A subtype of idiopathic ventricular fibrillation and its relevance to catheter ablation and genetic variants

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Introduction

Idiopathic ventricular fibrillation (VF) develops in structurally normal hearts and comprises various clinical entities.[1] In particular, site-specific premature ventricular complexes (PVCs), such as PVCs originating from the right ventricular outflow tract[2] or left ventricular papillary muscles,[3,4] have been reported to provoke idiopathic VF. PVCs originating from papillary muscles and the moderator band (MB) in the right ventricle (RV) are also among the causes of ventricular arrhythmias (VAs).[5,6]

Case report

A 57-year-old male patient had his first syncopal episode during desk work, and he regained consciousness spontaneously after a few minutes. He was admitted to our hospital for a medical examination. He had no history of previous syncope, other illnesses, or familial cardiac sudden death. On admission, his electrocardiogram (ECG) showed that the PVCs emerged with a bigeminal cycle with a coupling interval of 360 ms (Figure 1A). The QRS morphology was relatively narrow, with a duration of 138 ms, and had a left bundle branch block (LBBB) pattern with a precordial transition later than lead V_4. The intrinsicoid deflections in the precordial leads were 55 ms. The frontal plane axis of the PVCs was left superior, with a positive QRS complex in leads I and aVL. The characteristics implied that the PVC originated from the MB in the RV. An intensive examination including coronary computed tomography, echocardiography, and cardiac magnetic resonance imaging could not detect any structural heart disease.

The ECG monitor revealed a nonsustained polymorphic ventricular tachycardia (VT) on the next morning, which was triggered by an LBBB-type PVC (Figure 1B). To rule out any genetic arrhythmias such as Brugada syndrome, long QT syndrome (LQTS), or early repolarization syndrome, pharmacologic tests, such as those with pilsicainide (class Ic sodium channel blocker), epinephrine, isoproterenol, and disopyramide (class Ia sodium channel blocker), were performed. However, none of the pharmacologic responses was associated with any specific disease. We also noticed J waves in the inferolateral leads, but we concluded that they were bystanders because they lacked dynamicity before the onset of the VA or drug administration.

Because the PVC could trigger a polymorphic VT, which was responsible for his syncope, catheter ablation targeting the PVC was performed. The patient provided written informed consent before the procedure. An electrophysiological study was performed with the patient under deep sedation. A 3.5-mm saline-irrigated mapping ablation catheter (NaviStar Thermocool SF, Biosense Webster, Diamond Bar, CA) was inserted into the RV utilizing a steerable sheath. From the left femoral vein, an intracardiac echocardiography (ICE) catheter (Soundstar, Biosense Webster, CA) was advanced up into the right atrium. Radiofrequency (RF) energy was delivered with 30–35 W and a saline irrigation rate of 8 or 15 mL/min.

We mapped the earliest activation site of the PVC, which was located on the free wall of the RV, and the ICE results revealed the insertion of the MB on the free wall of the RV as well (Figures 2A and 2B). Pace mapping from the earliest activation site exhibited a morphology similar to that of the PVC (Figure 2C). At that site, an early potential was seen at the onset of the PVC. The local activation at the successful ablation site preceded the onset of the QRS of the PVC by 25 ms, and a sharp potential like a Purkinje potential was recorded by the ablation catheter (Figure 2D). During sinus rhythm, the potential was observed to precede the QRS wave (Figure 2E). The CARTO image and ICE demonstrated that the earliest activation site matched the location of the MB (Figures 3A and 3B).

After a radiofrequency energy delivery, the PVCs disappeared and the ECG exhibited a complete right bundle branch block (Figure 3C). Following that, the same PVC could no longer be induced by programmed stimulation under an isoproterenol infusion. The patient underwent an implantable cardioverter-defibrillator (ICD) implantation for secondary

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KEY TEACHING POINTS

- Premature ventricular complexes originating from the moderator band are responsible for ventricular arrhythmias, and catheter ablation is the among the possible therapies.
- Bipolar electrocardiograms may have Purkinje potentials at the successful ablation site, and intracardiac echocardiography may be useful.
- Ankyrin-B syndrome should be considered as a differential diagnosis of idiopathic ventricular fibrillation.

prevention. During 6 months of follow-up, he has experienced no further episodes of syncope or ICD therapies.

In our institute, we analyze the patient's genome by using the Next Generation Sequencer (MiSeq, Illumina, San Diego, CA) with a commercially available gene panel targeting 4813 genes associated with known clinical phenotypes (TruSight One, Illumina). Nucleotide variants, including a small insertion or deletions that would affect the amino acid sequences or could affect the splice sites, were annotated. We defined a variant as a mutation of which the minor allele frequency was <0.02 in all public databases. We detected a heterozygous single T-to-A nucleotide substitution at the position 4603 of the *ANK2* gene (NM_020977.3), which encoded ankyrin-B, leading to a replacement of tryptophan by arginine at amino acid residue 1535 (W1535R; NP_066187.2). This rare variant was confirmed by the Sanger method (Figure 3D). Family screening was not performed, because consent could not be obtained from the patient's parents or child.

We retrospectively reviewed the incidence of *ANK2* mutations in patients with inherited primary arrhythmia syndrome (IPAS) who underwent genetic screening in our university hospital. All patients who harbored *ANK2* variants resulting in a nonsynonymous substitution of the amino acid are shown as a supplementary table. *ANK2* mutations were identified in various IPASs such as Brugada syndrome, idiopathic VF, LQTS, and short QT syndrome.

Discussion

The MB is a component of the septomarginal trabeculation, which crosses from the septum to the free wall of the RV. The MB plays a pivotal role in the conduction system

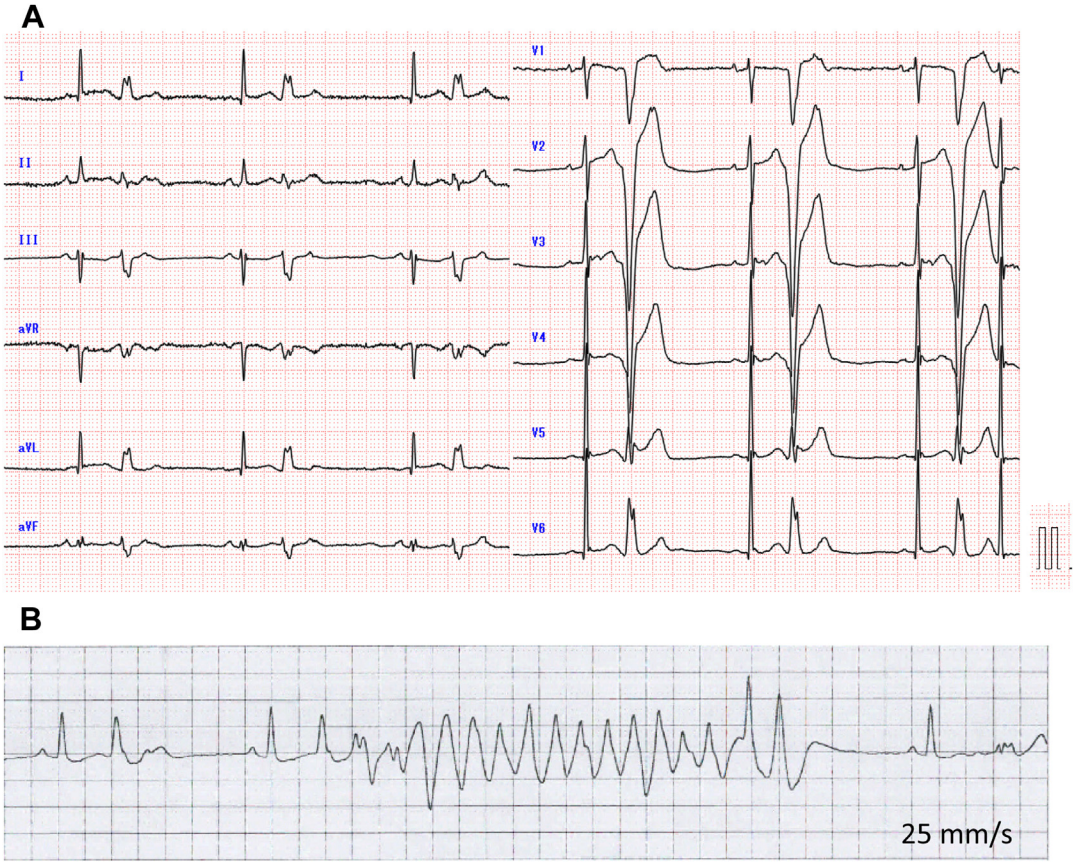

Figure 1 The 12-lead electrocardiogram (ECG) of the premature ventricular complexes and ECG monitor recording of the ventricular arrhythmia. **A:** 12-lead ECG. The premature ventricular contraction exhibited a left bundle branch block morphology. The heart rate was 65 beats per minute, and no Brugada-type ECG sign was evident. The PR and QTc intervals were within normal range. **B:** The ECG monitor recording after admission. A few seconds of premature ventricular complexes were observed preceding the ventricular arrhythmia.