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Review article

Early repolarization syndrome and Brugada syndrome: Is there any linkage?

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Abstract

Early repolarization syndrome (ERS) is characterized by the presence, in most cases in mid-to-lateral precordial leads, of a J wave on the downsloping portion of the QRS complex, followed by an elevation of the ST-segment with upward concavity. ERS is considered a benign electrocardiographic pattern of ventricular repolarization and, thus far, clinical interest in this syndrome has been confined to its differential diagnosis from myocardial infarction and pericarditis. Brugada syndrome (BS), an inherited cardiac disease first described in 1992, exhibits a characteristic electrocardiographic pattern consisting of a J wave mimicking a right bundle branch block with typical ST-segment elevation in the right precordial leads. Believed to be a normal repolarization variant for more than three decades, the syndrome is now known instead to be associated with a high incidence of life-threatening ventricular tachyarrhythmias and is responsible for a number of sudden deaths in young adults worldwide. Although clinical findings seem to differentiate the two syndromes, similarities between BS and ERS in terms of response to heart rate, pharmacologic agents, and neuromodulation could suggest a linkage in their pathophysiological mechanism. The authors review the clinical and experimental data in order to test this hypothesis.

Keywords: Early repolarization syndrome; Brugada syndrome; Arrhythmias; Sudden death

1. Introduction

ERS is an electrocardiographic variant of normal ventricular repolarization [1,2].

It is considered benign, and clinical interest in this syndrome has been confined to the differential diagnosis from other conditions characterized by ST-segment elevation, such as myocardial infarction and pericarditis [3].

The electrocardiographic features of the so-called "Brugada pattern" may be present in asymptomatic individuals or associated with several pathologic conditions [4]. In a few cases, it is an expression of an inherited cardiac disease that was first described in 1992 and called "Brugada syndrome" [5]. This syndrome is characterized by a high incidence of life-threatening ventricular tachyarrhythmias and is responsible for a number of sudden deaths in young adults worldwide [6].

Although clinically different, the two syndromes share similarities in terms of response to heart rate, pharmacologic agents, and neuromodulation that could be explained by a linkage in their pathophysiological mechanism [7]. It is important to verify this hypothesis because the arrhythmogenic potential of ERS is still unknown and some authors question its "innocence" [8].

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2. Early repolarization syndrome

ERS is a common electrocardiographic pattern, with a prevalence of 1–2% in the normal population [9]. Its prevalence is higher (10%) in the general athletic population, reaching 100% in selected groups of endurance-trained subjects [10]. Rare in the elderly, it is predominant in men and has been associated with cocaine use, defect and/or hypertrophy of the interventricular septum, obstructive hypertrophic cardiomyopathy, and additional left ventricular chorda [11–14]. A familial predisposition has been reported and could be related to a genetic factor involved in determining the syndrome [1].

The electrocardiographic criteria for the ERS are a J wave on the downsloping portion of the QRS complex, often visible as a notch, and an ST-segment elevation with upward concavity; a reciprocal ST-segment depression in aVR is an additional characteristic (Fig. 1).

An increase in QRS amplitude is often present and, recently, Boineau identified an interesting anomaly in the depolarization phase: an asymmetric QRS complex, with slurring and a reduced slope angle of the ascending positive R wave, and an extremely rapid intrinsecoid deflection [15].

The alterations are predominant in mid-to-lateral precordial leads but can also occur more laterally (leads I, aVL, V_5 and V_6), inferiorly (leads II, III, aVF), and anteriorly (leads V_1 and V_2). A concomitant inhomogeneous repolarization with irregular QT intervals and bifid T waves, in which the first T peak represents a greater degree of Q–T shortening, may be present [8].

The rapid pacing or the exercise normalizes the electrocardiogram, but the magnitude of the ST-segment elevation may vary markedly in the same patient, regardless of heart rate [16,17]. Magnetic measurement of ST and TQ segments unequivocally demonstrates that ST-segment elevation is not due to ischemic myocardial injury [18].

Prior clinical interest in this syndrome has been related to its differential diagnosis from other conditions characterized by ST-segment elevation in order to avoid a dangerous misdiagnosis.

3. Brugada syndrome

In recent years, another clinical syndrome associated with a prominent J wave and ST-segment elevation in the absence of structural heart disease has been identified: the "Brugada syndrome", discovered in 1992 by Pedro and Joseph Brugada [5]. In this syndrome, the J wave mimics a right bundle branch block, with ST-segment elevation localized in the right precordial leads (Fig. 2).

Three types of Brugada waves have been identified. In type I, the ST-segment elevation is triangular and the T waves may be inverted in leads V_1–V_3; in type II, the downward displacement of the ST-segment lies between two elevations of the segment in leads V_1 through V_3 but does not reach the baseline, whereas in type III the middle part of the segment touches the baseline. The T waves in types II and III may not be inverted [4].

A high incidence of ventricular arrhythmias characterizes the syndrome: when they occur, life-threatening arrhythmias consist of polymorphic ventricular tachycardia that evolves into ventricular fibrillation, with an estimated prevalence as high as 40–60% [19].

Brugada syndrome exhibits autosomal dominant inheritance with SCN5A, which encodes the cardiac sodium channel as the only gene with a proven involvement in about 25% of patients [20]. The effect is a Na reduction, resulting from

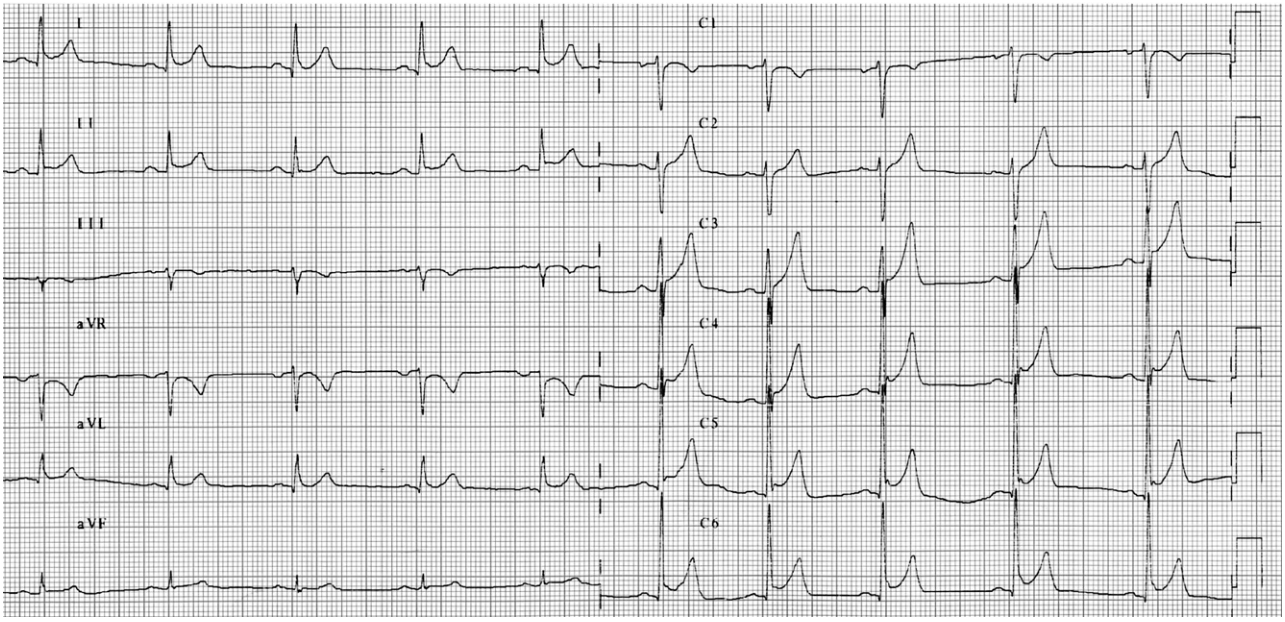

Fig. 1. Early repolarization syndrome.