Progression of Electroanatomic Substrate and Electric Storm Recurrence in a Patient With Brugada Syndrome

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In December 2011, a 39-year-old man resuscitated from out-of-hospital cardiac arrest caused by ventricular fibrillation received the diagnosis of Brugada syndrome on the basis of a spontaneous Brugada type 1 ECG pattern (Figure 1A). Before implantation of a cardioverter-defibrillator, the patient, after providing written informed consent, underwent a 3-dimensional electroanatomic mapping of the right ventricle (RV) as part of a clinical research study approved by ethics committee of our institution. A localized low-voltage area with delayed and fragmented potentials was evident in both bipolar and unipolar voltage maps in the anterior RV outflow tract. The patient was discharged with no antiarrhythmic medication and was free of arrhythmic events at implantable cardioverter-defibrillator interrogation for 1 year.

In January 2013, he was admitted at our institution again for arrhythmic storm with multiple consecutive appropriate implantable cardioverter-defibrillator shocks resulting from recurrent ventricular fibrillation.

Continuous ECG monitoring documented frequent monomorphic ventricular extrasystoles with left bundle-branch block morphology and an inferior axis and frequent R-on-T phenomenon triggering multiple episodes of ventricular fibrillation (Figure 1B). He was treated with isoproterenol infusion, leading to electric storm suppression and cardiac rhythm normalization.

As indicated in the research study in the case of arrhythmic events, 3-dimensional RV electroanatomic mapping was repeated and documented an increase (from 1 to 14.2 cm² and from 10.2 to 19.8 cm² in the bipolar and unipolar maps, respectively) of the RV outflow tract low-voltage area previously documented (Figure 2A–2D). To investigate the pathologic substrate of the low-voltage area and the possible mechanisms of disease progression and arrhythmias recurrence, we also performed a CARTO-guided RV endomyocardial biopsy, drawing 3 myocardial samples from an area with both bipolar and unipolar low voltages. In addition, during the same procedure, we performed endocardial radiofrequency ablation to abolish low-voltage fractionated potentials in the anterior RV outflow tract. Interestingly, radiofrequency applications in the inferior portion of the low-voltage area repeatedly evoked sustained polymorphic ventricular tachycardias self-terminating at radiofrequency pulse cessation, but in 3 cases degenerating into ventricular fibrillation and requiring external defibrillation (Figure 3). Histological analysis of endomyocardial biopsies showed the presence of myocardial inflammation with focal necrosis of adjacent myocytes and no evidence of fibro fatty substitution (Figure 4). The patient was discharged on therapy with quinidine 150 mg 3 times daily. After a follow-up of 18 months, he is asymptomatic and free of arrhythmic events at implantable cardioverter-defibrillator interrogation. Genetic analysis failed to identify mutations in the main genes so far associated with the syndrome.

To the best of our knowledge, this is the first description of electroanatomic substrate progression associated with the recurrence of ventricular fibrillation in a patient with Brugada syndrome. Our case suggests that electroanatomic and structural abnormalities underlie the ECG and arrhythmic features of Brugada syndrome and that the progression of these abnormalities can be associated with arrhythmia recurrence. Further studies are needed to define the prevalence of electroanatomic abnormalities in Brugada syndrome and to clarify the role of myocardial inflammation in electroanatomic substrate progression and arrhythmogenesis. Similarly, the potential role of electroanatomic mapping in monitoring disease progression and in prognostic stratification in Brugada syndrome warrants further investigation.

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Disclosures
Dr Notarstefano is a consultant for Biosense Webster. The other authors report no conflicts.

References

Figure 1. A, A 12-lead rest ECG obtained in 2011 showing a spontaneous type 1 Brugada pattern in leads V1 and V2. B, Continuous ECG monitoring (in 2013) showing frequent monomorphic ventricular ectopic beats with left bundle-branch block morphology and an inferior axis, as well as frequent R-on-T phenomenon triggering ventricular fibrillation. The type 1 Brugada pattern can be observed in lead V1.
Figure 2. Three-dimensional electroanatomic maps obtained in 2011 (A and B) and 2013 (C and D). A low-voltage area is present in the anterior right ventricular outflow tract in both bipolar (A) and unipolar (B) maps in 2011. In 2013, an extension of the abnormal voltage area can be observed in both bipolar (C) and unipolar (D) maps. In the bipolar maps, purple indicates electroanatomic normal tissue with a voltage amplitude ≥1.5 mV; red indicates electroanatomic scar tissue with a voltage amplitude <0.5 mV; and intermediate colors represent the low-voltage electroanatomic border zone (voltage amplitude >0.5 and <1.5 mV). In the unipolar maps, purple indicates electroanatomic normal tissue with voltage amplitude ≥5.5 mV; red indicates tissue with low voltage (amplitude <3.5 mV); and intermediate colors represent the low-voltage electroanatomic border zone (voltage amplitude >3.5 and <5.5 mV).
Figure 3. A, Bipolar map. Radiofrequency applications (red dots) in the right ventricular outflow tract low-voltage area. Black arrow indicates the site of low and fragmented potential shown in the right inset. White arrow indicates the site of biopsy. B, Nonsustained and sustained polymorphic ventricular tachycardia degenerating into ventricular fibrillation after a radiofrequency pulse is started in the area, indicated by the gray dot and arrowhead in A.

Figure 4. Histology of CARTO-guided right ventricular endomyocardial biopsies obtained from the right ventricular outflow tract low-voltage area showing inflammatory infiltrates (arrows) with interstitial edema (asterisks) and focal myocyte necrosis (arrowheads; hematoxylin and eosin stain; magnification, ×100).
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