We herein describe two patients with Brugada syndrome in whom J-waves were successfully modified by drugs. Case 1 was a 54-year-old man who presented with repeated ventricular fibrillations (VF) and J-point elevation in the right precordial and lateral leads. After administration of cilostazol (200 mg/d), J-waves disappeared and coved-type ST-segment elevation changed to a saddleback-type for 25 months. Case 2 was a 31-year-old man who presented with a VF storm and J-point elevation in the lateral leads. After administration of quinidine (300 mg/d), J-waves and coved-type ST-segment elevation disappeared for 20 months. J-wave disappearance and coved-type ST-segment elevation were followed by VF suppression, probably due to transient outward potassium current ($I_{to}$) suppression.

Key words: Brugada syndrome, J-wave syndrome, pharmacological therapy, ventricular fibrillation, cilostazol, quinidine

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Introduction

The concept of J-wave syndrome has recently been proposed because the presence of electrocardiographic J-waves (J-point elevation) plays a crucial role in ventricular fibrillation (VF) pathogenesis (1). The J-wave is thought to be the consequence of a transmural voltage gradient caused by a predominant expression of transient outward potassium currents ($I_{to}$) in the epicardium, as observed in Brugada syndrome (BrS) and J-wave-prominent idiopathic VF (IVF) (2). The J-wave may be augmented prior to VF episodes, and its pharmacological suppression controls these VF episodes (3-6). Quinidine is effective in suppressing VF storms and recurrences, but its availability is limited (7, 8). Cilostazol has been shown to be effective in preventing VF recurrence in BrS and IVF (9, 10); however, the long-term effect of these drugs on J-waves and VF recurrence is poorly understood in BrS.

We herein describe two cases from unrelated families who were diagnosed as BrS. Oral cilostazol or quinidine effectively abolished J-wave and coved-type ST-segment elevation in both patients and prevented VF recurrence during their long-term follow-up.

Case Reports

Case 1

A 54-year-old man was admitted to our hospital because of nocturnal syncope. He had no family history of syncope or sudden death. The cardiovascular system examination was normal. The presence of structural heart disease was excluded, and his standard 12-lead electrocardiogram (ECG) showed normal sinus rhythm and normal QT interval (Fig. 1A). However, he exhibited coved-type ST-segment elevation in leads V1 and V2, and J-waves with ascending ST segment in leads V3-V6, with a maximum amplitude of 0.3 mV (arrows in Fig. 1A).

During the electrophysiological study, VF was repeatedly
induced by triple extra-stimuli from the right ventricular outflow tract. Following a diagnosis of BrS, the patient was implanted with an implantable cardioverter-defibrillator (ICD) and discharged without administration of an anti-arrhythmic drug. Because his brain magnetic resonance imaging revealed an old lacunar infarction, clopidogrel sulfate (75 mg/d) was administered for secondary prevention.

Twelve months later, he experienced two consecutive ICD shocks due to VF episodes during sleep. An ECG showed both coved-type ST-segment elevation in the V1 lead and prominent J-waves in leads V4-V6 (arrows in Fig. 1B) as previously observed. His heart rate was relatively slow (57 beats/min), and we switched from clopidogrel sulfate to cilostazol (200 mg/d). On cilostazol, the patient’s heart rate increased to 76 beats/min, and coved-type ST-segment elevation and J-waves were no longer observed (Fig. 1C). He has been followed on the drug and has not experienced VF for 25 months.

**Case 2**

A 31-year-old man was admitted because of syncope immediately after waking up in the early morning. His father had died suddenly at the age of 36 in his sleep, and his grandfather had died suddenly in his 60s after an early morning walk. DNA screening for an SCN5A mutation was negative.

The patient’s cardiovascular system was normal. His 12-lead ECG showed normal sinus rhythm (53 beats/min) and J-waves with an ascending ST segment in leads I and V3-V6 and a horizontal ST segment in the aVL lead (arrows in Fig. 2A). ECG recorded at higher intercostal spaces did not fill the criterion of a typical ECG pattern for BrS (arrow head in Fig. 2A). The pure sodium channel blocker pilsicainide was given at a dose of 1 mg/kg and failed to induce the characteristic ECG pattern of BrS. VF was not induced by one to three extrastimuli applied to the right ventricle apex and outflow tract. He underwent an ICD implantation and was discharged without any anti-arrhythmic agent.

Forty-one months after discharge, he experienced two ICD shock deliveries during sleep. A month later, an electrical storm (≥3 VF episodes/24 h) occurred at night. His ECG recorded immediately after the storm showed J-waves in leads I and V6 and ST-segment elevation in leads V1 and V2 (arrows in Fig. 2B). Recordings from the higher intercostal spaces showed coved-type ST-segment elevation in the V2 lead, which was compatible with BrS (arrow head in Fig. 2B).

Quinidine was started at 300 mg per day, which increased the patient’s heart rate from 53 to 62 beats/min, and VF was prevented. Both J-waves and ST-segment elevation were abolished by the drug (Fig. 2C). With quinidine, late potentials on the signal-averaged ECG were normalized: LAS<sub>40</sub> from 60 to 35 μV, and RMS<sub>40</sub> from 3 to 22 ms. He was discharged on quinidine and has not experienced VF recurrence for the past 20 months.

**Discussion**

In both BrS and J-wave-associated IVF, electrical storms are known to be controlled by isoproterenol or quini-
Figure 2. Twelve-lead ECGs after the first syncopal episode (A), after the VF storm (B), and during the administration of quinidine (C). The bottom panel shows the upper third intercostal ECGs.

dine (3-6, 11-13). As alternatives, cilostazol has been shown to be effective in preventing VF recurrence (9, 10). We described two cases of BrS associated with J-waves. Either cilostazol or quinidine was able to suppress VF recurrence and abolish any ECG signs of early repolarization.

Mechanistically, quinidine inhibits $I_{to}$ currents and diminishes the transmural voltage gradient, thus reducing $I_{to}$-mediated J-waves (2). Cilostazol, a selective inhibitor of phosphodiesterase III, is an antiplatelet drug with vasodilatory action. This drug increases cellular cAMP levels and increases L-type calcium currents ($I_{ca}$), and like isoproterenol, it counteracts $I_{to}$, resulting in attenuation or abolishment of the electrical inhomogeneity of action potentials. The reduced electrical inhomogeneity of action potentials would prevent phase-2 re-entry and subsequent VF, thereby leading to the diminution or disappearance of coved-type ST-segment elevation or J-waves. However, it still remains poorly understood whether the attenuation of J-wave amplitude is a hallmark of drug efficacy on a long-term basis.

It has been reported that some BrS patients exhibit J-waves and that their presence is a predictor of arrhythmic events or poor outcomes in BrS (14, 15). In addition, the fact that electrical storms can be controlled by isoproterenol or quinidine with concomitant J-wave attenuation in J-wave-associated IVF implies an important role of J-waves for VF occurrence (6). In the present study, VF recurred when the patients showed prominent J-wave augmentation, suggesting their pro-arrhythmic roles. Although both cilostazol and quinidine were effective in preventing VF in BrS and J-wave-associated IVF, the details of the underlying mechanism of action remain to be elucidated.

The authors state that they have no Conflict of Interest (COI).

References

9. Tsujiya T, Ashikaga K, Honda T, Arita M. Prevention of ventricular fibrillation by cilostazol, an oral phosphodiesterase inhibi-

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