Appearance of J wave in the inferolateral leads and ventricular fibrillation provoked by mild hypothermia in a patient with Brugada syndrome

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Introduction

Patients with Brugada syndrome (BrS) are recognized as having a high risk for sudden cardiac death owing to ventricular fibrillation (VF). The electrocardiogram (ECG) pattern in BrS is dynamic and variable, and often the typical pattern is concealed.[1–3] Multiple factors have been shown to influence ST-segment elevation in BrS patients and suspected cases of BrS. These factors include changes in heart rate, body temperature, autonomic tone,[1–4] glucose-induced insulin production, full stomach test,[5,6] sodium channel blockers,[1,2,7] and so on. A high prevalence of the J wave in the inferolateral leads was reported in patients with idiopathic ventricular fibrillation compared with control subjects in a case-control study.[8] Subsequent studies confirmed a high prevalence of J wave as a risk marker for VF in various pathologic conditions, including BrS,[9] vasospastic angina,[10,11] acute myocardial infarction,[12] and hypothermia.[13,14] A J wave in the inferior leads was also associated with increased cardiac mortality in the general population.[15] Appearance and augmentation of the J-wave amplitude were modulated by various factors, including hypothermia, bradycardia, and increased vagal tone.[16,17] Several reports indicated that patients who had BrS with inferolateral J wave had a worse prognosis than those without.[7,18] If BrS patients showing inferolateral J wave have a wide range of the arrhythmogenic substrate, these patients may have a high risk for VF provoked by the modifiers of the J wave. We present a case of BrS in which VF was provoked by mild hypothermia with appearance of prominent J wave in inferolateral leads.

KEYWORDS Brugada syndrome; J wave in inferolateral leads; Ventricular fibrillation; Hypothermia; Sudden cardiac death
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Case report

A 39-year-old man with an episode of nocturnal agonal respiration was transferred to the hospital by ambulance. In the ambulance, VF was detected and, with appropriate shocks by the automated external defibrillator, converted to sinus rhythm (Figure 1A). A 12-lead ECG showed coved-type ST-segment elevation (type 1 ECG) in the second and third intercostal space recordings of the right precordial leads (V_1–V_2) (Figure 1B). Echocardiography showed diffuse mild hypokinesis of the left ventricular wall and ejection fraction was 50%, but no major structural abnormality of the heart was detected. Coronary angiography revealed no significant obstructions in the major coronary branches. The patient was diagnosed as having BrS. He had similar episode 7 years prior. No VF events or sudden cardiac death had been observed in his family members.

On admission to the coronary care unit, his 12-lead ECG displayed coved-type ST-segment elevation in V1 but did not show a J wave in any other leads. He underwent therapeutic hypothermia with a target temperature of 34°C for 24 hours. After the patient reached target temperature, ECG showed J waves in the lateral leads (time 14:56, V_5–V_6), and then after 34 minutes in the inferior lead (time 15:30, II-III-aVF) (Figure 2). With decreased heart rate, the amplitude of the J wave in the inferolateral leads gradually augmented. At the same time, ST-segment elevation in the V_1–V_3 lead newly appeared (time 17:30, Figure 2). With augmentation of J waves in the inferolateral leads, VF was initiated by short-coupled ventricular premature contractions (VPCs) exhibiting right bundle branch block with superior axis (Figure 3). VF was terminated by electrical defibrillation. J-point elevation in the inferolateral leads and ST-segment elevation in the right precordial leads disappeared with isoproterenol infusion.

After several days, circadian variation of ST-segment elevation in the right precordial leads was observed, but J waves in the inferolateral leads never appeared in response to conditions favorable for Brugada-type ECG, which

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KEY TEACHING POINTS

- Brugada syndrome (BrS) with inferolateral J waves carried a worse prognosis than BrS without.
- The basic mechanisms for ST-segment elevation in the right precordial leads and J wave in the inferolateral leads are similar, with increased electrical heterogeneity, but they are influenced by different modifiers.
- Augmentation of J waves in the inferolateral leads in patients with BrS represents an electric heterogeneity over extensive regions of the ventricles, which may cause ventricular fibrillation triggered by ventricular premature contractions originating from the inferior wall of the left ventricle, the same area for the genesis of the J wave.

included an intravenous administration of pilsicainide, glucose tolerance test, and treadmill exercise test. Late potential was positive (f-QRS: 136 ms, LAS40: 66 ms, RMS40: 6 μV) by signal-averaged ECG. VF was reproducibly inducible by programmed ventricular stimulation at the right ventricular apex but was not induced at the right ventricular outflow tract (RVOT). VF could not be induced by programmed ventricular stimulation at the right ventricular apex or RVOT after isoproterenol administration. During electrophysiological testing, the ECG showed coved-type ST-segment elevation in the right precordial leads, but J waves in the inferolateral leads were not observed at any time. The patient underwent implantable cardioverter-defibrillator implantation for secondary prevention of VF.

Discussion

This case was diagnosed as BrS according to the HRS/EHRA/APHRS consensus recommendation,[3] as the patient was a VF survivor showing type 1 Brugada ECG at the higher intercostal lead positions of V_1–V_2 without association of major structural heart diseases. During therapeutic hypothermia after resuscitated VF, he developed J waves in the inferolateral leads, and with augmentation of J-wave amplitude, short-coupled VPCs originating the inferior wall of the left ventricle triggered the initiation of VF. After the body temperature was warmed up to 37°C, J waves never

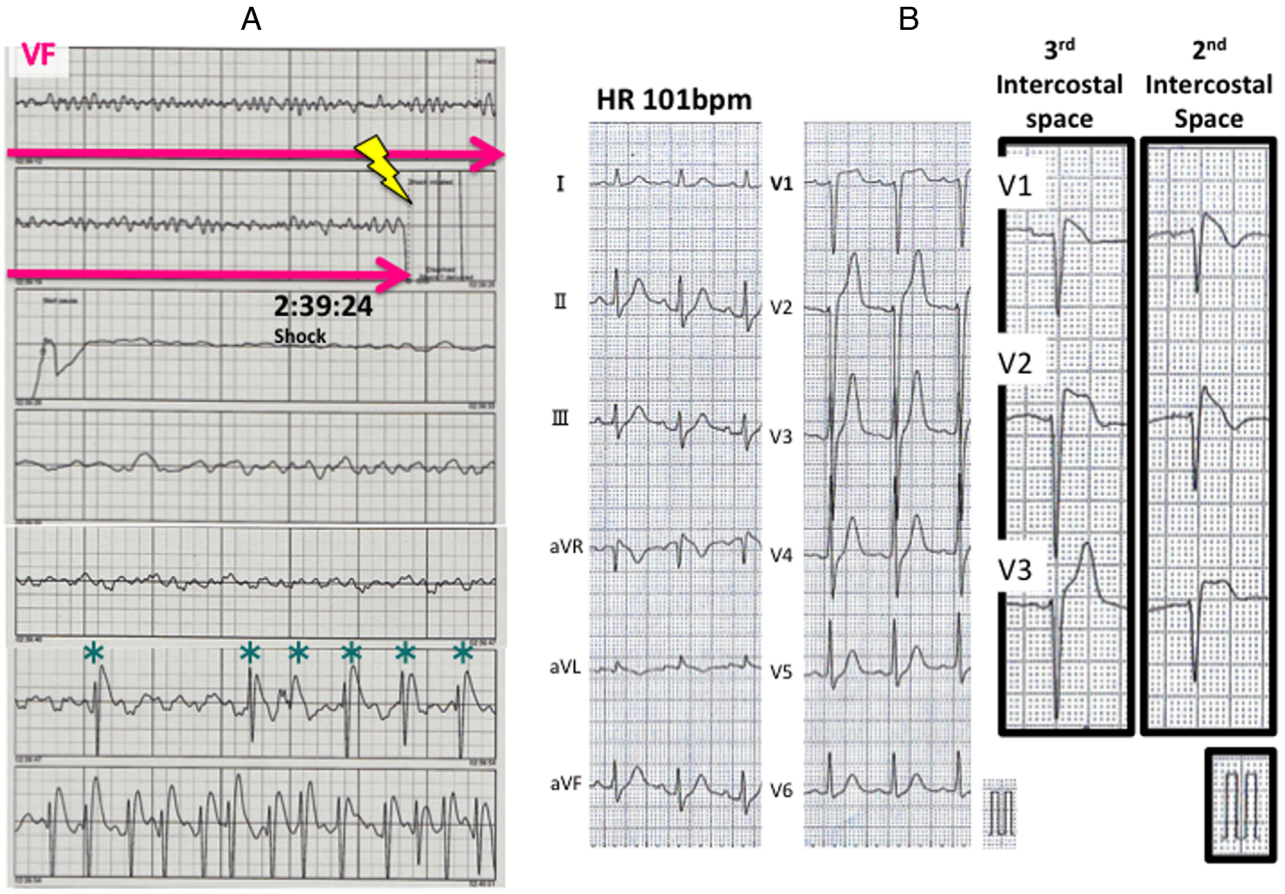

Figure 1 **A:** The automated external defibrillator detected ventricular fibrillation (VF), and the shock was delivered. After return of spontaneous circulation, the automated external defibrillator monitor showed prominent coved-type ST-segment elevation (*). **B:** The 12-lead electrocardiogram showed coved-type ST-segment elevation in the second and third intercostal space recordings of the right precordial leads (V_1–V_2) (*right panel*) but did not show J wave in any leads (*left panel*). HR = heart rate; bpm = beats per minute.

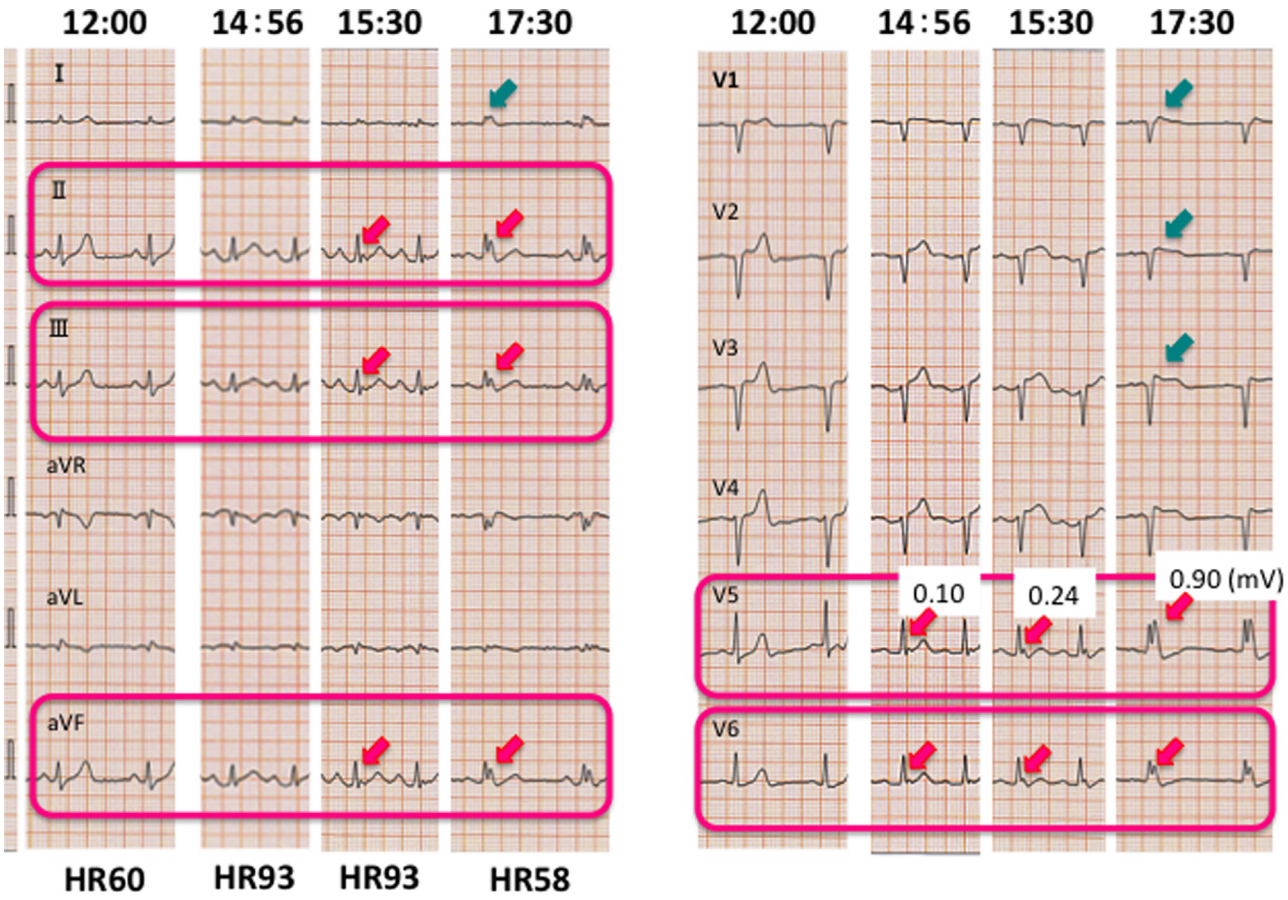

Figure 2 After a target temperature of 34°C was achieved, 12-lead electrocardiogram showed the elevation of J-point first in the lateral leads (V_5–V_6), followed by development in the inferior leads (II, III, aVF). In association with a lower heart rate, the amplitude of J waves in the inferolateral leads gradually increased. Moreover, ST-segment elevation in the right precordial leads (V_1–V_3) newly appeared. HR = heart rate.

appeared despite slow heart rate and circadian variation of ST-segment elevation in the right precordial leads.

The mechanism of ST-segment elevation in the right precordial leads in BrS was explained by the transmural voltage gradient during early repolarization phase at the RVOT.[17,19] Action potentials of epicardial cells of the RVOT show a prominent notch during early repolarization because of well-developed transient outward potassium current (Ito), while endocardial action potentials lack this notch owing to a less developed Ito. With augmentation of Ito or decreased inward sodium or calcium current, the notch of epicardial action potential becomes larger and leads to the appearance of shortened action potentials in some regions. As a result, dispersion of repolarization increases among contiguous cells, which provides an appearance of phase 2 reentry leading to the development of polymorphic ventricular tachycardia and VF. Although this concept has been supported mainly by experimental studies, clinical relevance is not fully achieved and different explanations have been proposed.[20]

Yan and Antzelevitch[13] proposed a similar explanation for the mechanism of J wave in the inferolateral leads to that of the ST-segment elevation in the right precordial leads of BrS. The voltage gradient caused by the presence and absence of the notch and Ito between the epicardial and endocardial cells in the inferior and lateral wall of the ventricle produces a J-wave configuration in the ECG. Conditions that augment or reduce Ito could modify the manifestation of J waves in the ECG. When Ito was augmented or current kinetics altered by exposure to hypothermia, bradycardia, or Ito agonist, the epicardial notch and J wave were augmented. Reduction of Ito by application of Ito blockers decreased the notch and J waves.[17] With further increase in the Ito-mediated notch, dispersion of repolarization becomes markedly augmented, conditions that favor the development of "phase 2 reentry" and initiation of polymorphic ventricular tachycardia / VF.[17] According to this hypothesis, the mechanism of the ST-segment elevation in BrS and J wave in the inferolateral leads is explained by voltage differences between endocardial and epicardial cells. The principal difference between them is the myocardial region responsible for manifestation of ECG changes and the origin of arrhythmias; the case of BrS is in the RVOT and the case with J wave in inferolateral leads is in the inferior region of the left ventricle.

Actually, there are similar behaviors between ST-segment elevation (V_1–V_3) in BrS and the J wave in inferolateral leads in response to various modifying conditions.[1,2,17] The amplitudes of both conditions are augmented by slow heart rate, pause, short-long-short sequence and by increased vagal tone,

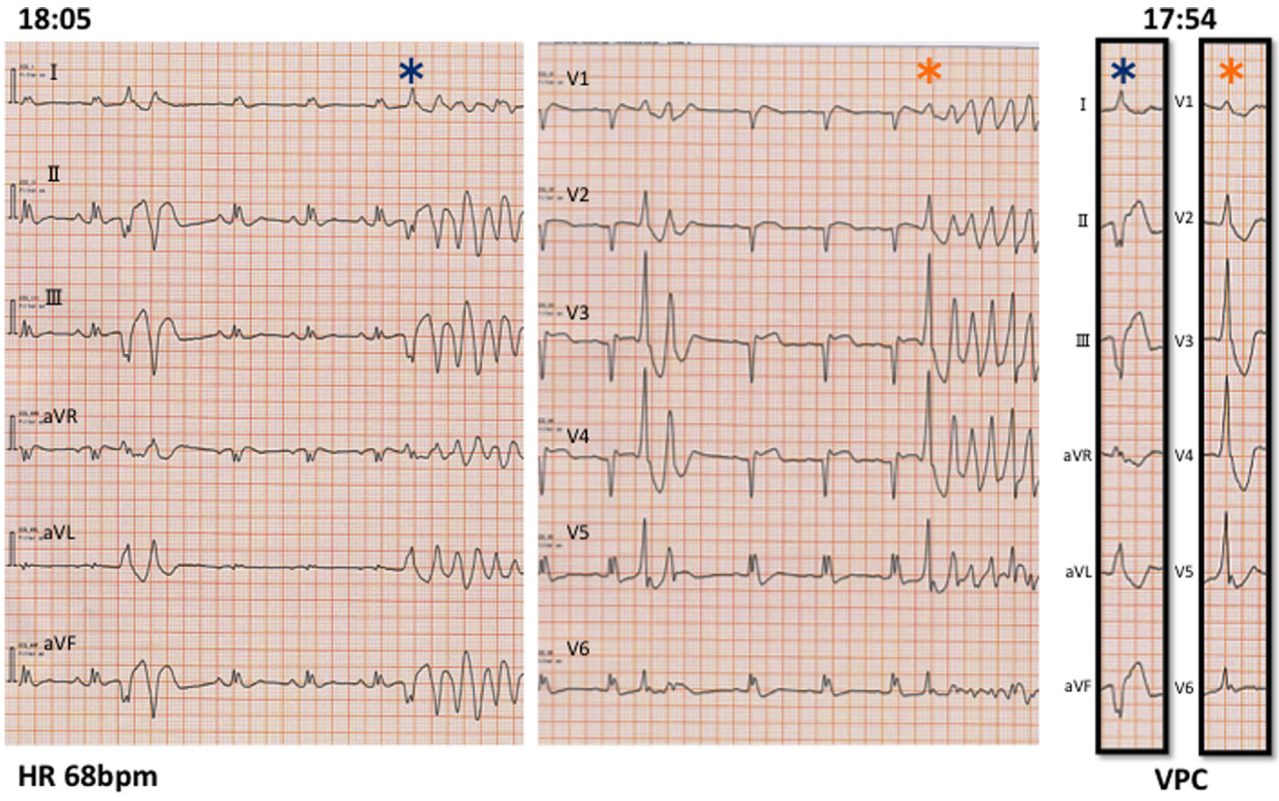

Figure 3 Ventricular fibrillation started after short-coupled ventricular premature contractions (VPC) exhibiting right bundle branch block with superior axis. HR = heart rate; bpm = beats per minute.

and they are suppressed by isoproterenol. There are, however, trivial differences between them. For example, although quinidine attenuates both conditions, other class I drugs such as pilsicainide and ajmaline augment the ST-segment elevation in BrS but attenuate J-wave amplitude in inferolateral leads.[2,21–23] High body temperature is claimed to be a risk for arrhythmic events in BrS, but low temperature induces development and augmentation of J-wave amplitude.[2,13]

In our case, J waves in the inferolateral leads were never observed at normal body temperature, even under conditions that augment ST-segment elevation and increased arrhythmogenic risk in BrS. Furthermore, J waves appeared at mild hypothermia (34°C), which was reported to be a marginal temperature for their development in the clinical setting.[24] Even at mild hypothermia, the amplitude of J waves in the inferolateral leads became augmented, leading to the development of VPCs. The focus of these VPCs, judged by the morphology, was suggested to be the inferior wall of the left ventricle, where the patient's J wave might be formed by increased heterogeneity of repolarization in the same area. These findings are in contrast to the area of ST-segment elevation and arrhythmia origin in BrS, where the RVOT was responsible for such events.[17,19]

The ST-segment elevation in the right precordial leads in this case became apparent at mild hypothermia, similarly to the J wave in the inferolateral leads, but after warm-up to 37°C the ST-segment elevation in the right precordial leads underwent circadian variation in amplitude but the J waves never appeared. The patient's first attack of VF appeared to originate at a different area from the one provoked by hypothermia, since no J wave in the inferolateral leads was noted after the resuscitation from the first event and ST-segment elevation was noted in the right precordial lead positions. A trigger for his first VF attack was not clear, but increased vagal tone might play a role, since the attack occurred during sleep, a condition that was different from the hypothermia with his second VF. These results suggest that basic mechanisms for ST-segment elevation in the right precordial leads and J wave in the inferolateral leads are similar, with increased electrical heterogeneity, but they are influenced by different modifiers to trigger arrhythmic events. Further patients with BrS showing J waves in the inferolateral leads might be explained by increased risk for VF owing to additional arrhythmic modifier than those without J waves.[7,18] Without clarifying the role of such modifiers, risk stratification in BrS may not be easily assigned.

Augmentation of the J wave in the inferolateral leads in patients with BrS represents an electric heterogeneity in an extensive region of ventricles that may develop VF triggered by VPC originating from the inferior wall of the left ventricle in association with J waves.

Conclusions

We report a case of a patient with BrS resuscitated from VF who underwent therapeutic hypothermia. At mild hypothermia, he developed J waves in the inferolateral leads with increasing amplitude, leading to the development of VPCs from the inferior wall of the left ventricle and degenerating into VF.

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