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Ventricular fibrillation associated with complete right bundle branch block

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Abstract

BACKGROUND—A substantial number of patients with idiopathic ventricular fibrillation (IVF) present with no specific electrocardiographic (ECG) findings.

OBJECTIVE—To evaluate complete right bundle branch block (RBBB) in patients with IVF.

METHODS—Patients with IVF showing complete RBBB were included in the present study. Structural and primary electrical diseases were excluded, and provocation tests were performed to exclude the presence of spastic angina or Brugada syndrome (BrS). The prevalence of complete RBBB and the clinical and ECG parameters were compared either in patients with IVF who did not show RBBB or in the general population and age and sex comparable controls with RBBB.

RESULTS—Of 96 patients with IVF, 9 patients were excluded for the presence of BrS. Of 87 patients studied, 10 (11.5%) patients showed complete RBBB. None had structural heart diseases, BrS, or coronary spasms. The mean age was 44 ± 15 years, and 8 of 10 patients were men. Among the ECG parameters, only the QRS duration was different from that of the other patients with IVF who did not show complete RBBB. Ventricular fibrillation recurred in 3:2 in the form of storms, which were well suppressed by isoproterenol. Complete RBBB was found less often in control subjects (1.37%; $P < .0001$), and the QRS duration was more prolonged in patients with IVF: 139 ± 10 ms vs 150 ± 14 ms ($P = .0061$).

CONCLUSIONS—Complete RBBB exists more often in patients with IVF than in controls. A prolonged QRS complex suggests a conduction abnormality. Our findings warrant further investigation of the role of RBBB in the development of arrhythmias in patients with IVF.

Keywords

Sudden death; Idiopathic ventricular fibrillation; Right bundle branch block; Electrocardiogram; Brugada syndrome

Introduction

Ventricular fibrillation (VF) occurring in subjects without a specific definitive diagnosis or known mechanism is referred to as idiopathic ventricular fibrillation (IVF). Brugada syndrome (BrS), a type of IVF, exhibits a spontaneous ST-segment elevation in the right precordial leads (V_1 – V_3) as a diagnostic electrocardiographic (ECG) marker.^{1,2} In other cases, prominent J waves or J point elevation in the inferior and/or lateral precordial leads has been shown to be associated with an increased risk for ventricular tachycardia (VT)/VF.^{3–7} However, a substantial number of patients with IVF show no such characteristic signs on their ECGs.^{4,7}

A normal ECG is usually a requirement for defining a VF as “idiopathic,” and therefore right bundle branch block (RBBB) would be one of the exclusion criteria for IVF. However, we recently encountered a patient with IVF who showed complete RBBB as the sole abnormal finding. Structural heart diseases were ruled out, and the presence of BrS and coronary spasms was excluded by provocation tests. The patient developed a VF storm, which responded to isoproterenol, as reported in the cases of BrS and other J wave syndromes.^{8–10}

We undertook a case-control study, with the aim to assess the prevalence of RBBB and clinical characteristics in a series of patients with IVF. The prevalence of complete RBBB and its ECG characteristics were compared against the general population.

Methods

Study population

The study included patients admitted to 6 hospitals from April 1998 to March 2012 in whom VF was documented along with the absence of structural heart disease. All the initial episodes of VF occurred out of hospital and were defibrillated by emergency personnel. None of the VF episodes were precipitated by fever or other transient conditions. All patients met the following entry criteria:

1. a documented episode of VF at the time of cardiac arrest or after admission;
2. the absence of structural heart disease and the presence of normal cardiac function;
3. negative serology tests for inflammatory diseases (white blood cell, C-reactive protein, erythrocyte sedimentation rate) and no abnormal blood chemistry;
4. absence of coronary artery disease or coronary spasm; and
5. no known primary electrical diseases, which include long or short QT intervals, catecholaminergic polymorphic VT,¹¹ and Wolff-Parkinson-White syndrome.

Cardiac catheterization and electrophysiological study

Cardiac catheterization was performed to exclude structural heart diseases and coronary artery diseases. Coronary spasm was excluded by a negative provocation test using either acetylcholine or ergometrine. Briefly, after the exclusion of significant stenosis, acetylcholine was injected into the left coronary artery in incremental doses of 50 and 100

mg (in 10 mL of 0.9% saline) over 20 seconds. Acetylcholine was then injected into the right coronary artery, as described above. If acetylcholine did not induce coronary spasms, 50 mg of intracoronary ergonovine maleate was injected into the right coronary artery and the left coronary artery over a period of 5 minutes. The end point was the development of total or subtotal occlusion or the completion of drug infusion.¹²

Exclusion

BrS was excluded by the absence of the type 1 ST-T pattern in leads V₁–V₃ and those patterns recorded at the second intercostal space as well as by the lack of induction of type 1 ECG by class I drugs.^{2,13} The dosages of the drugs used in provocation testing for BrS were as follows: pilsicainide 1 mg/kg/10 min IV, flecainide 400 mg p.o., and procainamide 10 mg/kg/10 min IV. The end point was the development of type 1 BrS ECG pattern or the completion of drug infusion. Coronary spasm was excluded by a negative provocation test using acetylcholine and/or ergometrine.

Catecholaminergic polymorphic VT was ruled out by patient's history, infusion of isoproterenol at electrophysiological study (EPS), or exercise stress testing. Short and long QT syndromes were excluded by ECG findings. Invasive studies and provocation tests were performed after obtaining written and informed consent.

Controls

The control group consisted of 4092 men and 3185 women between 20 and 69 years of age, who underwent annual health examinations in our clinic. All subjects showed normal results on physical examination and exhibited no overt heart failure. When abnormal findings were uncovered, the presence of cardiac disease was ruled out by echocardiography or exercise stress testing. Sudden cardiac death was ruled out in all the members of the subject's family.

The prevalence of complete RBBB was determined for each decade of life for comparison with that in patients with IVF. From the subjects showing complete RBBB, 55 of comparable age and sex were randomly chosen and the ECG parameters were compared with those of patients with IVF who showed RBBB.

Definition

Complete RBBB was defined as a late R (R_s) wave presenting in lead V₁ or V₂ with a slurred S wave in leads I and/or in lead V₆ with a prolonged QRS duration of >120 ms. The QRS duration was measured from the beginning of the QRS complex to the J point, which was defined as the point of transition from the R wave to the ST segment.^{4,5,14}

The diagnoses of BrS and early repolarization were based on the consensus report,^{2,13} and J waves were positive if the J point showed an amplitude of ≥0.1 mV above the isoelectric line in at least 2 contiguous leads in the inferior or precordial leads or in lead I or aVL.^{3–7}

ECG interpretation and data analysis

If patients who showed complete RBBB were identified in patients with IVF who met all the inclusion criteria, then BrS or other electrical diseases were ruled out. ECGs were read by 2 cardiologists to diagnose complete RBBB, BrS, and early repolarization syndrome (ERS). For ECGs with discrepant interpretations, a consensus was reached by a discussion between the 2 readers.

The ECG parameters were compared between patients with IVF who showed RBBB and patients with IVF who did not show RBBB for the basic rhythm and the RR, PR, and QT intervals in a standardized manner; the QT interval was corrected by using the Bazett

formula.¹⁵ The prevalence of complete RBBB and ECG parameters were compared with those of controls.

Statistical analysis

Numerical values are expressed as mean $\pm$ SD, and categorical variables are expressed either as absolute numbers or as a percentage. The differences between groups were analyzed by using the Mann-Whitney-Wilcoxon test for continuous variables and the Pearson χ^2 test for categorical variables. Statistical analyses were performed with SPSS, version 12.0 (SPSS Inc, Chicago, IL). A 2-sided *P* value of $<.05$ was considered statistically significant. The study was approved by the internal board of the School of Medicine at Keio University.

Results

Patients with IVF who showed RBBB

From 1998 to 2011, we evaluated 96 patients with IVF, 12 of whom showed RBBB on admission. No structural heart disease was detected. In 2 patients, BrS was diagnosed from the appearance of the type 1 ST-segment elevation in the right precordial leads, which was disclosed via spontaneous appearance of typical 1 ST-segment elevation in one patient (Figure 1)¹⁶ and after use of a class Ic drug in the other. The remaining 10 (11.4%) patients were included in the present study. A diagnostic ECG pattern of BrS was not induced in 9 patients who received a sodium block challenge: pilsicainide in 6 patients, flecainide in 2 patients, and procainamide in 1 patient. One patient was not tested, but repeated ECGs that included higher intercostal space recording were negative for BrS during her hospitalization. None of the patients had symptoms suggestive of chest pain, and they were negative on exercise stress test. Provocation of a coronary spasm was negative in all 8 patients tested. At EPS, programmed electrical stimulation induced VF in 5 of 7 patients studied.

The patient characteristics are summarized in Table 1. The mean age of the patients was 44 ± 15 years (range 21–66 years), and 8 of 10 patients were men. VF occurred in the early morning ($n = 4$), evening ($n = 2$), around midnight ($n = 3$), or in the daytime ($n = 1$).

ECG of patients with IVF who showed RBBB

An R wave in lead V_1 and a slurred S wave in lead V_6 or I were observed in 9 patients (cases 1–9), and 1 patient showed an r or s wave in lead V_1 but showed an R wave in lead V_2 (Figure 2). The QRS duration was >120 ms in all patients: 150 ± 14 ms. Three patients displayed a mild prolongation of the PR interval of >0.20 seconds. Left axis deviation of the frontal electrical axis $>30^\circ$ was observed in 2 patients. J wave-like deflections were observed in the inferior leads in 4 patients (cases 3, 4, 6, and 8 in Figure 2) within the widened QRS complexes. In 1 patient, a partial resolution of RBBB occurred during EPS, which led to the appearance of J waves in leads I and aVL (Figure 3).

Comparisons between patients with IVF who showed RBBB and patients who did not show RBBB

The age of 10 patients with IVF who showed RBBB was higher but nonsignificant compared with remaining 77 patients with IVF: 44 ± 15 years vs 38 ± 14 years, respectively ($P = .2713$). The ECG parameters were similar between the 2 groups except for the QRS duration (Table 2). RBBB resulted in only a slight prolongation of the QT interval, as shown in lead II.

Typical J waves were observed at the terminal part of the QRS complex in 42 of 77 (54.5%) patients with IVF who did not show RBBB as reported earlier.^{4,7} J wave-like deflections

were found to be buried within the QRS complexes in the inferior leads in 4 of our 10 (40%) patients with RBBB (Figure 2).

RBBB in controls

Complete RBBB was found in 1.37% of 7277 subjects: 2.00% in male subjects ($n = 4092$) and 0.57% in female subjects ($n = 3185$). Complete RBBB increased with advancing age: 1.32%, 1.15%, 1.36%, 2.37%, and 3.66% for men and 0.00%, 0.68%, 0.51%, 0.58%, and 0.87% for women, respectively, for the third to seventh decades. Therefore, the prevalence of complete RBBB was higher in patients with IVF than in healthy controls ($P < .0001$). Electrographically, J wave-like notches were found in 29.0% of the control subjects with complete RBBB and in 40.0% of the patients with IVF who showed complete RBBB. The difference was not significant ($P = .4999$). Left axis deviation in frontal electrical axis was found in 10.0% vs 20.0% for controls and patients with IVF, respectively ($P = .2980$).

Among the ECG parameters, only the QRS duration was different ($P = .0061$; Table 2). The QT interval was prolonged in controls ($P = .0386$), but the corrected QT interval was not ($P = .3740$).

Course in hospital and outcomes

One patient rejected both further examination and the implantation of an implantable cardioverter-defibrillator (ICD), and the remaining patients were followed for 6.3 ± 2.5 years. Seven patients underwent ICD implantation, and 3 of these patients had VF recurrence, 2 in a state of VF storms that were controlled by isoproterenol infusion. VF was precipitated by short-coupled premature ventricular complexes (PVCs; Figure 4). One of 2 patients with VF storms received bepridil for chronic therapy, and the other was followed without antiarrhythmic drug therapy. Both had been free from VF recurrence.^{17,18} One patient was lost to follow-up, and the remaining patients survived.

Discussion

Ten patients were admitted for VF, and in all of them, structural heart diseases and primary electrical diseases including BrS and coronary spasms were excluded and were diagnosed to have IVF. Complete RBBB was the sole abnormal finding. VF recurred in 3, and a VF storm was controlled by isoproterenol that suggested a common underlying arrhythmogenic substrate to BrS or J wave-associated IVF. Furthermore, the prevalence of complete RBBB was higher, and the QRS duration in patients with IVF was prolonged than the control subjects who showed complete RBBB.

The higher prevalence of complete RBBB was confirmed in patients with VF compared to controls. In the literature, we can count 93 patients with IVF in whom the ECG findings were well described.^{19–24} Among them, 9 of 93 (9.7%) patients showed complete RBBB, which is similar to our finding: 12.5%. However, it is possible that some patients might have BrS. This is because most of them were diagnosed before 1992 while BrS was first reported in that year.¹ However, even in a recent report, Nam et al²⁵ included 1 patient with RBBB to non-BrS-type IVF on the basis of rigid criteria.

Although complete RBBB has generally been considered to be benign,^{14,26–30} a recent cohort study made it apparent that RBBB is associated with both cardiovascular risk and all-cause mortality.³¹ Furthermore, recent studies have reported that complete RBBB can conceal the BrS ECG phenotype, which can be unmasked when RBBB is resolved.^{16,32} Twelve-lead ECGs were recorded at least once every other day, including those during drug testing, exercise testing, or catheterization, which were performed on different days. ECGs at higher intercostal spaces were performed on another occasion of ECG recording. If

present, BrS would be highly disclosed by these repeatedly recorded ECGs. Notwithstanding, it will be difficult to totally dismiss the possibility that RBBB may have concealed the J wave manifestation in our patients with IVF. Pacing at the right ventricle might be used to resolve the RBBB pattern and disclose J waves (Figure 3).

Ameliorative response to isoproterenol, but not to beta-blockers, amiodarone, and sedative agents might provide a clue to the underlying arrhythmogenic substrate. These responses are consistent with those observed in patients with J wave syndromes.³³ Isoproterenol is known to normalize ST-segment elevation and to suppress VF in patients with BrS and other J wave syndromes.^{4,6,9,10,25} This can be explained by the fact that isoproterenol produces an inward shift in the balance of currents during the early phases of the action potential by increasing inward calcium currents.³³ So far, VF episodes were observed to be commonly initiated by PVCs with short coupling intervals and following a short-long-short sequence.^{25,34} Two of 3 patients showed PVCs with short coupling intervals (Figure 4). These observations prompt further speculation that complete RBBB may conceal ERS.³³

Study limitations

Although Chiale et al³² reported a useful maneuver to distinguish BrS in patients with RBBB, we have not performed “Chiale’s maneuver” in all patients. We need to collect this information from patients who were implanted with an ICD by using its pacing modality. Also, a recent study shows that the sternum appears to be the best location to detect the ST-segment elevation,³⁵ but we did not include recordings from the sternum at the third and second intercostal space. Furthermore, a drug challenge to unmask BrS was done by using procainamide, but the drug is notoriously known to be less sensitive than flecainide or pilsicainide. Therefore, for this purpose we have discontinued this drug.

In summary, contrary to common perceptions, it is likely that some patients with IVF also present with complete RBBB. A diagnosis of IVF in a survivor of VF is most of the time made by exclusion. Our study suggests that RBBB may still be compatible with this diagnosis, although patients with IVF are considered not to present with any abnormalities. To rule out concealed BrS or ERS in the presence of complete RBBB, right ventricle pacing during EPS or from ICD lead may be useful.

Conclusions

Our results demonstrate that complete RBBB is more common in patients with IVF than expected in the general population. From wider QRS complexes, advanced conduction abnormality was suggested, and pharmacologically, it was suggested to share common characteristics with BrS or J wave-associated IVF. The role of RBBB on the arrhythmogenesis needs to be further elucidated.

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ABBREVIATIONS

BrS	Brugada syndrome
ECG	electrocardiogram/ electrocardiographic

EPS	electrophysiological study
ERS	early repolarization syndrome
ICD	implantable cardioverter-defibrillator
IVF	idiopathic ventricular fibrillation
PVC	premature ventricular complex
RBBB	right bundle branch block
VF	ventricular fibrillation
VT	ventricular tachycardia

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Figure 1.

A case of Brugada syndrome complicated with complete right bundle branch block (RBBB). The patient is a 69-year-old man (case 11). The electrocardiogram on admission (**A**) showed complete RBBB; however, a peculiar ST-segment pattern, which was considered to represent Brugada syndrome, was observed on repeated electrocardiographic recordings (**B**). The patient showed coved-type ST-segment elevation when RBBB resolved spontaneously, as reported elsewhere.¹⁶

Figure 2.

Electrocardiograms of 10 patients with idiopathic ventricular fibrillation with right bundle branch block. A typical complete right bundle branch block pattern showing a late R wave in lead V₁ (cases 1–9) or lead V₂ (case 10) with a prolonged duration of the QRS complex of >120 ms can be observed. Left axis deviation is obvious in cases 7 and 10. J wave-like notches were observed in cases 3, 4, 6, and 8 (arrows) within the QRS complexes.

Figure 3.

Ventricular fibrillation (VF) onset and resolution of right bundle branch block (RBBB) during electrophysiological study. **A:** A 45-year-old man previously diagnosed as idiopathic ventricular fibrillation followed by implantable cardioverter-defibrillator implantation was admitted for a VF storm. The pilsicainide provocation test for both Brugada syndrome and coronary spasm was negative, but his ECG shows a typical pattern of complete RBBB: an R wave in lead V₁ and a slurred S wave in lead V₆ and other leads. A premature ventricular beat that originated from the inferobasal region of the right ventricle was repeatedly initiating the VF. **B:** During electrophysiological study, the degree of RBBB diminished after right ventricular pacing, which revealed J waves in lead I (arrow).

Figure 4.

Onset of ventricular fibrillation (VF). **A:** The patient was case 3. Soon after admission, VF occurred 11 times, initiated by short-coupled premature ventricular complex, and then VF subsided. **B:** The patient was case 4. VF occurred after admission and recorded on monitor electrocardiogram. The onset of VF was shown in the inset below, which showed premature ventricular complex with short coupling interval.

Table 1

Clinical characteristics of patients with IVF who showed complete RBBB

Case	Age	Sex	VF	Time of VF	FH	VF at EPS	ICD	Drug test	Acetylcholinest	VF recurrence	Effective drug	Outcome	Follow-up period (y)
1	45	M	+	Morning	-	+	+	Pilsicainide	+	+/+	Isoproterenol, bepridil	Alive	2
2	49	F	+	Morning	-	NA	-	Procainamide	+	-	Magnesium sulfate ?	Alive	7.4
3	49	M	+	Evening	-	NA	+	Flecainide	+	-	-	Alive	3.5
4	54	F	+	Midnight	-	+	-	-	-	-	-	Unknown [‡]	-
5	56	M	+	Midnight	+	+	+	Pilsicainide	+	+	-	Alive	8.2
6	41	M	+	Morning	-	NA	+	Pilsicainide	+	-	-	Alive	8.0
7	66	M	+	Day time	+	+	+	Pilsicainide	-	-	Sotalol?	Alive	5.3
8	21	M	+	Morning	-	+	-	Flecainide	+	-	-	Alive	6.4
9	21	M	+	Evening	-	-	+	Pilsicainide	+	-	-	Alive	10.1
10	36	M	+	Midnight	-	-	+	Pilsicainide	+	+/+	-	Alive	6.2
11 [§]	69	M	+	Night	-	+	+	-	+	+	-	-	1.8
12 [§]	60	M	+	Morning	-	+	+	Pilsicainide	-	+	Bepridil	Alive	15

Isoproterenol was given to suppress VF and was effective. Magnesium sulfate given to control VF, but its efficacy was not evident. A beneficial effect of bepridil was observed in 2 patients: 1 patient with IVF and 1 patient with BrS. The efficacy of sotalol was not evident.

BrS = Brugada syndrome; EPS = electrophysiological study; F = female; FH = family history of sudden death; ICD = implantable cardioverter-defibrillator; M = male; VF = ventricular fibrillation.

* Appropriate ICD shock delivery.

[‡]VF storm.

[‡]We could not follow the clinical outcome because this patient refused treatment and was discharged before further evaluation.

[§]These patients were diagnosed with BrS and excluded from this study.

+Positive; - Negative; ?An effect is uncertain.

Table 2

Comparisons between patients with IVF who showed RBBB and patients who did not show complete RBBB

	IVF cRBBB	IVF no cRBBB	Control cRBBB	P*	P [†]
Patient no. (no. of men, %)	10 (8, 80)	77 (68, 88.3)	55 (44, 80)	.4831	1.0000
Age (y)	44 ± 15	38 ± 14	44 ± 10	.2713	.6702
QRS duration (ms)	150 ± 14	104 ± 11	139 ± 10	<.0001	.0061
RR interval (ms)	879 ± 103	821 ± 150	973 ± 121	.3620	.1756
PR interval (ms)	172 ± 28	171 ± 32	162 ± 21	.8735	.2564
QT interval (ms) [‡]	395 ± 28	383 ± 25	412 ± 24	.2627	.0386
Corrected QT interval (ms)	425 ± 48	397 ± 38	417 ± 20	.0856	.3740
J waves, n (%)	-	42 (54.5)	-	.2572	-

IVF = idiopathic ventricular fibrillation; cRBBB = control right bundle branch block.

* Comparisons between 2 IVF groups.

[†] Comparisons between IVF and control RBBB groups.

[‡] The QT interval was measured in lead II.