The role of cardiac magnetic resonance imaging in the evaluation of malignant ventricular arrhythmias in Brugada syndrome

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Introduction

Brugada syndrome is a genetic disorder associated with an increased risk of sudden cardiac death related to ventricular arrhythmia.[1–3] Initial studies reported rates of syncope or sudden cardiac death ranging from 17% to 42%. Although typically considered channelopathy, subtle structural changes have been reported in this disease's histopathology and magnetic resonance imaging. This includes fibrosis, fatty infiltration, and inflammatory infiltrates with collagen deposition.[2,4]

We present a case of a young patient with a known history of Brugada syndrome from an *SCN5A* mutation who suffered a cardiac arrest and arrhythmias with exercise and was found to have a nonischemic cardiomyopathy. The case discusses explicitly the pathophysiology and diagnosis of Brugada syndrome, recommended care and management in patients diagnosed with Brugada syndrome, and the role of cardiac magnetic resonance imaging (cMRI) in these patients.

Case report

A 19-year-old male patient presented following cardiac arrest. The patient worked as a basketball team manager; he reported feeling dizzy and lightheaded at practice. He subsequently collapsed while exercising and became unresponsive. The patient was found to be pulseless, and cardiopulmonary resuscitation was started immediately by bystanders. The presenting rhythm detected on the automatic external defibrillator was ventricular fibrillation. He received 1 round of defibrillation with the return of spontaneous circulation.

The patient had a history of Brugada syndrome subtype 1, diagnosed as part of routine clinical and genetic screening of first-degree relatives owing to an R282C-SCN5A mutation also carried by his father. The R282C variant was initially called a variant of uncertain significance and then reclassified as a likely pathogenic mutation. His father was diagnosed with Brugada syndrome approximately 10 years earlier and was thought to have also had myocarditis owing to left ventricular scarring identified on cMRI. His father had no prior history of ventricular arrhythmias or cardiac arrest, and an implantable cardioverter-defibrillator (ICD) was placed for primary prevention.

The patient had been followed for Brugada syndrome for several years and had normal systolic function at that time. He was seen by electrophysiology 7 months before presentation at the outside facility. At that time, he had no ischemic changes or arrhythmias on stress testing, a 24-hour Holter monitor did not reveal any arrhythmias, and he declined programmed electrical stimulation, as he was doing well. The patient was asked to avoid excessive heat and illicit substances such as cocaine.

On arrival after transport, the patient was alert, oriented, and in no acute distress. He denied recent fevers, chills, exercise intolerance, sick contacts, tick bites that would suggest Lyme disease, orthopnea, shortness of breath, syncope, presyncope, chest pain, lower extremity edema, or substance use, including

KEY TEACHING POINTS

- Brugada syndrome may potentially trigger exercise-induced malignant ventricular arrhythmias.
- While structural abnormalities are not typical in Brugada syndrome patients, mutations in cardiac sodium channels may predispose them to develop nonischemic cardiomyopathy.
- Cardiac magnetic resonance imaging should be considered to identify anatomic risk factors for developing malignant arrhythmias in patients with Brugada syndrome.

KEYWORDS Brugada syndrome; Cardiac magnetic resonance imaging; Myocardial fibrosis; Sudden cardiac death; Ventricular arrhythmia
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cocaine, methamphetamine, alcohol, or cannabis. His medication list included an albuterol inhaler as needed for asthma. The physical exam was notable for a regular rate and rhythm, with no evidence of murmurs or bruits, no jugular venous distension, and no lower extremity edema.

Work-up included a high precordial electrocardiogram (ECG), which revealed a first-degree atrioventricular block (PR interval 230 ms) and a right bundle branch block with 2 mm coved ST elevation and T-wave inversions in leads V_1-V_2, and a left axis (Figure 1). Transthoracic echocardiography (TTE) revealed a left ventricular ejection fraction (LVEF) of 48% with no significant valvular abnormalities. Cardiac MRI revealed mildly reduced left and right systolic function with global hypokinesis. Delayed enhancement images revealed epicardial enhancement involving the basal inferior and inferolateral walls, suggesting myocardial fibrosis due to nonischemic etiologies (Figure 2). A troponin T was mildly elevated to 0.11 ng/mL the first day and 0.09 ng/mL the following day (reference range $<$0.10 ng/mL). The patient was transferred to the cardiovascular intensive care unit for further monitoring.

The patient met the criteria for secondary prevention with an ICD. Given his conduction disease, he underwent placement of a single-chamber transvenous ICD without complications and was subsequently discharged. The patient was followed in the cardiology clinic 2 weeks after discharge with a repeat TTE, revealing a stable LVEF of 45%. Given his findings of myocardial fibrosis and nonischemic cardiomyopathy, he was started on beta-blockade with metoprolol. Repeat genetic testing using a broad cardiomyopathy and arrhythmia panel identified no other pathogenic or likely pathogenic mutations.

The patient reported 2 episodes of palpitations and dizziness around 6 months after discharge and was found to have 2 episodes of atrial fibrillation and 2 episodes of nonsustained ventricular tachycardia on device interrogation. The patient declined to increase his dose of metoprolol at that time owing to side effects, including fatigue. He had stable left ventricular dysfunction on repeat TTE 8 months after admission with an LVEF of 45% and was started on lisinopril for further guideline-directed medical therapy. His mildly reduced ventricular function was suspected to be secondary to the *SCN5A* mutation. The patient continues to report intermittent palpitations and dizziness with intense exercise, associated with nonsustained ventricular tachycardia that has required antitachycardia pacing documented on ICD telemetry.

Discussion

Brugada syndrome is an autosomal dominant inherited arrhythmia syndrome caused by mutations affecting voltage-gated ion channels in the cardiac cell membrane, predisposing patients to sudden cardiac death. Around 20%–30% of patients present with a mutation in the *SCN5A* gene, which codes for the main cardiac sodium channel alpha subunit $Na_V1.5$. However, putative mutations in other ion channels and membrane proteins have been reported.[5] The diagnosis is made definitively by a type 1 ECG revealing $\geq$2 mm ST-segment elevation (spontaneous or following administration with sodium channel blockers) in at least 1 right precordial lead.[5,6] First-degree relatives of affected individuals should be screened with molecular genetic testing and ECG. An ICD is recommended in patients with Brugada syndrome who are survivors of an aborted cardiac arrest event and/or have spontaneous sustained ventricular tachycardia (class Ic).[5]

The etiology of this patient's sudden cardiac arrest is suspected to be secondary to ventricular arrhythmia from his underlying known Brugada syndrome type 1. Other differential

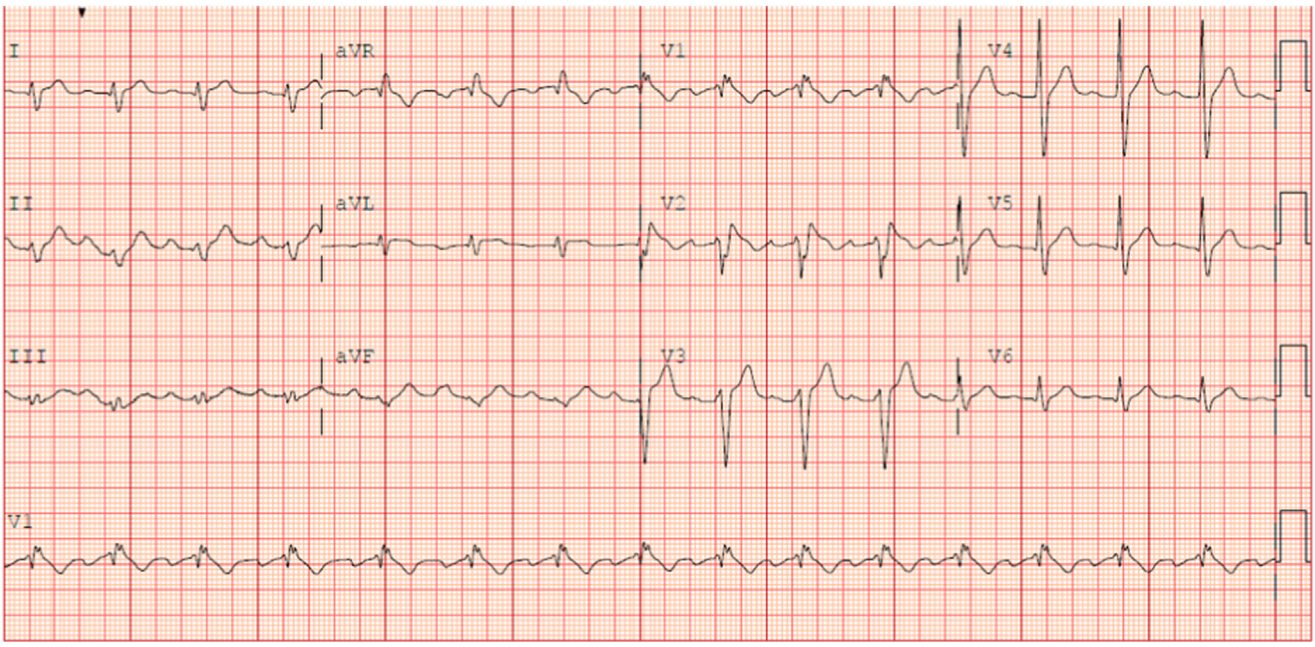

Figure 1 A high precordial electrocardiogram (ECG) demonstrating a 2 mm ST elevation and T-wave inversions in lead V_1-V_2. This is the only ECG abnormality that is potentially diagnostic of Brugada syndrome.

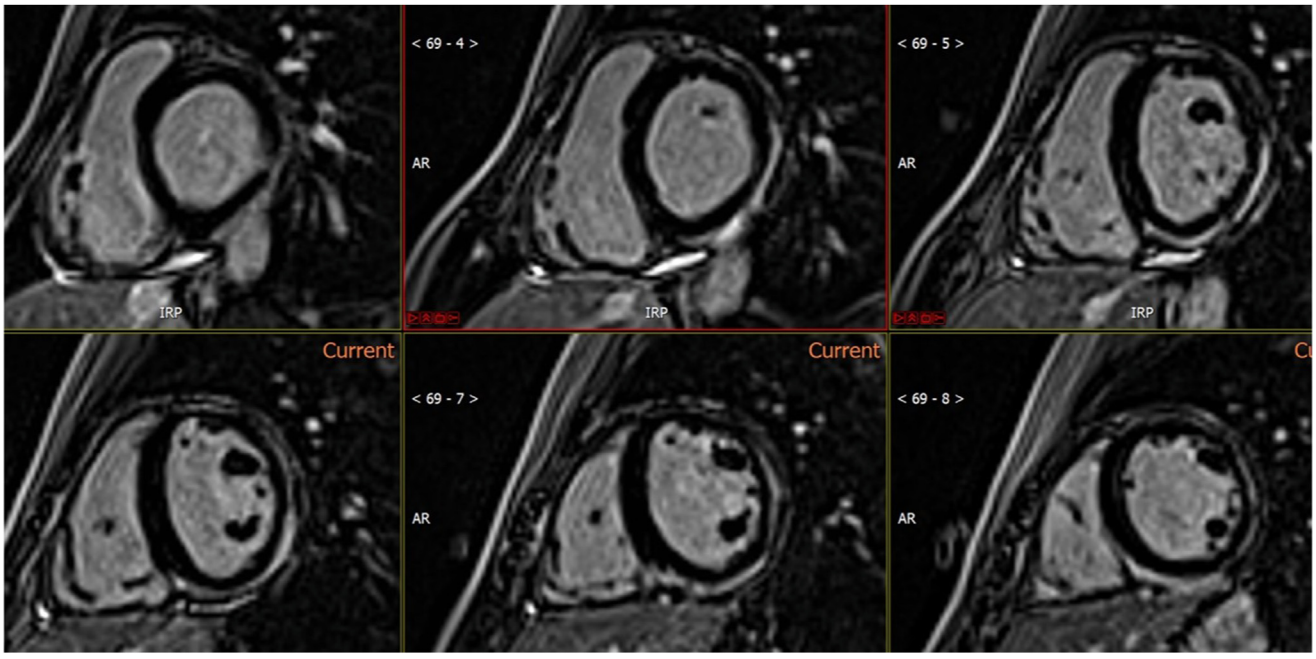

Figure 2 Cardiac magnetic resonance imaging showing epicardial enhancement involving the basal inferior and inferolateral walls, suggesting myocardial fibrosis due to nonischemic etiologies.

diagnoses were considered, such as arrhythmogenic right ventricular dysplasia, myocarditis, ischemic cardiac disease, coronary artery abnormalities, valvular pathologies, and substance abuse. However, these diagnoses were considered less likely given his known underlying arrhythmia syndrome and mutation. With regard to arrhythmogenic right ventricular dysplasia in particular, the patient did have mildly reduced biventricular function with enhancement in the basal inferior and inferolateral walls on cMRI, which can be seen in desmoplakin cardiomyopathy; however, genetic testing for desmoplakin mutations was negative.

The presented case concerns a patient with a history of Brugada syndrome type 1 who experienced aborted cardiac death while exercising and was subsequently diagnosed with mild nonischemic cardiomyopathy. While major structural abnormalities are not typically observed in Brugada syndrome patients, mutations in *SCN5A* can lead to the development of nonischemic cardiomyopathy.[6] The presence of Brugada syndrome and delayed enhancement on cMRI in both the patient and his father suggests that they likely result from the SCN5A-R282C mutation. Although the presence of fibrosis in Brugada syndrome does not itself indicate ICD placement by consensus guidelines, it could raise concern for increased arrhythmic risk. Clinical judgment is required in these at-risk patients for consideration of ICD placement.[7,8] We also speculate that the unusual exercise-induced arrhythmia phenotype may relate to the presence of both Brugada syndrome and nonischemic cardiomyopathy owing to the *SCN5A* mutation.

Conclusion

The present case underscores the potential for Brugada syndrome to lead to exercise-induced malignant ventricular arrhythmias. Cardiac MRI should be considered to identify anatomical risk factors contributing to malignant arrhythmia development in Brugada syndrome patients, especially in families where structural and/or functional abnormalities have been identified. Early identification of myocardial fibrosis at the initial presentation might have benefited this patient.

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