CASE REPORT

Brugada Syndrome Subject to Depolarization Abnormality of the Conduction System

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We report a patient who first developed Brugada syndrome (BS) after the conduction in atrioventricular (AV) node and the ventricular conduction system was disturbed. A type-1 Brugada ECG was unexpectedly unmasked after administration of a class IC antiarrhythmic agent for suppressing paroxysmal atrial fibrillation (paf), which had never been documented in the absence of such conduction disturbances, even after giving antiarrhythmic agents for paf. In addition, this patient was accompanied by sick sinus syndrome. This was an intriguing overlap syndrome case in that the development of BS might have been associated with the incidence of a conduction system disturbance.

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brugada syndrome; brady-tachycardia syndrome; Lenègre disease; right bundle branch block; atrioventricular block

Brugada syndrome (BS) is considered a subgroup of ventricular fibrillation (VF) occurring in patients without detectable structural heart disease which is characterized by ST-segment elevation in the right precordial leads, a right bundle branch block like morphology otherwise diagnosed as idiopathic VF.^{1,2} The current understanding is that BS merges with certain ventricular rhythm disorders.^{2–5} Recently, atrial rhythm disorders such as sick sinus syndrome, atrial standstill, and atrioventricular (AV) block have been reported as combined diseases with BS.^{6–9} The responsible gene for BS has been reported to be SCN5A which encode cardiac sodium channel¹⁰ and the mutations of SCN5A are also known to cause other cardiac rhythm disorders such as progressive cardiac conduction defects (Lenègre disease), AV block, sudden infant death syndrome, and type-3 long QT syndrome.^{2,5,7–11} Taking into account the recent progress in molecular biology into the genetic background of BS, it is conceivable that various phenotypes and their

overlap induced by such a responsible gene might occur.^{7,8,11} However, even if the gene mutation is found, it has not been completely disclosed which clinical phenotype appears. Moreover, the relation of incidental timings between BS and each coincidental disease has remained unclear.

This report presents an intriguing case of an overlap between BS, AV and bifascicular block, sinus node dysfunction, and paroxysmal atrial fibrillation (paf). Further, this case demonstrated unusual course of the development of BS in which the deterioration of the AV node or the ventricular conduction system might be associated with the genesis of BS.

CASE REPORT

A 64-year-old man was admitted to our hospital for an evaluation of his frequent chest discomfort, which was followed by light-headedness or near syncope. This patient experienced paf 12 months

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Figure 1. A 12-lead electrocardiogram (ECG) after the administration of disopyramide during atrial fibrillation (panel A) and after the restoration of sinus rhythm (panel B) 12 months before this admission. The ECG demonstrated neither a right bundle branch block nor left axis deviation. The PQ and QT intervals during sinus rhythm were within normal limits.

before his admission and paf could be terminated after the administration of disopyramide at a dose of 100 mg. The surface 12-lead electrocardiograms (ECG) during paf after injection of disopyramide and restoration of sinus rhythm (SR) are shown in Fig. 1. At that time, the ECGs demonstrated J-point elevation in leads V2-3 during paf and in lead V2 after conversion to SR (Fig. 1A and B, respectively) but such J-point elevation did not satisfy the criteria of diagnosis for BS.² It was noted that did neither a bundle branch block with QRS axis deviation nor AV block present. The PQ and QT intervals after the conversion to SR were within normal limits (180 ms and 400 ms, respectively) in the absence of any antiarrhythmic agents. On this admission, the 12-lead ECG exhibited normal SR, but the PQ interval was obviously prolonged to 280 ms as compared to that 12 months prior, resulting in a first degree of AV block (Fig. 2). In addition, complete right bundle branch and left anterior fascicular block, which was never previously documented, newly appeared. It seemed that this

ECG also exhibited coved-type ST elevation in leads V₁-V₂, but there was a slight notch in these leads coinciding with the end of the QRS wave in leads V₅-V₆. Such a notch might indicate that the QRS ended later in leads V₁-V₂, making coved-type ST elevation unlikely. A routine checkup including an echocardiogram revealed no structurally abnormal findings. The hematological and blood chemistry results were normal and no electrolyte abnormalities were observed. He developed paf again during his hospital stay and received pilsicainide at a dose of 50mg (class IC antiarrhythmic agent) to suppress paf. Paf terminated 30 min after beginning the drug injection, but 21 second of sinus arrest was documented following the termination (Fig. 3A). After administration of pilsicainide ST level in the right precordial leads was elevated and premature ventricular contraction (PVC) appeared without any symptoms (Fig. 3B). However, no more PVC couplets or nonsustained ventricular tachycardia occurred. Such ST elevation gave rise to another issue, that he might have concealed BS. In an

Figure 2. A 12-lead ECG on admission showing a prolonged PQ interval (280 ms) and complete right bundle branch block with a newly appearing left axis deviation.

electrophysiologic study, VF could be easily induced by double extrastimuli (S2–S3: 260–230 ms) with a basic cycle length of 600 ms from the right ventricular outflow tract. We then tried to assess the function of both sinus and AV nodes, but failed to obtain that data because paf was easily induced by the electrical stimulation.

We judged him to be a high risk patient of BS and implanted a dual chamber implantable cardioverter defibrillator (ICD), because VF could be induced by double extrastimuli¹² and we could not completely rule out that the near syncope which he had experienced was caused by VF, and in addition he might receive an antiarrhythmic drug therapy for paf but such drugs might render the incidence of VF greater. During a 12-month follow-up period after the ICD implantation, he did not experience any near syncope with a beta-blocker.

DISCUSSION

This was an intriguing case in that BS was developed after depolarization abnormality in AV node and the ventricular conduction system oc-

curred. In addition, our case coincided with a brady-tachycardia syndrome (paf and sick sinus syndrome), first degree of AV block, and bifascicular (right bundle branch and the left anterior fascicle) block and such an overlap has not been previously reported. It has been reported that the arrhythmogenicity of BS includes not only the ventricle but also the atrium.^{4,13,14} Moreover, other studies reported that the function of both the sinus and AV nodes have been attenuated in some of BS patients who did not have actually SSS or AV block.^{4,7–9,11}

On the other hand, it remains unknown whether or not such disturbed conduction is prerequisite for the development of BS. There was a recent study, which assessed the change of the AV and/or intraventricular conduction property in BS-type SCN5A mutation gene carriers,¹¹ where the intraventricular conduction worsened with aging in the mutated gene carriers and Lenègre disease was the most common phenotype. It was noteworthy that none of the patients who presented with Lenègre disease developed BS in the follow-up. Whereas, the clinical course presented here in that such

Figure 3. An ECG strip from the ambulatory monitor at the termination of paroxysmal atrial fibrillation (paf) after giving pilsicainide (panel A) and 12-lead ECG during sinus rhythm after pilsicainide (panel B). (A) A 21 second sinus pause was observed and a junctional escaped rhythm appeared 11.2 second after the termination of paf. (B) After the injection of pilsicainide, a coved-type ST elevation in the right precordial leads emerged and a premature ventricular contraction (PVC) occurred. The QRS configuration of PVC exhibited a left bundle branch block morphology with an inferior axis.

preceded depolarization abnormalities as AV and bundle branch block might be associated with the development of BS has not been reported. It might be concluded that the patients in whom the disturbed conduction in AV node or the ventricular conduction system newly emerges might have a risk for developing BS and caution should be taken to identify such patients who would be at a risk for lethal arrhythmias during the follow-up.

The study limitation was that it remained unclear whether or not this patient had already developed BS 12 months before this admission even though the ST level was not elevated after receiving disopyramide. The different responses to the various antiarrhythmic agents in BS have been known. However, it is possible that this patient did not develop BS 12 months before his admission because the amount of disopyramide administered was sufficient dose for antiarrhythmic action to block sodium channel and disopyramide as well as pilsicainide could cause ST elevation in the right precordial leads and unmask BS in concealed BS patients.^{2,15,16}

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