Isolated, premature ventricular complex–induced right ventricular dysfunction mimicking arrhythmogenic right ventricular cardiomyopathy

Antonio Berruezo, MD, PhD,[*†‡] Elena Efimova, MD,[§] Juan Acosta, MD,[‖] Beatriz Jáuregui, MD[*†]

*From the *Institut Clínic Cardiovascular, Hospital Clínic, Universitat de Barcelona, Barcelona, Spain, [†]Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain, [‡]Centro de Investigación Biomédica en Red (CIBER Cardiovascular), Instituto de Salud Carlos III, Madrid, Spain, [§]Department of Electrophysiology, Heart Centre Leipzig, Leipzig, Germany, and [‖]Arrhythmia Unit, Virgen del Rocío University Hospital, Seville, Spain.*

Introduction

We present the case of a 23-year-old woman with palpitations and frequent premature ventricular contractions (PVCs) with left bundle branch block morphology and superior axis. Structural heart disease was ruled out initially but, after a 2-year follow-up, new T-wave inversions appeared in inferior and precordial leads on the 12-lead electrocardiogram (ECG), and echocardiography showed dilatation of the right ventricle (RV) with posterior akinesia. Formally, these findings fulfilled the definite diagnosis of arrhythmogenic right ventricular cardiomyopathy (ARVC). Catheter ablation of the PVCs was performed, showing an unusual site of origin for idiopathic etiology (lateral subtricuspid region of the RV free wall). Successful PVC ablation resulted in complete normalization of electrocardiographic and echocardiographic parameters, suggesting that a pure PVC-induced RV cardiomyopathy should be considered before establishing the final diagnosis of ARVC based only on Task Force criteria (TFC).

KEY TEACHING POINTS

- The present case shows a new clinical entity consisting of isolated right ventricle (RV) cardiomyopathy induced by frequent premature ventricular contractions (PVCs), mimicking arrhythmogenic right ventricular cardiomyopathy (ARVC).
- The diagnosis of pure PVC-induced RV cardiomyopathy can fully overlap with that of ARVC. This new entity may fulfill enough Task Force criteria to be misdiagnosed as a "definite" ARVC.
- Pure PVC-induced RV cardiomyopathy should be considered in cases of RV systolic dysfunction and a high burden of PVCs arising from the RV, especially for those located in the free wall. Marked mechanical and electrical dyssynchrony of the RV are postulated as likely mechanisms for this entity.
- Successful PVC ablation in cases of pure PVC-induced RV cardiomyopathy results in complete normalization of electrocardiographic and echocardiographic parameters that mistakenly fulfilled the Task Force criteria for ARVC.

Case report

A 23-year-old woman was admitted to our hospital owing to mild palpitations and ventricular bigeminy on ECG. The 12-lead ECG showed frequent PVCs with left bundle branch block morphology and superior axis (Figure 1A). During the index admission, 24-hour Holter monitoring revealed a PVC burden of 47% (monomorphic), without nonsustained ventricular tachycardia episodes. Transthoracic echocardiography revealed no abnormalities and preserved left ventricle (LV) and RV function. The patient had no syncope, no family history of sudden cardiac death, and no history of participation in any competitive sport. A decision was made in favor of conservative treatment and beta-blocker therapy was initiated.

At 1-year follow-up, the PVC burden on 24-hour Holter monitoring was 35%. Cardiac magnetic resonance imaging

KEYWORDS Arrhythmogenic right ventricular cardiomyopathy; Catheter ablation; Premature ventricular complex; PVC-induced cardiomyopathy; Right ventricular dysfunction; Task Force criteria
(Heart Rhythm Case Reports 2018;4:222–226)

Address reprint requests and correspondence: Dr Antonio Berruezo, Arrhythmia Section, Cardiology Department, Cardiovascular Institute, Hospital Clinic, Associate Professor of Medicine, University of Barcelona, C/ Villarroel, 170, 08036 Barcelona, Spain. E-mail address: berruezo@clinic.cat.

https://doi.org/10.1016/j.hrcr.2018.02.006

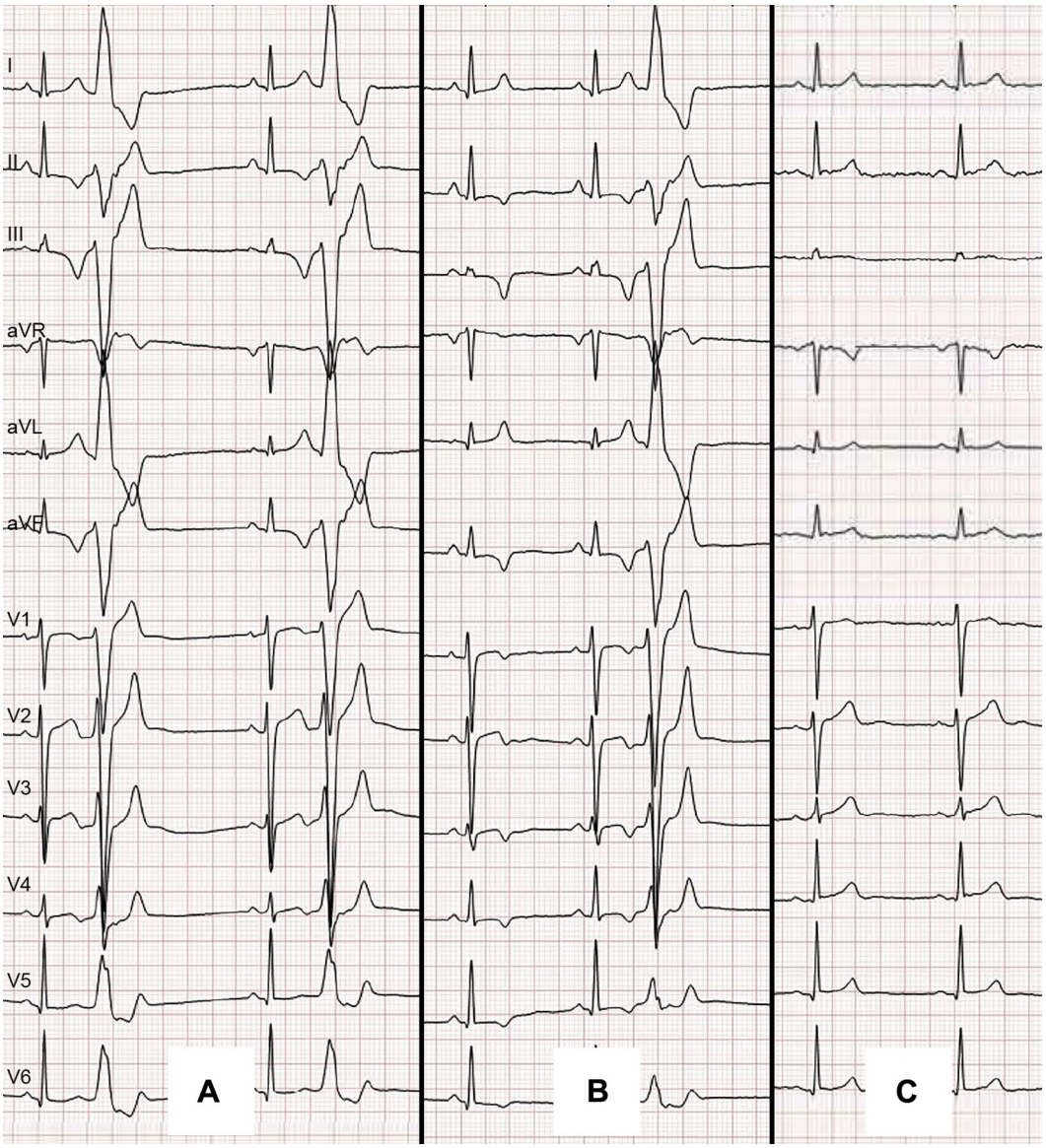

Figure 1 Electrocardiography recordings. **A:** At first admission, with premature ventricular contraction (PVC) bigeminy showing left bundle branch block morphology and superior axis. **B:** At 2-year follow-up, with a new appearance of T-wave inversion in inferior and precordial leads and fragmented QRS in lead III. **C:** After successful ablation (upright T waves, no PVCs).

(MRI) was performed, showing normal chamber dimensions with preserved biventricular function. No late gadolinium enhancement or regional motion abnormalities were found in the LV or RV. The patient remained oligosymptomatic despite frequent PVCs, and beta-blocker therapy was maintained. At 2-year follow-up, PVC burden remained high (45%) on 24-hour Holter. New T-wave inversions appeared in inferior and precordial leads on the 12-lead ECG (Figure 1B). For the first time, echocardiography showed a slightly dilated RV (right ventricular outflow tract diameter of 34 mm in parasternal long-axis and of 36 mm in short-axis view) with posterior akinesia. The LV size and function remained within normal limits. Formally, the presence of 1 major (RV dilatation with posterior akinesia) and 2 minor criteria (frequent PVCs, inverted T wave) fulfilled the definite diagnosis of ARVC.

Taking into account the impairment of the RV systolic function and unsuccessful conservative treatment, the patient was scheduled for catheter ablation of the PVCs. During activation mapping, the PVC earliest activation site was identified at the lateral subtricuspid region of the RV free wall (Figure 2). Considering that this was an unusual site of origin for idiopathic PVCs and that the patient met diagnostic criteria for ARVC, it was decided to perform endo-epicardial voltage mapping of the RV. Despite the normal endocardial bipolar voltage map, a few discrete, low-voltage areas could be seen in the unipolar map near (but not related to) the region of PVC origin (Figure 3). Consistently, the epicardial bipolar map showed a low-voltage area at the subtricuspid region of the RV free wall (Figure 3). No abnormal electrograms (ie, electrograms with delayed components) were identified in endocardial

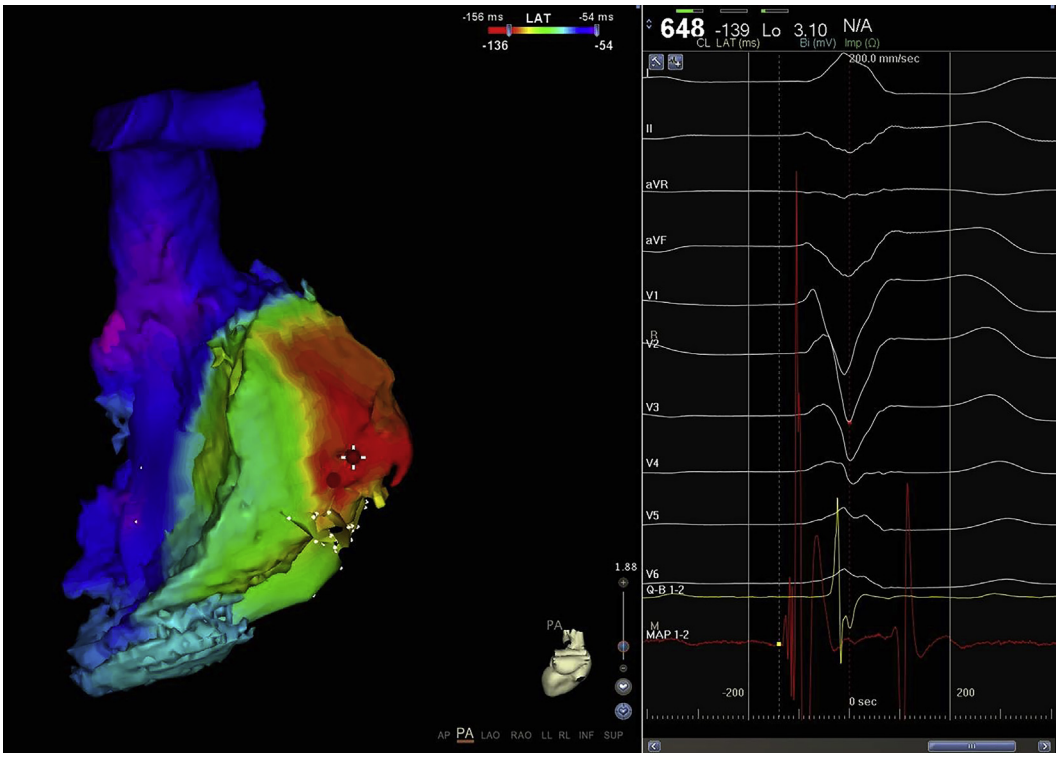

Figure 2 Activation mapping. The earliest activation site appears in the subtricuspidal lateral region. Red dots indicate radiofrequency applications.

and epicardial maps, thus unsupporting the diagnosis of ARVC. Ablation at the earliest endocardial activation site was successful, achieving a complete abolition of the PVCs.

One year after the procedure, follow-up echocardiography revealed normal RV dimensions without any wall motion abnormalities. Both echocardiographic and ECG parameters appeared completely normalized after successful PVC ablation, suggesting that ARVC had been an overdiagnosis (Figure 1C). A 3-year follow-up cardiac MRI also showed no abnormalities.

Discussion

To our knowledge, this case is the first description of PVC-induced isolated RV cardiomyopathy with a complete normalization of ECG and echocardiographic abnormalities after successful PVC ablation. The concept of LV dysfunction in the presence of frequent PVCs with improvement in LV function after PVC elimination is well recognized.[1–3] However, isolated RV systolic dysfunction induced by frequent PVC has not been previously described. The finding of a reduced RV function in combination with frequent PVCs, especially from a non–outflow tract origin in the RV, raises the suspicion of ARVC as the underlying pathology. The diagnosis of ARVC is currently based on 2010 TFC, considered to have improved diagnostic sensitivity and specificity for early and family ARVC forms in comparison with TFC 1994.[4] Liu and colleagues[5] validated the effect of the 2010 TFC on diagnosis and showed that 9.2% of patients fulfilling 1994 TFC for ARVC received a diagnosis other than ARVC, and 4.4% of the diagnoses were potential ARCV mimics. Similarly, Vermes and colleagues[6] showed an improved specificity, but not sensitivity, of diagnostic criteria for ARVC. Even when the diagnostic work-up is guided by the 2010 TFC (with presumably increased specificity), however, physicians still face a diagnostic dilemma: a possibility of under-recognition of early disease on one hand and overdiagnosis on the other. Not only does a correct identification of the "concealed phase" of ARVC remain challenging, but certain clinical entities produce ECG changes and RV morphologic abnormalities that could mimic ARVC and be misinterpreted.

According to the 2010 TFC, a definite diagnosis of ARVC can be made with 2 major criteria, 1 major and 2 minor criteria, or 4 minor criteria from 6 different categories.[4] Applying the current guidelines to our patient, frequent PVCs in the RV and RV impairment in combination with T-wave inversion was sufficient for the diagnosis of ARVC. The absence of sustained ventricular arrhythmias (VA), as in the present case, is also frequent in patients with a definite diagnosis of ARVC. In a recent study,[7] among 65 index patients without sustained VA at presentation, during a median 7-year follow-up, sustained VA were observed only in 48%. This would imply that, among patients without sustained VA at the moment of ARVC diagnosis, arrhythmic progression can be slower than previously thought, at least in a not negligible proportion of cases. On the other hand, an early involvement of the LV in ARVC, which may course with pan T-wave inversions but normal LV function, has

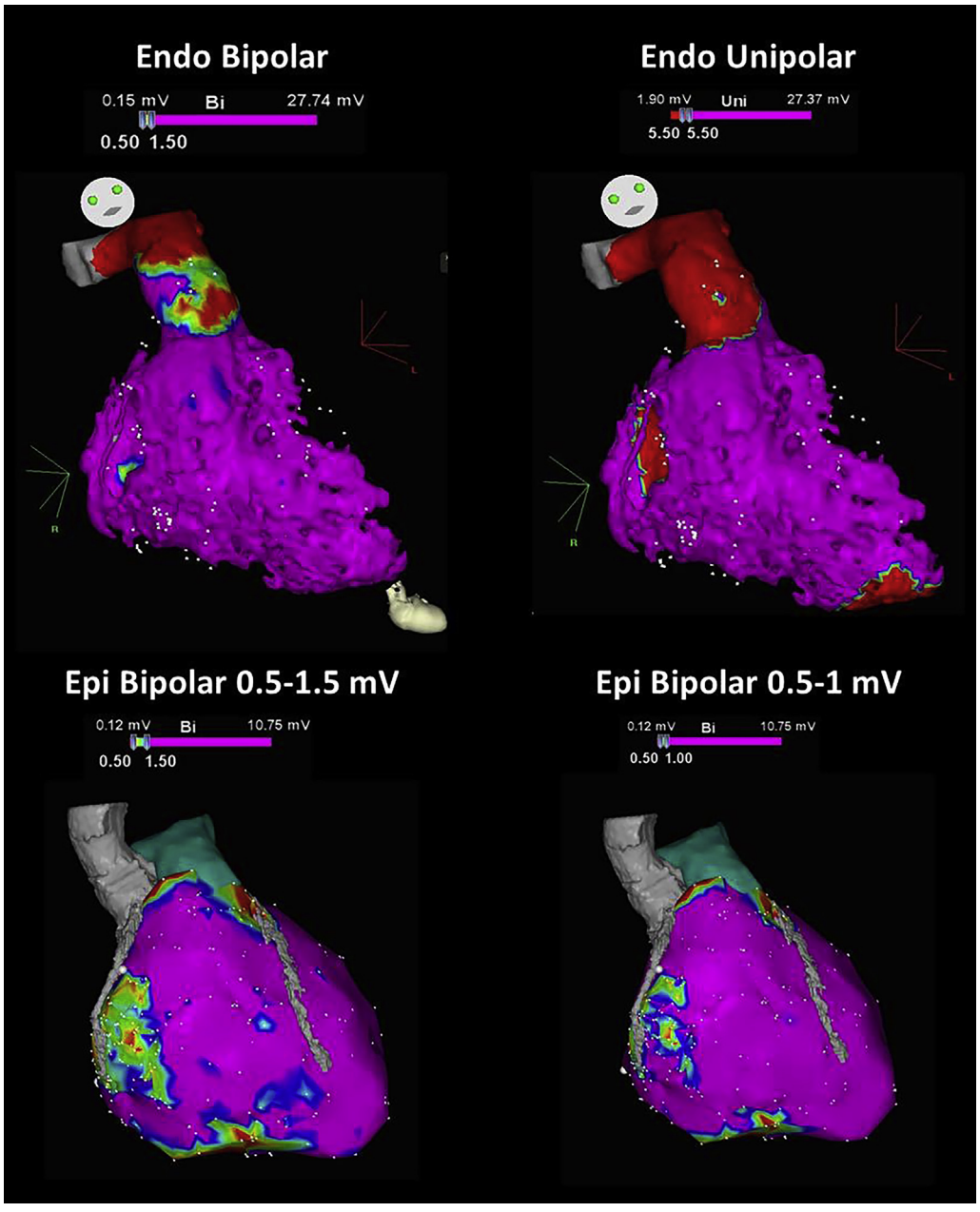

Figure 3 Electroanatomical mapping. **Above:** Endocardial (Endo) voltage mapping shows discrete unipolar low-voltage areas (red indicates <0.5 mV bipolar and <5.5 mV unipolar) in the subtricuspidal lateral and apical regions. **Below:** Epicardial (Epi) voltage mapping shows bipolar electroanatomical border zone (amplitude 0.5–1.5 mV on the left and 0.5–1.0 mV on the right) in the lateral wall below the tricuspid annulus.

already been reported[8,9] and could have explained the T-wave inversions in inferior and precordial leads in the present case. In fact, only 18% of all patients with ARVC and LV involvement (as seen in MRI) show reduced LVEF.[10]

Back to our case, successful PVC ablation led to recovery of RV function and the diagnosis of ARVC could be ruled out after morphologic and electrical normalization of the pathologic findings, suggesting that frequent PVCs had induced an ARVC pattern in our patient. It should be noted that frequent PVCs induced an isolated RV dysfunction in this case. No LV function or size abnormalities were observed throughout the entire follow-up period. To our knowledge, this condition has not been previously described in literature. Although we cannot provide a definitive explanation of isolated RV dysfunction, it remains possible that the specific PVC origin (subtricuspid region of RV free wall) could have contributed to the worsening of RV function by inducing mechanical and electrical dyssynchrony of the RV.

We should bear in mind that overdiagnosis of ARVC may have considerable consequences in terms of further disease management, such as indication for implantable cardioverter-defibrillator therapy. Thus, our patient with 4 minor criteria (RV dilatation, young age, T-wave inversion

in inferior and precordial leads, fragmented QRS) had a class IIb implantable cardioverter-defibrillator indication.[11]

A substantial number of previously described ARVC mimics (categorized as cardiac displacement, RV overload conditions, and myocardial scarring) should be ruled out before ARVC is definitively established. The role of cardiac MRI in the recognition of ARVC mimics with a structural basis has been elucidated by previous investigators.[12–14] However, the imaging techniques were not useful in our case to provide an alternative diagnosis to ARVC. It was the normalization of structural, functional, and electrocardiographic parameters after PVC ablation that enabled the diagnosis of PVC-induced RV cardiomyopathy mimicking ARVC.

Some authors have reported the importance of additional information derived from electroanatomical mapping.[15,16] In our patient, only discrete low-voltage areas were detected by unipolar mapping in the subtricuspid region of the RV free wall. Epicardial mapping was also performed, and the bipolar electrograms showed discrete low-voltage areas but without characteristics suggesting scarring (ie, delayed components). Despite the absence of abnormal electrograms that would contribute to ARVC diagnosis, the patient received close follow-up after the ablation procedure.

Conclusion

The present case shows a new clinical entity, isolated RV cardiomyopathy induced by frequent PVCs that mimics ARVC. Successful PVC ablation resulted in complete normalization of electrocardiographic and echocardiographic parameters, suggesting that pure PVC-induced RV cardiomyopathy should be considered before establishing the final diagnosis of ARVC based only on TFC. It remains possible that the PVC site of origin could have played a role in this entity by inducing a considerable mechanical and electrical dyssynchrony of the RV.

References

1. Yarlagadda RK, Iwai S, Stein KM, Markowitz SM, Shah BK, Cheung JW, Tan V, Lerman BB, Mittal S. Reversal of cardiomyopathy in patients with repetitive monomorphic ventricular ectopy originating from the right ventricular outflow tract. Circulation 2005;112:1092–1097.
2. Penela D, Van Huls Van Taxis C, Aguinaga L, et al. Neurohormonal, structural, and functional recovery pattern after premature ventricular complex ablation is independent of structural heart disease status in patients with depressed left ventricular ejection fraction: a prospective multicenter study. J Am Coll Cardiol 2013;62:1195–1202.
3. Zang M, Zhang T, Mao J, Zhou S, He B. Beneficial effects of catheter ablation of frequent premature ventricular complexes on left ventricular function. Heart 2014;100:787–793.
4. Marcus FI, McKenna WJ, Sherrill D, et al. Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the Task Force Criteria. Eur Heart J 2010;31(7):806–814.
5. Liu T, Pursnani A, Sharma UC, et al. Effect of the 2010 task force criteria on reclassification of cardiovascular magnetic resonance criteria for arrhythmogenic right ventricular cardiomyopathy. J Cardiovasc Magn Reson 2014;16–47.
6. Vermes E, Strohm O, Otmani A, Childs H, Duff H, Friedrich MG. Impact of the revision of arrhythmogenic right ventricular cardiomyopathy/dysplasia task force criteria on its prevalence by CMR criteria. JACC Cardiovasc Imaging 2011; 4:282–287.
7. Groeneweg JA, Bhonsale A, James CA, et al. Clinical presentation, long-term follow-up, and outcomes of 1001 arrhythmogenic right ventricular dysplasia/cardiomyopathy patients and family members. Circ Cardiovasc Genet 2015; 8:437–446.
8. Norman M, Simpson M, Mogensen J, Shaw A, Hughes S, Syrris P, Sen-Chowdhry S, Rowland E, Crosby A, McKenna WJ. Novel mutation in desmoplakin causes arrhythmogenic left ventricular cardiomyopathy. Circulation 2005; 112:636–642.
9. Sen-Chowdhry S, Syrris P, Prasad SK, Hughes SE, Merrifield R, Ward D, Pennell DJ, McKenna WJ. Left-dominant arrhythmogenic cardiomyopathy: an under-recognized clinical entity. Am Coll Cardiol 2008;52:2175–2187.
10. Sen-Chowdhry S, Syrris P, Ward D, Asimaki A, Sevdalis E, McKenna WJ. Clinical and genetic characterization of families with arrhythmogenic right ventricular dysplasia/cardiomyopathy provides novel insights into patterns of disease expression. Circulation 2007;115:1710–1720.
11. Corrado D, Wichter T, Link MS, et al. Treatment of arrhythmogenic right ventricular cardiomyopathy/dysplasia: an international task force consensus statement. Eur Heart J 2015;36:3227–3237.
12. Quarta G, Husain SI, Flett AS, Sado DM, Chao CY, Tomé Esteban MT, McKenna WJ, Pantazis A, Moon JC. Arrhythmogenic right ventricular cardiomyopathy mimics: role of cardiovascular magnetic resonance. J Cardiovasc Magn Reson 2013;11:15–16.
13. Macias C, Nakamura K, Tung R, Boyle NG, Kalyanam S, Bradfield JS. Importance of delayed enhanced cardiac MRI in idiopathic RVOT-VT: differentiating mimics including early stage ARVC and cardiac sarcoidosis. J Atr Fibrillation 2014;7:1097.
14. Rastegar N, Burt JR, Corona-Villalobos CP, Te Riele AS, James CA, Murray B, Calkins H, Tandri H, Bluemke DA, Zimmerman SL, Kamel IR. Cardiac MR findings and potential diagnostic pitfalls in patients evaluated for arrhythmogenic right ventricular cardiomyopathy. Radiographics 2014;34:1553–1570.
15. Corrado D, Basso C, Leoni L, et al. Three-dimensional electroanatomic voltage mapping increases accuracy of diagnosing arrhythmogenic right ventricular cardiomyopathy/dysplasia. Circulation 2005;111:3042–3050.
16. Pieroni M, Dello Russo A, Marzo F, Pelargonio G, Casella M, Bellocci F, Crea F. High prevalence of myocarditis mimicking arrhythmogenic right ventricular cardiomyopathy differential diagnosis by electroanatomic mapping-guided endomyocardial biopsy. J Am Coll Cardiol 2009;53:681–689.