Coexisting early repolarization pattern and Brugada syndrome: recognition of potentially overlapping entities

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Abstract

The Brugada type 1 electrocardiographic (ECG) pattern and the early repolarization pattern (ERP) are 2 ECG patterns characterized by the appearance of J waves. Although Brugada type 1 ECG pattern in the context of the Brugada syndrome (BrS) is well known for predisposing to life-threatening ventricular arrhythmias, it has only recently come to light that ERP, which was previously believed to be benign, may also be a marker for arrhythmogenic potential. ERP and BrS share many remarkable cellular, ionic, and ECG similarities and behave comparably in terms of their response to heart rate, pharmacologic agents, and neuromodulation. The extent to which ERP and BrS may overlap remains unclear. Here, we present an illustrated case of a symptomatic patient whose ECG signature evolved spontaneously from ERP alone to ERP with a concomitant Brugada type 1 ECG pattern over a short number of days. This case lends further strength to the notion that these 2 ECG patterns may be more closely related than had been initially thought.

Keywords: Early repolarization pattern; Brugada syndrome; Ventricular repolarization; Sudden cardiac death

Introduction

The Brugada type 1 electrocardiographic (ECG) pattern and the early repolarization pattern (ERP) are 2 ECG patterns characterized by the appearance of J waves. Although Brugada type 1 ECG pattern in the context of the Brugada syndrome (BrS) is well known for predisposing to life-threatening ventricular arrhythmias, it has only recently come to light that ERP, which was previously believed to be benign, may also be a marker for arrhythmogenic potential. Early repolarization pattern and BrS share many remarkable cellular, ionic, and ECG similarities and behave comparably in terms of their response to heart rate, pharmacologic agents, and neuromodulation.

Early repolarization pattern is a common ECG finding that affects 1% to 9% of the general population and is more common in African Americans and athletes. Although no consensus definition exists, it has previously been defined by elevation of the J point (QRS-ST junction) of at least 1 mm (0.1 mV) above baseline in at least 2 contiguous leads, in the inferior leads (II, III, and aVF), lateral leads (I, aVL, and V4 to V6), or both. It can manifest either as “slurring” of the QRS (a smooth transition from the QRS segment to the ST segment) or “notching”—a positive J deflection inscribed on the S wave. Early repolarization pattern was initially thought to be entirely benign, but recent evidence suggests otherwise.1,2

Brugada syndrome is a clinical ECG entity predisposing to ventricular arrhythmia and sudden cardiac death (SCD). It is defined electrocardiographically by a characteristic pattern including J point and ST-segment elevation 2 mm or greater, followed by a negative T wave in the right precordial leads. The ECG of patients with BrS can change over time between type 1 “coved” and types II and III “saddle-back” patterns and even show transient normalization. The BrS pattern has been closely linked to SCN5A gene mutations affecting sodium channel function.3

The extent to which ERP and BrS may overlap remains unclear.4 Both ERP and BrS have been described simultaneously in different members of the same family,5 and some have even proposed classifying them as part of a spectrum of disease.6 Here, we present what is, to the best of our
knowledge, the first illustrated case of a symptomatic patient whose ECG signature evolved spontaneously from ERP alone to ERP with a concomitant Brugada type 1 ECG pattern over a short number of days. This case lends further strength to the notion that these 2 ECG patterns may be more closely related than had been initially thought.

Clinical case

A 20-year-old Brazilian male professional soccer player presented for assessment, complaining of 2 presyncopal episodes and 1 syncopal episode in the preceding 30 days. The 2 presyncopal episodes occurred coinciding with defecation. Both episodes were associated with lightheadedness, diaphoresis, and nausea. The syncopal episode occurred at rest with no prodromal symptoms. His medical history was unremarkable; he had successfully passed 2 prior precompetitive clinical ECG screenings.

The patient’s family history was significant for the sudden, unexplained death of a paternal uncle at the age of 35 years. The patient volunteered that his brother was being followed up by a cardiologist because of “cardiac arrhythmia” but was unable to provide further detail.

Fig. 1. Panel A, Twelve-lead ECG from a 20-year-old man, showing sinus bradycardia, J waves (arrow) with concave up ST-segment elevation in leads V4 to V6 and the inferior leads. These features are considered to be consistent with ERP. Panel B, Twelve-lead ECG from the same 20-year-old man, recorded 72 hours later. The ERP persists, and there is now sinus bradycardia with a Brugada type 1 ECG pattern (coved type) in leads V1 to V3. The ST-segment elevation seen in lead aVR has been identified as a potential high-risk marker for ventricular arrhythmia in patients with BrS.
Cardiovascular examination revealed bradycardia at 45 beats per minute with physiologic sinus arrhythmia and a blood pressure of 110/70 mm Hg. The remainder of the physical examination was unremarkable. The patient denied consumption of any medications or recreational drugs. His diagnostic tests included a normal echocardiogram and negative tilt table testing. Genetic screening for BrS was negative (Kit ProMetic Life Sciences Inc, Quebec, Canada).

His initial 12-lead ECG (Fig. 1A) showed sinus bradycardia at 44 beats per minute. There were positive Sokolow voltage criteria for left ventricular hypertrophy and a normal QTc interval (367 milliseconds). In the left precordial leads, there are deep and narrow Q waves and a notch (J wave) on the terminal portion of the QRS complex. There is concave up ST-segment elevation, followed by a positive T wave in the inferior leads and from V4 to V6. All these features were considered to be consistent with ERP.

A second 12-lead ECG (Fig. 1B), obtained 72 hours later, showed sinus bradycardia at 44 beats per minute but a completely different ventricular repolarization pattern in the right precordial leads. A Brugada type 1 ECG pattern (coved type) can be seen in leads V1 to V3. An accentuated J wave across the precordial and limb leads can also be observed. There is new ST-segment elevation in lead aVR with a negative T wave and a large U wave. The QTc interval remains 367 milliseconds. Morphologies of the right precordial leads at admission and 72 hours later are compared in Fig. 2.

An electrophysiology study delivering 2 extrastimuli induced ventricular fibrillation. The patient was offered an implantable cardioverter defibrillator (ICD) but declined. He was prescribed oral quinidine at a dose of 300 mg every 6 hours. A second electrophysiology study 2 months later, using up to 3 extrastimuli, repeated 2 months later, failed to show inducible arrhythmia.

Discussion

Since it was first reported on by Shipley in the 1940s, elevation of ST segments in the absence of structural heart disease, conduction system disease, or chest pain, occurring particularly in young, athletic individuals, had long been labeled a normal variant referred to as ERP. The first in vitro findings that suggested ERP may not be as benign as previously thought came from the work of Gussak and Antzelevitch in 2000. More recently, the retrospective analysis of Haissaguerre et al showed that among patients with a history of idiopathic ventricular fibrillation, there was an increased prevalence of ERP compared with controls (31% vs 5%; P < .001).

The prevalence of ERP varies between 1% and 9%. It shows a definite male bias (77%) and is more commonly observed in younger individuals (27.5%). The ECG pattern is frequently observed in athletes, African Americans, cocaine abusers, and patients with hypertrophic obstructive cardiomyopathies.

The degree to which ERP and BrS may overlap remains undetermined. A recent study by Sarkozy et al found that up to 11% of patients with BrS may also have an ERP on their ECGs. Both BrS and ERP have been identified
predominately in young, otherwise healthy men, have a predisposition to familial occurrence, and can display transient ECG normalization. Both also share many common characteristics in terms of response to heart rate, pharmacologic agents, and neuromodulation. Brugada syndrome has been linked to mutations in both sodium channels (eg, SCN5A, GPD1L) and calcium channels (eg, CACNA1C, CACNB2b). Where recent large cohort studies have demonstrated evidence for a heritable basis for ERP, a genetic marker and its pattern of inheritance are yet to be identified.

In a recent review, some experts have argued that based on their similarities in terms of demographics, ECG signatures, and response to neuromodulation, ERP and BrS represent parts of a continuous spectrum of phenotypic expression that they have proposed classifying under the umbrella term of “J-wave syndromes.” The authors divide J-wave syndromes into subtypes based on risk and morphology. Type 1 is associated with ERP predominantly in the inferior or inferolateral leads and is associated with a higher level of risk. Type 2 displays an ERP predominantly in the inferior or inferolateral leads and is associated with the highest level of risk for development of malignant arrhythmias. Brugada syndrome pattern represents a fourth type and, by far, the highest risk of SCD. A basic mechanism linking these entities is yet to be determined but may stem from perturbations in the transient outward current (Ito), which is responsible for J-wave formation. This may be due to a decrease in inward sodium or calcium channel currents or an increase in outward potassium currents. Conversely, they could exist as completely separate entities and be sometimes seen together due to the relatively high prevalence of ERP in the general population.

In the presented case, a symptomatic patient with ERP and a Brugada type 1 ECG pattern underwent an electrophysiology study before being offered an ICD. The role of the electrophysiology study in the evaluation of BrS remains controversial. Of note, the patient’s ECG displayed ST elevation in lead aVR—this has been proposed as a high-risk marker for arrhythmia. When the patient declined an ICD, the decision was made to prescribe him oral quinidine, which appears to be a reasonable alternative to an ICD in at-risk patients with BrS and in those with ventricular fibrillation associated with ERP. Currently, there is a paucity of data to guide risk stratification and management of patients with ERP. Recently, Rosso et al found, on retrospective analysis of a case-control study, that identifying a J wave in a young adult’s ECG would only increase the probability of SCD from 3.4:100 000 to 11:100 000.

The appearances of both ERP and BrS in the same patient lend further strength to the notion that ERP may not be as benign as previously believed. The diagnostic value of the J wave as a marker of arrhythmogenicity and the possibility of overlap between these entities are yet to be determined. Prospective studies and further electrophysiologic and genetic information will help to clarify the clinical significance of and relationship between ERP and BrS.

References