nutritionist regarding weight loss strategies. She was referred for cardiac genetics evaluation after discharge, the results of which are pending.

ABBREVIATIONS AND ACRONYMS

AAOCA = anomalous aortic origin of a coronary artery

ACAOS = anomalous coronary artery from the opposite sinus

ECG = electrocardiogram

HOCM = hypertrophic obstructive cardiomyopathy

ICD = implantable cardioverter-defibrillator

LQTS = long QT syndrome

LVOT = left ventricular outflow tract

MRI = magnetic resonance imaging

NSVT = nonsustained ventricular tachycardia

OHS = obesity hypoventilation syndrome

RCA = right coronary artery

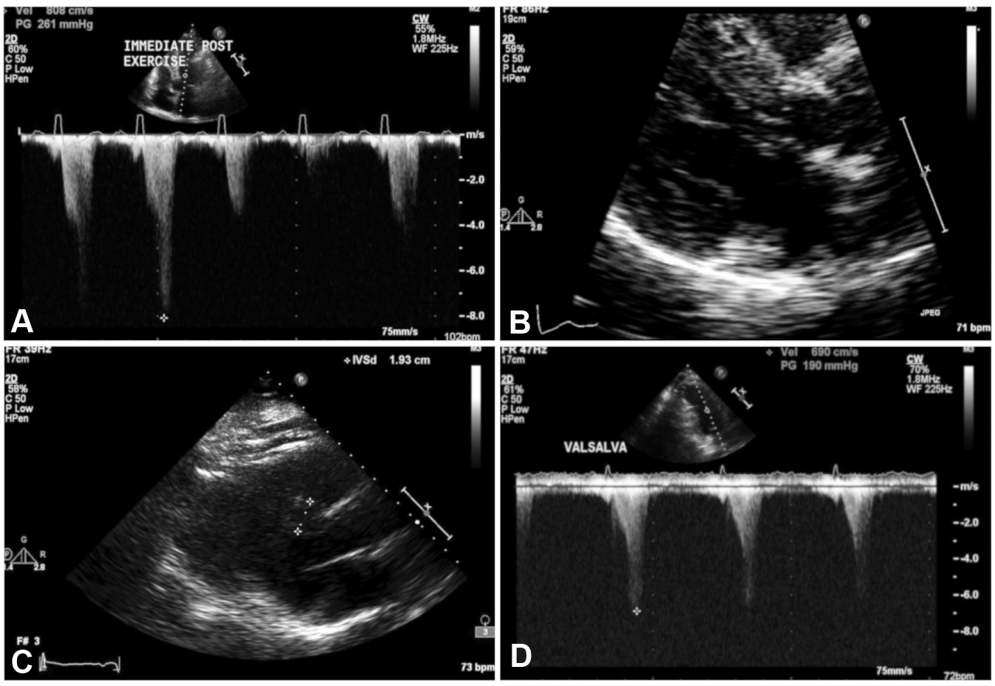
SCD = sudden cardiac death

TABLE 1 Timeline of the Patient's Clinical Course

Time	Event
Before hospital admission	
Month 1	Echocardiogram at rest only showing LVOT gradient of 70 mm Hg and IVSd at 1.8 cm, ECG showed QTc of 438 ms.
Month 3	Left heart angiography shows no coronary artery disease, LVEDP of 36 mm Hg, and anomalous origin of the right coronary artery.
Month 6	Stress echocardiogram showing rest LVOT of 71 mm Hg and post-exercise at 261 mm Hg (Figure 1A) with evidence of SAM (Figure 1B) and mild MR.
Month 7	Holter monitor showing 17 runs of NSVT.
After hospital admission	
Day 1	Cardiac MRI showing LVH, ejection fraction of 85%, no evidence of delayed enhancement. ECG with borderline prolonged QTc of 497 ms.
Day 3	CTA showing the anomalous origin of the RCA arising from the left coronary cusp (Figure 2).
Day 6	EKG with normal sinus rhythm at 60 bpm, LVH with QRS at 116 ms, and prolonged QTc of 582 ms (Figure 3).
Day 8	Presurgical echo with Valsalva showing the IVS at 1.93 cm (Figure 1C), LVOT gradient of 190 mm Hg (Figure 1D), and PW of 1.7 cm.
Day 9	Surgery: LV myomectomy with resection of subaortic obstruction, unroofing of RCA with re-implantation, and tricuspid valve annuloplasty.
Day 15	LVOT gradient of 7 mm Hg and no evidence of SAM.
Day 21	Dual chamber (single coil) ICD implantation for primary prevention.
Day 22	Discharged.

CTA = computed tomography angiography; ECG = electrocardiogram; ICD = implantable cardioverter-defibrillator; IVS = interventricular septum; IVSd = interventricular septum thickness at end-diastole; LV = left ventricle; LVEDP = left ventricular end-diastolic pressure; LVH = left ventricular hypertrophy; LVOT = left ventricular outflow tract; MR = mitral regurgitation; MRI = magnetic resonance imaging; NSVT = nonsustained ventricular tachycardia; PW = posterior wall thickness; RCA = right carotid artery; SAM = systolic anterior motion.

FIGURE 1 Echocardiographic Evaluation of HCM



(A) Echocardiographic evaluation of hypertrophic cardiomyopathy. Post-exercise left ventricular outflow tract (LVOT) gradient of 261 mm Hg. **(B)** Septal anterior motion causing severe LVOT obstruction post-exercise. **(C)** Valsalva interventricular septal thickness of 1.93 cm. **(D)** Valsalva LVOT gradient of 190 mm Hg.

DISCUSSION

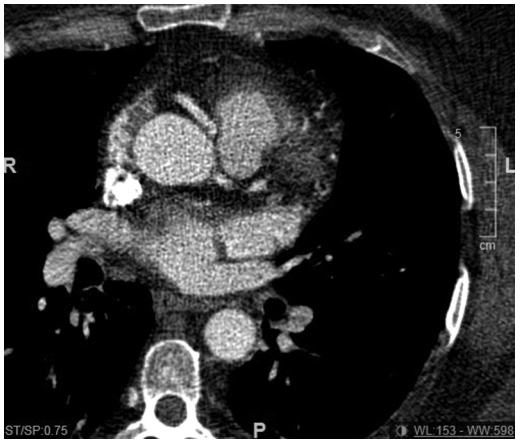
Approximately 300,000 to 400,000 people die from SCD in the United States each year (1). There are many etiologies of SCD, of which myocardial ischemia is the most common. Encountering a patient with four risk factors for SCD, namely, HOCM, acquired long QT syndrome (aLQTS), anomalous aortic origin of a coronary artery (AAOCA), and OHS, is very rare and carries a significant risk of mortality. Nonetheless, it could be treatable with surgical intervention when diagnosed and addressed in a timely manner.

We chose to report this unique case due to the presence of 4 rare risk factors for SCD in a single patient. The probability of having all 4 risk factors simultaneously is ~0.014% given the prevalence of HOCM at 0.2% (2), AAOCA at 0.17% (3), aLQTS at 0.7% (4), and OHS at 0.6% (5).

HOCM can be hereditary or acquired. In this patient, obesity and long-standing hypertension may have contributed to her left-ventricular hypertrophy and LVOT obstruction (genetic testing is currently pending). The rate of SCD in HOCM is ~1% per year (6). HOCM is characterized by myocyte disorganization and hypertrophy, which can cause myocardial ischemia and autonomic abnormalities leading to VT or fibrillation. Medical therapy alone is not sufficient to prevent SCD. Therefore, HOCM patients may benefit from ICD placement for primary prevention and, rarely, may require myomectomy in addition to medical therapy, as with our patient (7,8).

LQTS is more common in HOCM, occurring in 1 of 8 people with HOCM compared with <1 of 200 healthy adults in the absence of QT-prolonging medications, and corresponds with the degree of hypertrophy and LVOT obstruction (9). Our patient had normal QTc at diagnosis, but developed LQTS by the time of admission. Her aLQTS may have developed due to initiation of QT-prolonging drugs (e.g., disopyramide) or worsening hypertrophy and obstruction. Given the propensity of HOCM patients to develop aLQTS and the pro-arrhythmic potential of LQTS, QTc should be evaluated in all HOCM patients.

FIGURE 2 CT Coronary



Right anomalous coronary artery from the opposite sinus with an interarterial course

Anomalous coronary artery from the opposite sinus (ACAOS) is a well-documented cause of SCD secondary to myocardial ischemia. RCA anomalies (as in our patient) are more common and associated with less morbidity than left coronary anomalies. Several variables affect the risk and detection of AAOCAs. There is a major discrepancy in detection of AAOCA using echocardiogram (incidence: 0.17%) versus coronary angiography (1.07%) (3). ACAOS is further stratified on coronary angiogram to high interarterial course (between the aorta and pulmonary artery) and low interarterial course (between the aorta and right ventricular outflow tract), with the high interarterial course carrying a significantly higher risk of SCD (10). Other factors that may increase risk of SCD are acute takeoff angle, slit-like ostium, compression of the intramural segment by the aortic valve commissure, and compression of the coronary artery between the aorta and pulmonary trunk.

Given the low incidence of SCD, high variability in the detection and clinical relevance of anatomical anomalies, along with the absence of clear symptoms in high-risk patients, optimizing cost efficiency of screening and interventions is a major challenge.

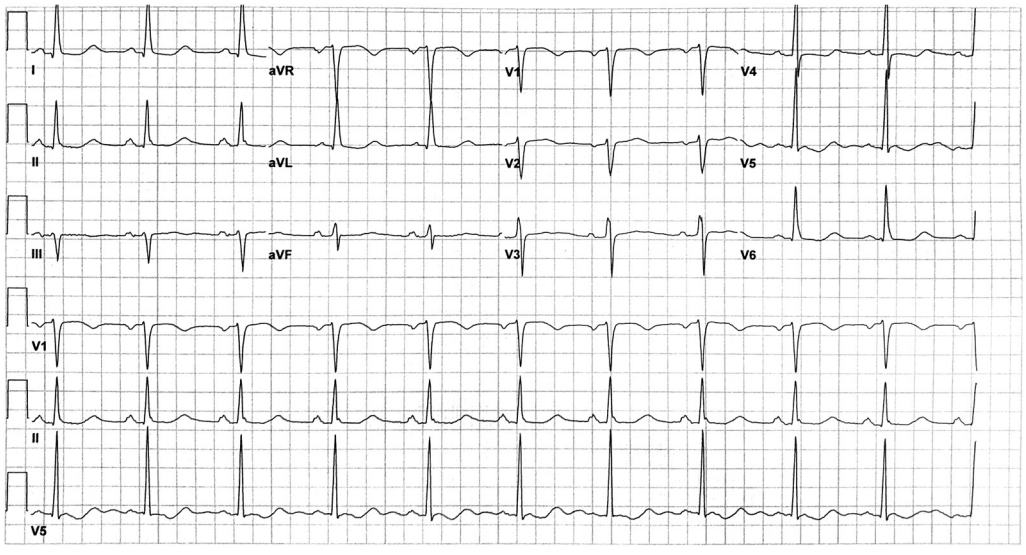
FOLLOW-UP

Repeat echocardiogram showed LVOT gradient of 7 mm Hg and no evidence of systolic anterior motion. Repeat ECG showed QTc of 497 ms. She continues to take diltiazem 360 mg daily. On follow-up, she continues to report intermittent chest pain, but has not experienced recurrent syncope.

CONCLUSIONS

Our patient was symptomatic with multiple syncopal episodes in the context of right ACAOS coinciding with three other possible causes of SCD (aLQTS,

FIGURE 3 Electrocardiogram Demonstrating Normal Sinus Rhythm, Left Ventricular Hypertrophy, Left Atrial Enlargement, and Prolonged QTc Interval of 582 ms



JACC: CASE REPORTS, VOL. 2, NO. 6, 2020
JUNE 2020:930–4

HOCM, and Pickwickian syndrome). Through careful outpatient monitoring, appropriate use of maximal medical therapy, and multidisciplinary coordination, a patient with hypertrophic cardiomyopathy and multiple risk factors for SCD was able to defy the odds of death in the riskiest and rarest of circumstances.

ADDRESS FOR CORRESPONDENCE: Dr. Ara H. Rostomian, Division of Cardiology, Kaiser Permanente-Los Angeles Medical Center, 1526 North Edgemont Street, 2nd Floor, Los Angeles, California 90027. E-mail: ara.h.rostomian@kp.org.

REFERENCES

1. Deo R, Albert CM. Epidemiology and genetics of sudden cardiac death. Circulation 2012;125:620–37.

2. Semsarian C, Ingles J, Maron MS, Maron BJ. New perspectives on the prevalence of hypertrophic cardiomyopathy. J Am Coll Cardiol 2015;65:1249–54.

3. Angelini P. Coronary artery anomalies. Circulation 2007;115:1296–305.

4. Yu H, Zhang L, Liu J, et al. Acquired long QT syndrome in hospitalized patients. Heart Rhythm 2017;14:974–8.

5. Balachandran JS, Masa JF, Mokhlesi B. Obesity hypoventilation syndrome: epidemiology and diagnosis. Sleep Med Clin 2014;9:341–7.

6. Hayashi M, Shimizu W, Albert CM. The spectrum of epidemiology underlying sudden cardiac death. Circ Res 2015;116:1887–906.

7. Zamorano JL, Anastasakis A, Borger MA, et al. 2014 ESC guidelines on diagnosis and management of hypertrophic cardiomyopathy: the task force for the diagnosis and management of hypertrophic cardiomyopathy of the European Society of Cardiology (ESC). Eur Heart J 2014;35:2733–79.

8. Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: Executive summary. J Am Coll Cardiol 2018;72:e91–220.

9. Johnson JN, Grifoni CJ, Bos M, et al. Prevalence and clinical correlates of QT prolongation in patients with hypertrophic cardiomyopathy. Eur Heart J 2011;32:1114–20.

10. Lee H-J, Hong YJ, Kim HY, et al. Anomalous origin of the right coronary artery from the left coronary sinus with an interarterial course: subtypes and clinical importance. Radiology 2012;262:101–8.

KEY WORDS cardiac risk, cardiomyopathy, coronary vessel anomaly, genetic disorders, obesity, primary prevention