Brugada-like Electrocardiographic Pattern Unmasked by Fever

Rie WAKITA,1 MD, Ichiro WATANABE,1 MD, Yasuo OKUMURA,1 MD, Takeshi YAMADA,1 MD, Yasuhiro TAKAGI,1 MD, Tatsuya KOFUNE,1 MD, Kimie OKUBO,1 MD, Riko MASAKI,1 MD, Hidezou SUGIMURA,1 MD, Naohiro OSHIKAWA,1 MD, Satoshi SAITO,1 MD, Yukio OZAWA,1 MD, and Katsuo KANMATSUSE,1 MD

SUMMARY

Brugada syndrome is characterized by right bundle branch block morphology and ST-segment elevation in the right precordial leads and a propensity to develop ventricular arrhythmias. Mutations in a cardiac sodium channel gene have been linked to this syndrome, and the ionic mechanisms responsible for the electrocardiographic phenotype are temperature-dependent. This case report describes a patient in whom a typical Brugada ECG pattern developed during fever and could be reproduced at normal body temperature by administration of pilsicainide. (Jpn Heart J 2004; 45: 163-167)

Key words: Brugada syndrome, Fever, Pilsicainide, Ventricular premature beat, Electrocardiogram

BRUGADA syndrome is characterized by an electrocardiographic (ECG) pattern consisting of elevated ST segments in precordial leads V1-V3 and a morphology similar to that of right bundle branch block along with a propensity for life-threatening ventricular arrhythmias in the absence of structural heart abnormalities.1) A genetic basis has been proposed and mutations in a cardiac sodium channel gene have been reported as the substrate for the syndrome in some patients.2) The ECG pattern may be dynamic over time and may include transient normalization. Several pathophysiological conditions and some pharmacological interventions are known to affect the ionic currents underlying the ECG expression of the syndrome. The administration of class I antiarrhythmic drugs may unmask the ECG abnormalities.3) Some experimental data suggest that body temperature above the physiological range may aggravate the dysfunction of the mutant channel, thus raising the possibility that patients with Brugada syndrome may display...
a more abnormal ECG pattern or even be at a higher risk of arrhythmias during a febrile state.4)

**CASE REPORT**

A 35-year-old Japanese man visited the Emergency Department of Nihon University Hospital because he was experiencing a high fever. His symptoms included chills, fever, and miliary eruptions over his entire body. He was diagnosed as having measles and was admitted to the Emergency Department. He had no family history of sudden death, nor had he experienced any episodes of syncope. On admission his body temperature was 40.3°C. Physical examination revealed that he had Koplik's spots in his mouth, but was otherwise normal. Chest X-rays showed normal heart size, and no consolidation in the lungs. The electrocardiogram on admission showed sinus tachycardia (heart rate: 114 beats/min) and a typical Brugada pattern with right bundle branch block morphology and prominent coved-type ST-segment elevation in the right precordial leads (Figure 1). Creatinine kinase, myocardial bound isoenzyme, troponin I levels, and serum electrolytes were normal and the patient did not complain of chest pain nor dis-

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**Figure 1.** Twelve-lead electrocardiogram on admission at a body temperature of 40.3°C. Note the coved-type ST-segment elevation in the right precordial leads. BT = body temperature; HR = heart rate; bpm = beats per minute.
comfort. The patient became afebrile (36.7°C) on hospital day 8. The repolarization abnormalities disappeared in his electrocardiogram, which showed normal QRS and T-wave patterns and minimal ST-segment elevation in leads V2 and V3. However, a signal-averaged electrocardiogram showed positive late potentials (filtered QRS duration: 128 msec, duration of low-amplitude signal < 40 µV in the terminal filtered QRS complex: 58 msec, root mean square voltage of the terminal 40 msec in the filtered QRS complex: 6.4 µV).\(^5\) There was no evidence of structural heart disease as shown by a normal echocardiogram and normal myocardial perfusion tomography after treadmill exercise up to 12 metabolic equivalents. On discharge, the patient was asymptomatic and afebrile. A pilsicainide challenge test was conducted 6 weeks after discharge.\(^6\) A 12-lead electrocardiogram showed flat T waves in lead V1 and minimal ST-segment elevation in leads V2 and V3 (Figure 2). Following the IV administration of 1 mg/kg of pilsicainide, the QRS widened from 108 msec to 120 msec, and ST-segment elevation in the leads V1~V3 was detected within 5 minutes, and frequent ventricular premature beats of left bundle branch block morphology and inferior axis appeared (Figure 3). An electrophysiological study was not performed because the patient refused. We recommended that in future he promptly consult an emergency room for ECG monitoring if a fever develops.

**ECG before administration of pilsicainide**

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Figure 2. Twelve-lead electrocardiogram after the patient became afebrile (36.7°C). Abbreviations as in Figure 1.
DISCUSSION

Brugada syndrome is not an uncommon condition, and reports on its prevalence have shown that it is present in various ethnic groups, including the Japanese population. There have been many studies to investigate the cellular basis of the syndrome. One hypothesis proposed to explain the molecular basis of Brugada syndrome is that of reduced myocardial sodium current and the resulting imbalance of inward and outward currents, particularly in the right ventricular epicardium, where disproportionate expression of the transient inward current creates a transmural voltage gradient and dispersion of repolarization. Molecular genetic studies have shown the reduced myocardial sodium current to be caused by disease-associated mutations in the SCN5A gene. Dumaine, et al reported that in an in vitro study, the ionic mechanisms responsible for the ECG phenotype of Brugada syndrome are temperature-dependent. Several clinical reports have indicated that a febrile state unmasked the syndrome or exacerbated ST-segment elevation and arrhythmogenesis. Our present report supports the temperature-dependent nature of the underlying ion channelopathy of Brugada syndrome. It seems clear that this patient did have Brugada syndrome as indi-

Figure 3. Twelve-lead electrocardiogram after pilsicainide administration. Note the ST-segment elevation in the right precordial leads and premature ventricular contractions of left bundle branch block pattern with inferior axis. Abbreviations as in Figure 1.
cated by a structurally normal heart and positive response to pilsicainide challenge. The role of body temperature in diagnosis and arrhythmogenesis in Brugada syndrome warrants further investigation.

REFERENCES


