Jpn Circ J 2001; **65:** 483–486

Arrhythmias in Patients With Brugada-Type Electrocardiographic Findings

Hideki Itoh, MD; Masami Shimizu, MD; Hidekazu Ino, MD;
Kazuyasu Okeie, MD; Masato Yamaguchi, MD; Noboru Fujino, MD;
Hiroshi Mabuchi, MD; Hokuriku Brugada Study Group*

Brugada syndrome is characterized by marked ST-segment elevation in the right precordial leads (Bru-ECG) and is associated with a high risk for sudden death. However, it is unclear whether the arrhythmogenesis is caused by the mechanisms responsible for Bru-ECG. The present study investigated the risk of arrhythmias in patients with Bru-ECG by retrospectively analyzing 30 patients (28 men; mean age, 51±14 years) with Bru-ECG. Aborted sudden cardiac death (ventricular fibrillation or syncope) occurred in 9 patients (30%); paroxysmal atrial fibrillation was present in 9 (30%) patients in addition to malignant ventricular arrhythmias, and some type of arrhythmic event (aborted sudden cardiac death or paroxysmal atrial fibrillation) occurred in 15 patients (50%). Of all the arrhythmic events, 93% occurred at night or early in the morning, and 92% had pronounced ST-segment elevation. These results suggest that Bru-ECG may be associated not only with an increased risk of ventricular tachyarrhythmias but also with an increased risk of paroxysmal atrial fibrillation, and that the arrhythmogenesis may be related to the pronounced ST-segment elevation. (*Jpn Circ J* 2001; **65:** 483–486)

Key Words: Brugada syndrome; Paroxysmal atrial fibrillation; Sudden death; ST-segment elevation; Arrhythmogenesis

In 1992, Brugada and Brugada described 8 cases of aborted sudden death in patients without demonstrable structural heart disease but with a characteristic electrocardiogram pattern (Bru-ECG) consisting of right bundle-branch block and ST-segment elevation in leads V_{1-3}.[1] More prominent ST-segment elevation in the right precordial leads has been observed immediately before or after episodes of aborted sudden cardiac death in some patients[2,3] but asymptomatic patients with Bru-ECG have been described[4–6] Brugada et al also reported that the incidence of arrhythmic events is similar in symptomatic and asymptomatic patients with Bru-ECG[7] These reports suggest that all patients with characteristic Bru-ECG are at risk for sudden cardiac death, but the variety of arrhythmic events associated with the Bru-ECG and the relationship between the occurrence of arrhythmic events and ST-segment elevation is unknown. Therefore, we investigated the characteristics of arrhythmic events in patients with the Bru-ECG.

Methods

Patients

Data on 30 patients (28 men; mean age, 51±14 years, 5 patients >65 years) with the Bru-ECG were recruited from September 1, 1998 until October 1, 2000 by the Second Department of Internal Medicine, Kanazawa University or its associated hospitals and were analyzed in terms of arrhythmic events. Eight patients were having a health examination, 7 were in hospital for diseases other than cardiac disease, and 15 were in the department of cardiology. Twenty-four had 'coved type' and 6 patients had 'saddle-back type' ST-segment elevation on initial presentation (Fig 1). Ten patients (33%) had family members with aborted sudden cardiac death (eg, case 5 is the father of case 7). Clinical data, including electrocardiographic findings, did not differ between those patients in whom aborted sudden cardiac death (SCD group) occurred and those in whom it did not (non-SCD group) (Table 1). None of the patients suffered from chest pain during the appearance of the Bru-ECG. Patients with angina pectoris and acute myocardial infarction were excluded on the basis of laboratory findings, exercise tests or coronary angiography. Echocardiography findings, including cardiac function and cardiac chamber sizes, were normal in all patients. All 22 patients who underwent an exercise test above 6.8 METS had negative findings with decreased or unchanged ST-segment elevation. All 14 patients who underwent coronary angiography had normal findings. Programmed electrical investigations were performed in 4 SCD patients and 4 from the non-SCD group. A maximum of 3 ventricular extrastimuli were delivered and 3 of the SCD patients had ventricular fibrillation. Flecainide (2 mg/kg per 10 min) or oral pilsicainide (100–150 mg/day) were administrated to 7 patients and the sodium channel blockers elevated the ST-segment in all 7. The ST-segment changed markedly in 28 patients and 2 normalized during the follow-up period.

ECG Measurement

All ECG measurements were performed by a single experienced investigator who was unaware of the clinical information. The QT interval was measured from the beginning of the QRS complex to the end of the T wave and corrected for heart rate using Bazett's formula: QTc =

(Received November 20, 2000; revised manuscript received January 24, 2001; accepted February 15, 2001)
The Second Department of Internal Medicine, School of Medicine, Kanazawa University, Kanazawa, Japan
*The names and institutions of the investigators are listed in Appendix
Mailing address: Hideki Itoh, MD, The Second Department of Internal Medicine, School of Medicine, Kanazawa University, 13-1 Takara-machi, Kanazawa 920-8640, Japan. E-mail: i-yoko@rj8.so-net.ne.jp

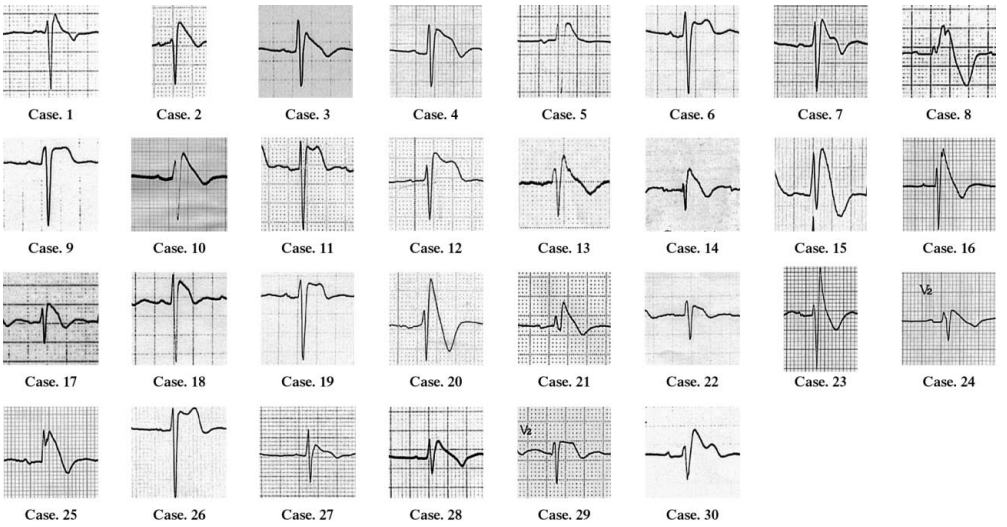

Fig 1. Lead V_2 ECGs in patients with the characteristic Brugada syndrome ECG at the time of presentation. Twenty-four patients had the 'coved type' ST-segment elevation and 6 patients had 'saddle-back type' ST-segment elevation.

Table 1 Comparision of Clinical Characteristics

	SCD group (n=9)	*non-SCD group (n=21)*	*p value*
Age (years)	*44±12*	*53±14*	*NS*
Gender (M/F)	*8/1*	*20/1*	*NS*
Family history of SCD	*4*	*4*	*NS*
Electrocardiographic findings			
Coved/saddle-back ST segment	*7/2*	*16/5*	*NS*
STj (mV)	*0.50±0.11*	*0.59±0.31*	*NS*
ST40 (mV)	*0.38±0.11*	*0.39±0.15*	*NS*
PR (ms)	*157±20*	*180±51*	*NS*
QRS (ms)	*91±24*	*90±14*	*NS*
QTc ($ms^{1/2}$)	*382±60*	*363±41*	*NS*
RR (ms)	*844±137*	*836±210*	*NS*
Age at aborted SCD onset (years)	*44±12*	*–*	
Time of aborted SCD onset			
21.00–09.00 h / 09.00–21.00 h	*9/0*	*–*	
AF	*3*	*4*	*NS*
EF (%)	*67±7*	*67±7*	*NS*

SCD, sudden cardiac death; aborted SCD, syncope or aborted sudden cardiac death; AF, paroxysmal atrial fibrillation; EF, ejection fraction; STj, ST-segment elevation measured at the J point from the baseline in lead V_2; ST40, ST-segment elevation measured at 40 ms from the baseline in lead V_2; QTc, $QT/RR^{1/2}$.

$QT/RR^{1/2}$.[8] The QRS width was measured from the beginning of the Q wave to the end of the S wave (J point). The ST-segment elevation above the baseline (PR line) was measured at the J point (STj) and 40 ms after the J point (ST40) in lead V_2. The other parameters were measured in lead V_5.

Characteristic ECG of Brugada Syndrome

A diagnosis of Bru-ECG was based on (1) ST-segment elevation in leads V_1 to V_2/V_3; (2) STj ≥ ST40; (3) ST40 ≥0.2 mV; and (4) characteristic ECG findings as judged by 2 cardiologists.

Detection of Arrhythmic Events

We retrospectively analyzed arrhythmic events in patients with the Bru-ECG and defined their occurrence as either the first appearance of aborted SCD (ventricular fibrillation or syncope)[7] or arrhythmias with antiarrhythmic therapy. We analyzed the arrhythmic events that occurred spontaneously appeared when the patients were not taking any medications, excluding those events induced by electrophysiologic studies, and we compared the ST-segment elevation during the arrhythmic events with the ST-segment elevation on initial presentation.

Results

Arrhythmic Events in Patients With Bru-ECG

Nine patients (30%), including 4 with ventricular fibrillation and 5 with syncope, had experienced aborted SCD (cases 1–9). Onset age was 44±12 years. Paroxysmal atrial fibrillation (AF) was present in 9 of the 30 patients (30%) (cases 7–15). The total arrhythmic events, including aborted SCD and/or paroxysmal AF, occurred in 15 patients (50%).

Characteristics of Arrhythmic Events in Patients With Bru-ECG

Of all arrhythmic events, 93% (14/15 arrhythmic events)

Table 2 Arrhythmic Events in Patients With Brugada-Type Electrocardiographic Findings

Patient no.	Onset age (years) / Gender	Arrhythmic events	Time of arrhythmic event		ST-segment elevation†	
			Aborted SCD	AF	Aborted SCD	AF
1	24/M	Aborted SCD	day	/	NA	/
2	37/M	Aborted SCD	night	/	NA	/
3	45/M	Aborted SCD	22.00 h	/	–	/
4	51/M	Aborted SCD	21.00 h	/	+	/
5	53/M	Aborted SCD	7.00 h	/	+	/
6	58/M	Aborted SCD	22.00 h	/	+	/
7	24/M	Aborted SCD/AF	23.00 h	21.00 h	+	+
8	52/F	Aborted SCD/AF	8.00 h	8.00 h	+	+
9	53/M	Aborted SCD/AF	20.00 h	2.00 h	+	+
10	45/M	AF	/	23.00 h	/	+
11	<50/M	AF	/	NA	/	NA
12	<65/M	AF	/	NA	/	NA
13	70/M	AF	/	NA	/	+
14	72/M	AF	/	17.00 h	/	+
15	77/M	AF	/	night	/	+

†ST-segment when arrhythmic events spontaneously appeared without taking medications including antiarrhythmic drugs. Aborted SCD, ventricular fibrillation or syncope; AF, paroxysmal atrial fibrillation; +, positive; –, negative; NA, not available.

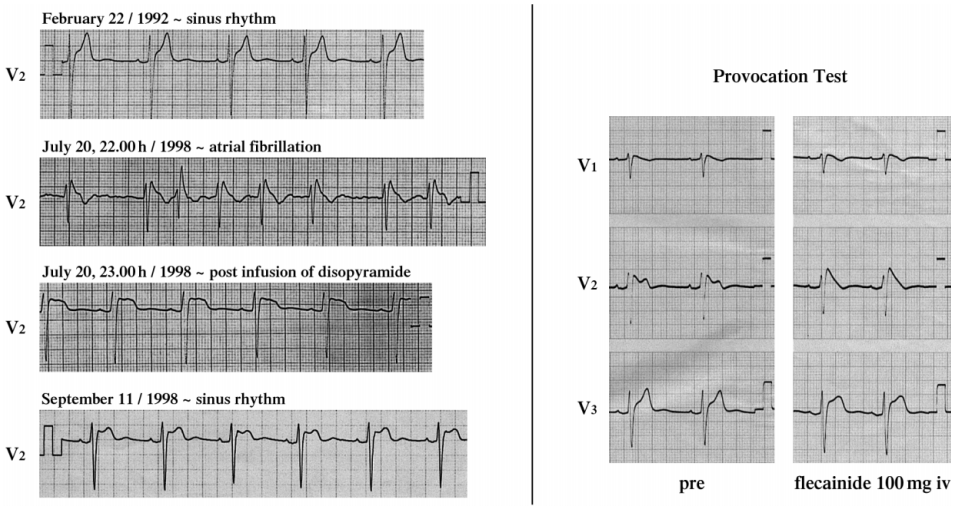

Fig 2. Lead V_2 ECG in a 45-year-old male patient with characteristic ECG of Brugada syndrome. Note the ST-segment elevation in V_2 and atrial fibrillation. When sinus rhythm was restored, the ST-segment elevation decreased. The infusion of flecainide (100 mg/10 min) increased ST-segment elevation and produced the 'coved type' ST segment.

occurred at night or early in the morning. Most events at night occurred after dinner, and 92% (13/14 arrhythmic events) had pronounced ST-segment elevation just after the arrhythmic event (Table 2).

The findings in a 45-year-old man with paroxysmal AF and ST-segment elevation are shown in Fig 2. He had not suffered from aborted SCD and had the 'coved type' ST-segment elevation during the arrhythmic event. The ST-segment elevation changed to a 'saddle-back type' morphology after the patient was converted to sinus rhythm with disopyramide therapy and the elevation decreased during sinus rhythm. The infusion of flecainide (100 mg/10 min) increased the ST-segment elevation.

Discussion

We have shown that Bru-ECG is associated with a high incidence of paroxysmal AF and aborted SCD, and that ST-segment elevation is most prominent during or immediately after the arrhythmic event.

Characteristic ECG of Brugada Syndrome and Paroxysmal Atrial Fibrillation

Many studies have demonstrated that the Bru-ECG is associated with an increased risk of ventricular tachyarrhythmias[9,10] but we have demonstrated that paroxysmal AF occurs in 30% of patients with the Bru-ECG. Ventricular fibrillation is observed more frequently at night in patients with this syndrome[1,11] and it has been suggested that increased vagal activity and decreased sympathetic activity may play an important role in the arrhythmogenesis[2]

In the present study, not only ventricular arrhythmias but also AF occurred at night and early in the morning and based on these findings, we hypothesize that the occurrence of AF in patients with the Bru-ECG may be influenced by autonomic nervous activity, as with ventricular arrhythmias.

A number of drugs, including adrenergic and cholinergic agents, are able to modulate the degree of ST-segment elevation in patients with Brugada syndrome[1,12] so ST-segment elevation might be influenced by autonomic tone, which should induce malignant ventricular arrhythmias.

Study Limitations

We did not analyze information on the inducibility of aborted SCD and paroxysmal AF. Furthermore, it is also unknown how ST-segment elevation in the right precordial leads, which represent the reporarization of the ventricle, would induce the electrophysiologic changes in the atria that may cause paroxysmal fibrillation. We speculate that electronic injury exists not only in the ventricular myocardium but also in the atria. We need further long term follow-up studies.

Conclusions

Malignant ventricular arrhythmias and paroxysmal atrial fibrillation occurred frequently in patients with the Bru-ECG and were associated with pronounced ST-segment elevation.

Acknowledgments

We would like to thank Noriko Ooba and Hideo Futamata for the analysis of electrocardiograms in patients with Brugada syndrome, and Satoru Sakagami, the First Department of Internal Medicine, School of Medicine, Kanazawa University for the collection of patients.

This work was presented in part at the 49th Annual Scientific Session of the American College of Cardiology, Anaheim, California, March 2000.

References

1. Brugada P, Brugada J: Right bundle branch block, persistent ST segment elevation and sudden cardiac death: A distinct clinical and electrocardiographic syndrome. *J Am Coll Cardiol* 1992; **20:** 1391–1396
2. Kasanuki H, Ohnishi S, Ohtuka M, Matsuda N, Nirei T, Isogai R, et al: Idiopathic ventricular fibrillation induced with vagal activity in patients without obvious heart disease. *Circulation* 1997; **95:** 2277–2285
3. Matsuo K, Shimizu W, Kurita T, Inagaki M, Aihara N, Kamakura S: Dynamic changes of 12-lead electrocardiograms in a patient with Brugada syndrome. *J Cardiovasc Electrophysiol* 1998; **9:** 508–512
4. Takenaka S, Emori T, Koyama S, Morita H, Fukushima K, Ohe T: Asymptomatic form of Brugada syndrome. *Pacing Clin Electrophysiol* 1999; **22:** 1261–1263
5. Fuziki A, Usui M, Nagasawa H, Mizumaki K, Hayashi H, Inoue H: ST segment elevation in the right precordial leads induced with class IC antiarrhythmic drugs: Insight into the mechanism of Brugada syndrome. *J Cardiovasc Electrophysiol* 1999; **10:** 214–218
6. Matana A, Goldner V, Stanic K, Mavric Z, Zaputovic L, Matana Z: Unmasking effect of propafenone on the concealed form of the Brugada phenomenon. *Pacing Clin Electrophysiol* 2000; **23:** 416–418
7. Brugada J, Brugada R, Brugada P: Right bundle-branch block and ST-segment elevation in leads V1 through V3. *Circulation* 1998; **97:** 457–460
8. Bazett HC: An analysis of the time-relations of electrocardiograms. *Heart* 1920; **7:** 353–370
9. Brugada J, Brugada P: Further characterization of the syndrome of right bundle branch block, ST segment elevation, and sudden cardiac death. *J Cardiovasc Electrophysiol* 1997; **8:** 325–331
10. Atarashi H, Ogawa S, Harumi K, Hayakawa H, Sugimoto T, Okada R, et al: Characteristics of patients with right bundle branch block and ST-segment elevation in right precordial leads. *Am J Cardiol* 1996; **78:** 581–583
11. Matsuo K, Kurita T, Inagaki M, Kakishita M, Aihara N, Shimizu W, et al: The circadian pattern of the development of ventricular fibrillation in patients with Brugada syndrome. *Eur Heart J* 1999; **20:** 465–470
12. Miyazaki T, Mitamura H, Miyoshi S, Soejima K, Aizawa Y, Ogawa S: Autonomic and antiarrhythmic drug modulation of ST segment elevation in patients with Brugada syndrome. *J Am Coll Cardiol* 1996; **27:** 1061–1070

Appendix

Hokuriku Brugada Study Group

Mitsuru Nagata and Kenshi Hayashi, The Second Department of Internal Medicine, School of Medicine, Kanazawa University; Kuniyoshi Shimizu, and Touru Matsuyama, Kouseiren Takaoka Hospital; Hiroyuki Yoshio, Yoshio Clinic; Masatoshi Ikeda and Nariaki Terashima, Ishikawa Prefactural Central Hospital; Tameto Onoe, Wajima General Hospital; Kousei Ueda, Hiroaki Hirase and Koutarou Ooe, Komatsu Municipal Hospital; Sumio Mizuno and Hiromasa Kokado, Fukui Cardiovascular Hospital; Yutaka Nitta, Toyama Red-Cross Hospital; Masanobu Namura, Taketsugu Tsuchiya and Yujirou Tanabe, Kanazawa Cardiovascular Hospital; Ei Kawasaki, Kanazawa West Hospital; Sigeru Oota, Oota Hospital; Tsutomu Araki, Kanazawa Saiseikai Hospital; Junichi Hirai, Fukui Prefactural Hospital; Kikuo Yasuda, Yasuda Hospital; Norihiko Sugihara, Sugihara Hospital; Masahiro Minamoto, Naruwa General Hospital; Takeshi Nakao, Nakao Hospital; Hirohito Sanada, Tatsunokuchi Hospital; Sinya Takeda, Yokohama Sakae Kyousai Hospital; Tetsuji Sumitani and Etsurou Araie, Takaoka Municipal Hospital.