Persistent Abnormal Value of Late Potential in Brugada Syndrome Associated with Hypokalemia

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Hypokalemia accentuates the electrocardiographic (ECG) pattern of Brugada syndrome. We report two patients with Brugada syndrome and hypokalemia-induced lethal events. Despite concealing the typical ECG pattern with normalization of serum potassium levels, late potentials were persistently detected by signal-averaged ECG, even at the 18-month follow-up. An implantable cardioverter defibrillator was inserted to prevent sudden cardiac death.

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Brugada syndrome; hypokalemia; late potential

Low potassium levels are associated with Brugada syndrome and the occurrence of ventricular arrhythmia.^{1,2} However, no studies have shown late potentials (LPs) detected by signal-averaged electrocardiography (ECG) after restoring serum potassium levels in patients with Brugada syndrome.

CASE 1

A 50-year-old man was being transported following syncope. In the ambulance, he experienced ventricular fibrillation (VF), which was successfully treated with direct current shock. His body temperature was 37.0°C and chest x-ray and echocardiogram were normal. Blood chemistry showed hypokalemia (2.6 mEq/L). The 12-lead ECG on admission showed an ECG aspect compatible with pattern of Brugada in precordial leads (Fig. 1A). The Brugada ECG was normalized with restoration of serum potassium (3.6 mEq/L, Fig. 1B). No further arrhythmic events occurred during hospitalization. Cardiac catheterization revealed no significant stenosis in the coronary arteries. During the electrophysiological study, VF was reproducibly induced by programmed stimuli from the right ventricle. An intravenous pilisicainide (50 mg) test exaggerated the

ECG pattern of Brugada syndrome (Fig. 1C). An implantable cardioverter defibrillator (ICD) was implanted to prevent sudden cardiac death.

CASE 2

A 53-year-old man who suffered sudden cardiopulmonary arrest was referred to our hospital for cardiopulmonary resuscitation. His body temperature was 39.2°C. Laboratory evaluation revealed leukocytosis (16,400 mm³), elevated C-reactive protein (8.85 mg/dL), and hypokalemia (3.0 mEq/L). Echocardiography showed normal wall motion of the left ventricle. Chest x-ray and computed tomography (CT) scan confirmed pneumonia. The 12-lead ECG revealed complete right bundle branch block with a coved-type ST-segment elevation in precordial leads (Fig. 1D). An intravenous infusion of potassium and intravenous administration of antibiotics were initiated. Serum potassium was 3.9 mEq/L on day 2, with normalization of coved ST elevation, irrespective of marked febrile state (Fig. 1E). No significant stenosis was observed in the coronary arteries. VF was reproducibly induced by programmed stimuli from the right ventricle. An ICD was inserted to prevent sudden death.

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Figure 1. ECG patterns of two patients with Brugada syndrome and hypokalemia-induced lethal events. (A) A 12-lead ECG of Case-1 on admission showed an ECG aspect compatible with pattern of Brugada. (B) Normalization of the ECG upon restoration of serum potassium levels. (C) An intravenous pilsicainide (50 mg) test reproduced the ECG pattern of Brugada syndrome. (D) A 12-lead ECG of Case-2 at Emergency Room revealed complete right bundle branch block with a coved-type ST-segment elevation in precordial leads. (E) Normalization of the ST-segment elevation upon restoration of serum potassium, even in the presence of high fever.

LPs BY SIGNAL-AVERAGED ECG

The LPs were analyzed using a signal-averaged ECG System (FCP7541, Fukuda Denshi Co., Tokyo, Japan). Three parameters were assessed via a computer algorithm: (1) the filtered QRS duration; (2) the root mean square voltage of the terminal 40 ms in the filtered QRS complex (RMS_{40}); and (3) the duration of low-amplitude signals $<40 \mu V$ in the terminal filtered QRS complex (LAS_{40}). LPs were considered abnormal when two criteria ($RMS_{40} < 20 \mu V$ and $LAS_{40} > 38$ ms) were met.³ Despite the normalization of serum potassium level, LPs were persistently abnormal in both patients before discharge and even at the 18-month follow-up (Table 1).

DISCUSSION

In both cases, hypokalemia was clearly associated with Brugada syndrome and the occurrence of lethal events. We implanted an ICD because latent conduction delay was evident even when typical ECG patterns were masked. Abnormal LP values were persistently observed at the 18-month follow-up, irrespective of serum potassium levels.

The ECG features of Brugada syndrome are often concealed but can be unmasked or modulated by many factors.⁴⁻⁷ Hypokalemia is also known to be associated with Brugada syndrome and occurrence of the polymorphic ventricular tachyarrhythmia.^{1,2} In consistence with previous case reports, the Brugada ECG pattern was observed when the serum

Table 1. Serum Potassium Levels and LPs (by Signal-Averaged Electrocardiogram) of Two Cases Presenting with Brugada Syndrome and Hypokalemia-Induced Lethal Events

	Case-1		Case-2	
	Before Discharge	After 18 Months	Before Discharge	After 18 Months
Serum potassium level (mEq/L)	4.0	4.4	4.2	3.9
fQRS (ms)	117	119	194	175
RMS ₄₀ (μ V)	13.3	13.8	2.4	5.5
LAS ₄₀ (ms)	41	40	136	116

fQRS = the filtered QRS duration; LAS₄₀ = the duration of low-amplitude signals $<40 \mu$ V in the terminal filtered QRS complex; RMS₄₀ = the root mean square voltage of the terminal 40 ms in the filtered QRS complex.

potassium levels were 2.6 mEq/L (Case 1) and 3.0 mEq/L (Case 2), respectively. A febrile state also accentuates the Brugada ECG pattern and precipitates VF.⁶ Case 2 exhibited a coved-type Brugada ECG pattern with hypokalemia and high body temperature. The characteristic ST-segment elevation was normalized with intravenous potassium infusion, even in the presence of high fever. In both cases, hypokalemia was mainly related to a Brugada ECG pattern. The cause of hypokalemia was not known and these patients had no prior drug use, and urinary potassium excretion levels and blood endocrine activity were also within the normal range.

A majority of spontaneous type 1 Brugada syndrome with a history of life-threatening events have demonstrated LPs.^{3,8} Multivariate analyses revealed that the presence of LPs is an independent predictor of sudden death. LPs have also been observed in a high percentage of Brugada syndrome patients with induced VF.⁹ Conduction delays, especially at the right ventricular outflow track, produce LPs in Brugada syndrome.⁹ Despite the restoration of serum potassium level, LPs were persistently abnormal even at the long-term follow-up. Ventricular tissue abnormality may exist irrespective of serum potassium levels in both patients.

CONCLUSION

Although the role of hypokalemia in Brugada syndrome is not so clear and has been rarely described, in the cases presented here, LPs were obvious even at the 18-month follow-up. These cases provided further evidence of risk for the future in Brugada syndrome associated with hy-

pokalemia. ICD implantation should be considered to prevent sudden cardiac death in these patients.

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REFERENCES

1. Araki T, Konno T, Itoh H, et al. Brugada syndrome with ventricular tachycardia and fibrillation related to hypokalemia. *Circ J* 2003;67:93-95.
2. Notarstefano P, Pratola C, Toselli T, et al. Atrial fibrillation and recurrent ventricular fibrillation during hypokalemia in Brugada syndrome. *Pacing Clin Electrophysiol* 2005;28:1350-1353.
3. Ikeda T, Sakurada H, Sakabe K, et al. Assessment of noninvasive markers in identifying patients at risk in the Brugada syndrome: Insight into risk stratification. *J Am Coll Cardiol* 2001;37:1628-1634.
4. Shimizu W. Acquired forms of Brugada syndrome. In Antzelevitch C (ed.): *The Brugada Syndrome: From bench to bedside*. UK, Blackwell Futura, 2004, pp. 166-177.
5. Antzelevitch C, Brugada P, Borggrefe M, et al. Brugada syndrome: Report of the second consensus conference: Endorsed by the Heart Rhythm Society and the European Heart Rhythm Association. *Circulation* 2005;111:659-670.
6. Gavrielatos G, Letsas KP, Pappas LK, et al. Brugada electrocardiographic pattern induced during febrile state with marked leukocytosis. *Pacing Clin Electrophysiol* 2007;30:135-136.
7. Hayashi T, Mitani H, Goto K, et al. Alcohol-induced ventricular fibrillation in Brugada syndrome. *J Arrhythmia* 2009;25:32-35.
8. Ikeda T, Takami M, Sugi K, et al. Noninvasive risk stratification of subjects with a Brugada-type electrocardiogram and no history of cardiac arrest. *Ann Noninvasive Electrocardiol* 2005;10:396-403.
9. Kanda M, Shimizu W, Matsuo K, et al. Electrophysiologic characteristics and implications of induced ventricular fibrillation in symptomatic patients with Brugada syndrome. *J Am Coll Cardiol* 2002;39:1799-1805.