Brugada Syndrome

Marwan M. Refaat, MD, FHRS, FESC[a,b,c,d,*], Mostafa Hotait, MD[d], Melvin Scheinman, MD[e]

KEYWORDS

• Brugada syndrome • Diagnosis • Implantable cardioverter defibrillator • Sudden cardiac death

KEY POINTS

- Brugada syndrome might stay undetected in patients until surviving cardiac arrest.
- Despite the prominent advances in exploring the disease in the past 2 decades, many questions remain unanswered and the controversies continue.
- Despite all mutations identified to be associated with the disease, two-thirds of cases have a negative genetic test.
- Future studies should be directed toward modulating factors to help physicians in risk stratification and optimally implementing an implantable cardioverter defibrillator to prevent sudden cardiac death.

CASE PRESENTATION

A 26-year-old man presented for evaluation after several episodes of palpitations over the last year. During these episodes that commonly happen at night, his lips turn purple and he has difficulty breathing. He had recurrent episodes of syncope. His electrocardiogram (ECG) showed interventricular conduction delay and underwent a procainamide challenge that did not show the Brugada pattern. However, his genetic test showed an SCN5A mutation c.5219 C>T (p. Ser1710Leu) and was diagnosed with Brugada syndrome. His daughter was diagnosed with Brugada syndrome owing to compound heterozygosity with 2 mutations in the SCN5A gene: Arg1512Trp and Ser1710Leu. His wife had the SCN5A Arg1512Trp mutation. He had another daughter that carries the SCN5A Ser1710Leu mutation. The patient was to have an electrophysiology study and an implantable cardioverter defibrillator (ICD) implantation.

DISCUSSION

The Brugada syndrome affects predominantly middle-aged men with mean age of diagnosis around 40 years old and is mostly diagnosed by incidental ECG findings. Although previous reports showed disease prevalence ranging from 1:2000 to 1:100,000 in different parts of the world, these remain rough estimates owing to its incidental finding, dynamic ECG pattern, and masked characteristic.[1] It is inherited in an autosomal-dominant manner with incomplete penetrance. It has been highly associated with high risk of

Disclosure: None.

[a] Cardiac Electrophysiology, Cardiology, Department of Internal Medicine, American University of Beirut Faculty of Medicine and Medical Center, 3 Dag Hammarskjold Plaza, 8th Floor, New York, NY 10017, USA; [b] Department of Biochemistry and Molecular Genetics, American University of Beirut Faculty of Medicine and Medical Center, 3 Dag Hammarskjold Plaza, 8th Floor, New York, NY 10017, USA; [c] Department of Biochemistry and Molecular Genetics, American University of Beirut Medical Center, Beirut, Lebanon; [d] Cardiology Division, Department of Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon; [e] Division of Cardiology, Department of Medicine, University of California San Francisco Medical Center, San Francisco, CA, USA

* Corresponding author. Cardiology Division, Department of Internal Medicine, American University of Beirut Medical Center, PO Box 11-0236, Riad El-Solh, Beirut 1107 2020, Lebanon.
E-mail address: mr48@aub.edu.lb

Card Electrophysiol Clin 8 (2016) 239–245
http://dx.doi.org/10.1016/j.ccep.2015.10.036

sudden cardiac death. Patients are at high risk for sudden cardiac death with the cardiac event rate per year being 0.5% in asymptomatic patients, 1.9% in patients with syncope, and 7.7% in patients with aborted sudden cardiac death.[1–4] The syndrome is estimated to be responsible for 4% of all sudden cardiac deaths and 20% of sudden cardiac deaths among patients with structurally normal hearts.[1,3–5]

The Brugada syndrome is typically characterized by a right bundle branch block–like morphology along with 1 of 3 distinctive patterns of ST-segment elevation in the right precordial leads (V1–V3) on ECG in structurally normal hearts. Several Brugada syndrome cases with ST-segment elevation in inferior leads as well as the high lateral leads (I and avL) have been reported and showed a worse prognosis. According to these ST-segment patterns, the 2 Brugada consensus reports classified the disease into 3 types. Type 1 pattern has ST elevation of greater than 2 mm, giving rise to a coved-type ST segment, in electrical continuity with a negative T-wave and without a separating isoelectric (**Fig. 1**). Type 2 has a high take-off ST-segment elevation. In this variant, the J-point elevation (>2 mm) gives rise to a gradually descending elevated ST-segment (remaining >1 mm above the baseline) and a positive or biphasic T-wave. This ST-T segment morphology is referred to as the saddleback type. Type 3 is the coved- or saddleback-type with less than 1 mm ST-segment elevation. The Brugada pattern can be spontaneous or induced by procainamide, ajmaline, flecainide, or pilsicainide. Only type 1 pattern is pathognomonic of the Brugada syndrome; the other patterns are less significant. As for the definite diagnosis of Brugada syndrome, the ECG pattern should be combined with any of following clinical conditions: polymorphic ventricular tachycardia, ventricular fibrillation (VF), syncope, and early sudden cardiac death in the family (<45 years old). In addition to the ECG signs and clinical presentation, the diagnostic workup must exclude the following medical conditions that might mimic Brugada syndrome in ST segment elevation: acute pericarditis, Prinzmetal angina, acute pericarditis, and arrhythmogenic right ventricular cardiomyopathy.

Theories have emerged to explain the link between these ECG signs, possible underlying mechanisms and the increased susceptibility for ventricular arrhythmia.

Repolarization Versus Depolarization Theory

Although Brugada emerged as an exclusively cardiac channel dysfunction affecting the action potential (AP), other studies and even the first consensus report in 2002 included the possibility of underlying structural abnormality and recently investigators reported prevention of VF episodes in Brugada syndrome by catheter ablation over the anterior right ventricular outflow tract epicardium.

The repolarization theory is based on the transmural dispersion of repolarization and the unequal

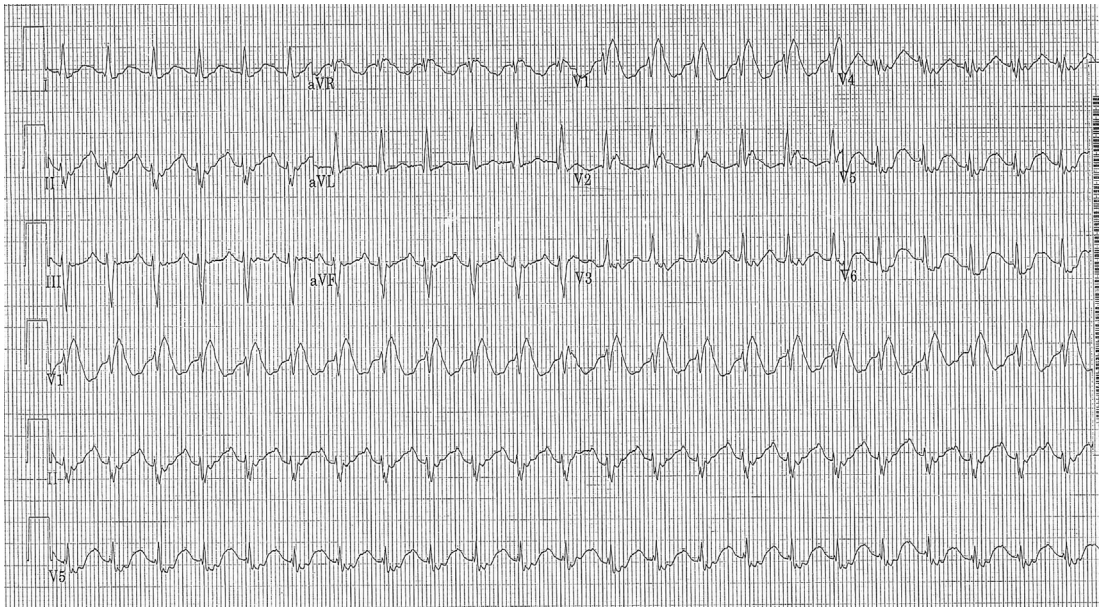

Fig. 1. Electrocardiogram of a patient with Brugada syndrome with a type 1 Brugada pattern.