Sinus Node Dysfunction Concomitant With Brugada Syndrome

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Background A genetic correlation between Brugada syndrome (BS) and sinus node dysfunction (SND) has been proposed, although the clinical and electrophysiologic characteristics of this concomitant condition are unknown.

Methods and Results The study comprised 5 patients with symptomatic BS (4 with spontaneous episodes of ventricular fibrillation (VF) and 1 with syncope) of whom 3 had a documented sinus pause >3 s (a 42- and 62-year-old man, and a 49-year-old woman). Only 1 of them had a family history of sudden death; 2 of them had also an episode of atrial fibrillation or flutter. Electrophysiologic study demonstrated prolonged sinus node recovery time in 2 patients (2.6 s and >5 s), in whom a cardiac pacemaker had been implanted before the diagnosis of BS was made after episodes of VF. Finally, all 3 patients received an implantable cardioverter defibrillator, including 2 upgrades from pacemaker.

Conclusions SND is not a rare concomitant disorder in BS and there is a possible genetic connection. (Circ J 2005; 69: 946–950)

Key Words: Brugada syndrome, Sinus node recovery time; Sinus pause; Ventricular fibrillation

Brugada syndrome (BS) is a well-known electrical disorder causing sudden cardiac death from ventricular fibrillation (VF).1,2 Although some patients with BS have atrial tachyarrhythmias3–5 and/or conduction disturbances1,6–8 there is limited information concerning sinus node dysfunction (SND).

Methods and Results

We present 5 patients with symptomatic BS, including 4 with spontaneous episodes of VF and 1 with syncope, who were referred to us. Structural heart disease was excluded in each patient by echocardiography (all patients), cardiac catheterization and coronary angiography (3 patients), single-photo emission computed tomography (3 patients), and exercise stress testing (2 patients). Of the 5 patients, we documented a sinus arrest >3 s in 3 cases: a 42- and 62-year-old man, and a 49-year-old woman (Table 1). Only 1 patient (Case 3) had a family history of sudden death; cases 1 and 3 had also had an episode of atrial fibrillation or flutter (AFL). Electrophysiologic study (EPS) demonstrated prolonged sinus node (SN) recovery time (SNRT) in 2 patients in whom a cardiac pacemaker had been implanted before the diagnosis of BS was made on the basis of spontaneous episodes of VF. Finally, all 3 patients received an implantable cardioverter defibrillator (ICD), including 2 upgrades from pacemaker.

Case Reports

Case 1 (Fig 1) In 1989 a 42-year-old man was re-admitted as an emergency for recurrent syncope. The previous year, he had had several syncopal episodes during and after dinner, and consulted a local clinic where his ECG showed AF that spontaneously converted to sinus rhythm. He was then referred to us. Holter ECG monitoring revealed no ventricular arrhythmias but showed a sinus pause of 3.6 s in the evening. The EPS demonstrated a prolonged SNRT of 2,550 ms and he was implanted with a VVI pacemaker. During re-admission in 1989 for recurrent syncope, he developed VF (Fig 1 Bottom) and was successfully defibrillated by external DC shock. His ECG revealed the typical Brugada pattern and the pacemaker was exchanged for an ICD.

Case 2 (Figs 2,3) A 62-year-old man was referred because of several syncopal episodes and typical Brugada ECG pattern. Two days after admission, ECG monitoring revealed asymptomatic episodes of sinus pause of 3.6 s in the evening. The EPS demonstrated a prolonged SNRT of 2,550 ms and he was implanted with a VVI pacemaker. During re-admission in 1989 for recurrent syncope, he developed VF (Fig 1 Bottom) and was successfully defibrillated by external DC shock. His ECG revealed the typical Brugada pattern and the pacemaker was exchanged for an ICD.

Case 3 (Fig 4) A 49-year-old woman was admitted for syncope. Her younger brother had died suddenly at the age of 30 years. The ECG showed AFL, incomplete right bundle-branch block, but no ST segment elevation. The duration of the flutter was indeterminable. Although the persistent AFL was terminated by rapid atrial pacing
during the EPS, sinus arrest with junctional escape beats followed. The SNRT was prolonged for more than 5 s. No ventricular tachyarrhythmias were induced during the EPS. Under the diagnosis of sick sinus syndrome and infrahisian conduction delay (His-ventricular interval 75 ms), a DDD pacemaker was implanted, but 10 months later she was admitted as an emergency because of recurrent syncope. A spontaneous episode of VF was documented in the emergency room during dual-chamber pacing (Fig 4 Bottom). After successful DC defibrillation, we changed the pacing mode from DDD to AAI for evaluation of ST elevation in the precordial leads. A saddleback-type ST elevation was observed in leads V1-3, which improved after infusion of isoproterenol. In spite of the type 2 ST elevation the diagnosis of BS was made; the previously implanted DDD pacemaker and lead system were removed, and implantation of a dual chamber ICD was performed.
Fig 2. Case 2: (Left) Twelve-lead ECG shows right bundle-branch block and the coved-type ST elevation in leads V1 and V2. (Right) ECG monitoring shows asymptomatic sinus pauses after midnight during sleep, with a maximum duration of 6.6 s.

Fig 3. Case 2: ECG from the ICD shows successful conversion of an episode of spontaneous ventricular fibrillation (VF) to sinus rhythm at 03.06 h.
Discussion

We have identified SND in 3 of 5 patients with symptomatic BS, which suggests it is not a rare concomitant. Ventricular tachyarrhythmias, supraventricular tachyarrhythmias\(^3\text{-}\(^5\)) and His-Purkinje conduction delay\(^1\text{-}\(^8\)) have been reported in patients with BS and it is thought that this arrhythmogenicity is related to downregulation of a channel mutation\(^2\text{-}\(^9\)).

Morita et al reported that SN function is attenuated in patients of BS with programmed electrical stimulation-induced VF compared with those without VF; however, their study did not include patients with clinically documented SND\(^10\). In our study, a sinus pause \(>3\) s was documented in 3 patients, 2 of them had prolonged SNRT. A genetic correlation between BS, long QT syndrome, and SND has been proposed\(^11\text{-}\(^14\)). Takehara et al reported a sodium channel mutation in SCN5A identified in BS associated with atrial standstill\(^15\). Prolongation of the action potential of SN cells and slowing of diastolic depolarization because of an abnormal sodium channel gene may contribute to SND\(^11\). A reduced sodium current could account for BS and a conduction disturbance in the sinoatrial region\(^15\). However, in the present study the precise mechanism of SND was not identified because we did not perform a genetic evaluation. Increased vagal tone may also partially contribute to sinus pause because in Case 1 the prolonged SNRT was normalized after intravenous atropine injection and in Case 2 the sinus pause only occurred at midnight during sleep.

In 2 patients (Cases 1 and 3), the diagnosis of BS was not made at initial admission because neither the typical ECG findings nor ventricular tachyarrhythmias was documented, and Case 1 was managed before publication of the initial paper by Brugada and Brugada\(^1\). Dynamic change in the ST segment, which sometimes seems normal, is well known in BS\(^9\). Therefore, in patients with sick sinus syndrome, if they have recurrent syncope after pacemaker implantation, ventricular tachyarrhythmias may be a possible cause and repeated ECG recording and provocation with sodium channel blocker could disclose latent BS\(^9\). On the other hand, SND may be another possible cause of syncope in BS.

Conclusion

Based on our results, we suggest that SND is not a rare concomitant disorder in BS and that there is a possible...
genetic connection. Although we studied a very small number of symptomatic patients with BS and did not perform genetic analysis, we speculate that, in some cases at least, BS may be a multiple conduction disorder, including not only the His-Purkinje system and ventricle, but also the SN and atrium, derived from ion channel mutations. A multicenter study involving a large number of patients is necessary to clarify the precise incidence of SND in BS.

References