A case report of arrhythmogenic ventricular cardiomyopathy presenting with sustained ventricular tachycardia arising from the right and the left ventricles before structural changes are documented

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Background Arrhythmogenic ventricular cardiomyopathy (AC) is a genetic progressive disease characterized by fibro-fatty replacement of either ventricles in isolation or in combination. Arrhythmogenic ventricular cardiomyopathy is frequently associated with ventricular tachycardia (VT) having a left bundle branch block (LBBB) morphology and much more rarely with VT having right bundle branch block (RBBB) morphology even when the left ventricle is involved. Cardiac magnetic resonance (CMR) imaging plays a key role in the diagnosis of AC. Sustained VT in AC may occur in the concealed stage of the disease before the manifestation of morphological abnormalities on echocardiogram; however, they almost always are accompanied by structural abnormalities of the ventricles on CMR.

Case summary A 54-year-old man presented with sustained VT of LBBB configuration consistent with the diagnosis of AC but with no right ventricular (RV) anomalies at repeat CMR. Ten years later, he developed sustained VT with RBBB morphology and structural changes at CMR compatible with RV involvement in the setting of AC. Two years later, he suffered from recurrent identical sustained RBBB-VT with typical CMR signs of left ventricular involvement. Genetic analysis was negative for any known mutation.

Discussion In the present report, we describe a patient with AC who first exhibited LBBB- and 10 years later RBBB-sustained VT. Contrasting with what is usually observed in patients with AC, documentations of the VT’s arising from either ventricle were found to precede the structural anomalies in the respective cardiac chambers. This case highlights that normal CMR does not exclude underlying AC contrary to the perceptions of many clinicians. In addition, it strongly encourages repeating CMR after 1–2 years when the diagnosis of AC is highly suspected.

Keywords Case report • Arrhythmogenic ventricular cardiomyopathy • Ventricular tachycardia • Cardiac magnetic resonance imaging • Cardiac ablation
Learning points

- Sustained ventricular tachycardia arising from the right and the left ventricles can be rarely observed in the same patient during the course of arrhythmogenic ventricular cardiomyopathy (AC).
- These tachycardias may occur before structural abnormalities of the ventricles are detected by cardiac magnetic resonance (CMR).
- When the diagnosis of AC is highly suspected but CMR is normal, repeating CMR after 1–2 years should be encouraged.

Introduction

Arrhythmogenic ventricular cardiomyopathy (AC) is a genetic, progressive disease characterized by fibro-fatty replacement of either ventricles in isolation or in combination.\(^1\,2\) Classically, it predominantly affects the right ventricle with frequent involvement of the left ventricle (LV).\(^1\,2\) Recent evidence now suggests the left-sided involvement is more common than previously thought, with isolated right ventricular (RV) involvement and evidence of left-sided disease present in 13% and 87% of AC-related deaths, respectively.\(^3\)

Arrhythmogenic ventricular cardiomyopathy is associated with a high risk of sustained monomorphic ventricular tachycardia (VT)\(^1\,2\) mainly with a left bundle branch (LBBB) morphology, suggesting an RV origin; in contrast, VT having a right bundle branch block (RBBB) morphology and suggesting a left ventricular origin, is rarely observed even in patients with left dominant AC.\(^4\)

Because of the anatomical, functional, and tissue-specific characteristics of AC, cardiac magnetic resonance (CMR) imaging plays a key role in the diagnosis work-up of AC.\(^4\,7\)

Sustained VT in AC may occur in the concealed stage of the disease before the manifestation of morphological abnormalities on echocardiogram; however, they almost always are accompanied by structural abnormalities of the ventricles on CMR.\(^8\,9\)

In the present report, we describe a patient with AC who first exhibited LBBB-VT and 10 years later RBBB-VT. Documentations of the VT’s arising from either ventricle were found to precede the CMR-detected structural anomalies in the respective cardiac chambers.

Timeline

| Age 54 | Presented with a left bundle branch block (LBBB)-ventricular tachycardia (VT), treated with beta-blockers |
| Age 56 | Presented with an LBBB-VT, cardiac magnetic resonance (CMR) was normal |
| Age 57 | Ablated for LBBB-VT, treated with beta-blockers and sotalol |
| Age 64 | Presented with a right bundle branch block (RBBB)-VT, CMR diagnostic for arrhythmogenic right ventricular dysplasia (ARVD) |
| Age 66 | Presented with an RBBB-VT, CMR diagnostic for ARVD + arrhythmogenic left ventricular dysplasia (ALVD) |

Case presentation

Our patient was a previously asymptomatic, apparently healthy 54-year-old man with no familial history of arrhythmias or heart disease or risk factors for coronary artery disease. He experienced several episodes of mild dizziness related to non-sustained, rapid (260/min) LBBB-VT that were unrelated to exercise (March 2007). Resting electrocardiogram (ECG), echocardiogram, coronary angiography, and CMR (June 2007) were normal. He was started with beta-blocker therapy and 2 years later (June 2009) underwent an exercise test without medication. During the test, he exhibited sustained VT (220/min) similar in morphology to that documented 2 years earlier (Figure 1). The VT morphology (LBBB + left QRS axis) was uncommon for idiopathic VT and raised a possible diagnosis of AC by 2010 Task Force Criteria (TFC). However, the ECG in sinus rhythm did not show any repolarization changes suggestive of arrhythmogenic right ventricular cardiomyopathy (ARVC), including epsilon sign or T-wave inversions in the right precordial leads.

In addition, repeat CMR performed at another centre (December 2009) yielded normal results. The patient continued to suffer from short episodes of palpitations on beta-blocker therapy and thus was recommended to undergo an electrophysiologic study (EPS) (March 2010). Normal AH and HV intervals were recorded. Sustained VT (190/min) identical in morphology to the clinical LBBB-VT was reproducibly induced with rapid RV pacing during isoproterenol infusion.

Ventricular tachycardia was well tolerated and could be mapped using standard mapping techniques. A very early endocardial activation was observed at the right ventricle close to the infero-lateral area of the tricuspid annulus (~49 ms). Ventricular tachycardia terminated at first application of radiofrequency pulse. An obvious late potential was found at areas close to the VT termination site. Radiofrequency pulses were applied at the same location of VT termination. No VT was inducible thereafter. Based on the clinical, ECG and EPS findings, the diagnosis of AC was highly suspected despite the lack of structural anomalies recognized on CMR. During the following 7 years (2010–2017), the patient was treated with sotalol due to a high degree of symptomatic multifocal ventricular activity. Fortunately, yearly exercise testing never exhibited VT.

On March 2017, at the age of 64 years, the patient was admitted for another episode of sustained VT (220/min), presumably attributed to discontinuation of sotalol treatment by the patient himself due to some bradycardia. The VT morphology (RBBB with a left QRS axis) (Figure 2) was different from that recorded in the past and suggested an arrhythmia arising from the LV. The arrhythmia was treated with electrical cardioversion. Echocardiogram and CMR disclosed for...
the first-time akinesia/dyskinesia of the RV basal free wall accompanying RV dilatation consistent with the definite diagnosis of AC according to the 2010 TFC (Figure 3); however, no obvious anomaly was found in the LV. Sotalol therapy was reinitiated. Genetic analysis (Comprehensive Genetic Arrhythmia Program at the University of San Francisco) included sequence analysis and deletion/duplication testing of 114 genes. No pathogenic sequence variants or deletions/duplications were identified.

Two years later (May 2019), while on sotalol, the patient had a pre-syncopal episode followed by palpitations with documented sustained VT (178/min) displaying a morphology of RBBB and left axis deviation identical to that recorded 2 years earlier. The arrhythmia was treated with electrical cardioversion. Electrocardiogram during sinus rhythm showed sinus bradycardia (54/min), low-voltage, narrow QRS complexes, suspected epsilon wave, normal PR and QT intervals with negative T waves in leads III and aVF.

Repeat CMR confirmed the morphological changes consistent with ARVC found earlier. Late gadolininium enhancement associated with segmental wall abnormalities were also observed for the first time in the lateral wall of the LV (Figure 4). Ablation of the RBBB-VT
could not be performed due to its non-inducibility with both RV and left ventricular stimulation; noteworthy was the lack of low-voltage area during mapping of the left ventricular endocardium and epicardium. However, sustained VT with an LBBB morphology (similar to that previously ablated) was again induced and consequently successfully ablated using a combined endo-epicardial approach. The patient received an implantable cardioverter-defibrillator.

Discussion

The present case demonstrates two unique findings in the setting of AC: (i) the occurrence of episodes of monomorphic VT arising from both ventricles, separately presenting a decade apart and (ii) the sustained VT arising from each ventricle pre-dated any structural manifestations suggestive of AC.

**Left bundle branch block and right bundle branch block-ventricular tachycardia**

Occurrence of both LBBB and RBBB-VT during the clinical course of a patient with AC is rare. A review of case reports comprising 14 patients with AVC who exhibited RBBB-VT (Table 1) revealed that only two of them also had spontaneous documentation of LBBB-VT.\(^{10,11}\) The most remarkable case was reported by Adams et al.\(^{11}\) from Belfast in a 7-year-old girl who exhibited in April 1961 her first episode of sustained VT (240/min) with RBBB morphology and inferior axis. During the following 10 years, she experienced 15 VT episodes.

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**Figure 3** Cardiac magnetic resonance (March 2017). Left panel: four-chamber view showing late gadolinium enhancement of the basal lateral right ventricular wall (arrow); right panel: short-axis view of the left ventricle showing no chamber involvement (no late enhancement).

**Figure 4** Cardiac magnetic resonance (May 2019). Left panel: four-chamber view showing the same right ventricular involvement as in Figure 3 (arrow); right panel: short-axis view showing late gadolinium enhancement in a non-ischaemic pattern involving the mid infero-lateral wall of the left ventricle (arrow).
Table 1  Prevalence of LBBB-VT among case reports of documented RBBB-VT in the setting of AC. AC, arrhythmogenic cardiomyopathy; CMR, cardiac magnetic resonance; CT, computer tomography; EPS, electrophysiologic study; F, female; LBBB, left bundle branch block; LV, left ventricle; M, male; N, no; NA, not available; NSVT, nonsustained ventricular tachycardia; PM, post-mortem examination; RBBB, right bundle branch block; RV, right ventricle; VT, sustained ventricular tachycardia; Y, yes.

| First author                      | Year publication | Gender | Age at first VT | LBBB-VT (Y/N) (spontaneous/EPS) | RBBB-VT (Y/N) (spontaneous/EPS) | First VT (spontaneous/EPS) | RV involvement (Y/N) | LV involvement (Y/N) |
|-----------------------------------|------------------|--------|-----------------|----------------------------------|----------------------------------|---------------------------|---------------------|---------------------|
| Webb et al.¹⁰                     | 1986             | F      | 47              | Y (spontaneous + EPS)            | Y (spontaneous + EPS)            | NA                        | Y ?!                | Y (angi)            |
| Martini et al.¹⁴                  | 1988             | M      | 23              | Y (EPS)                          | Y/spontaneous                    | RBBB                      | Y (angi)            | Y (angi)            |
| Sen-Chowdhry et al.⁴              | 2008             | F      | 81              | N                                | Y/spontaneous                    | RBBB                      | N                   | Y (PM)              |
| Ine et al.¹ⁱ                      | 2010             | F      | 67              | Y (EPS)                          | Y (EPS)                          | NA                        | Y (angi + biopsy)   | Y (angi + CT)       |
| Navarro-Manchon et al.¹⁶          | 2011             | M      | 37              | N                                | Y (spontaneous)                  | RBBB                      | Y (CMR)             | Y (CMR)             |
| Hsiao et al.¹⁷                    | 2012             | M      | 57              | N                                | Y (spontaneous)                  | RBBB                      | Y (CMR)             | Y (CMR)             |
| te Riele et al.¹⁸                 | 2013             | F      | 44              | N                                | Y (spontaneous)                  | RBBB                      | Y (CMR)             | NA                  |
| Groeneweg et al.¹⁹                | 2013             | F      | 51              | Y (EPS) (NSVT)                   | Y (spontaneous + EPS)            | RBBB                      | Y (angi)            | Y (angi)            |
| Havranek et al.²⁰                 | 2015             | M      | 35              | Y (EPS)                          | Y (spontaneous + EPS)            | RBBB                      | Y (angi)            | Y (angi)            |
| Chakraborty et al.²¹              | 2016             | M      | 40              | No                               | Y (spontaneous)                  | RBBB                      | Y (biopsy)          | Y (CMR)             |
| Guglielmi et al.²²                | 2016             | M      | 56              | N                                | Y (spontaneous)                  | RBBB                      | N                   | Y (CMR)             |
| Rabey et al.²³                    | 2016             | M      | 68              | N                                | Y (spontaneous)                  | RBBB                      | N                   | Y (CMR)             |
| Barbosa-Barros et al.²⁴           | 2017             | M      | 52              | N                                | Y (spontaneous)                  | RBBB                      | N (CMR)             | Y (CMR)             |
| Adams et al.¹¹                    | 2019             | F      | 7               | Y (spontaneous)                  | Y (spontaneous)                  | RBBB                      | Y (CMR)             | N? (CMR)            |
episodes. After a 47-year arrhythmia-free period, she exhibited VT (220/min) with LBBB morphology and inferior axis. The diagnosis of severe AC was made by echocardiography and CMR. Interestingly, the RBBB-VT was not addressed by the authors. However, the LV was quoted as ‘undilated’ on CMR. Genetic testing was negative for pathogenic variants (P. Mckeeown, personal communication).

Abnormal cardiac magnetic resonance vs. ventricular tachycardia occurrence

Te Riele et al. demonstrated electrical abnormalities on ECG (pre-cordial T-wave inversion, epsilon waves) and Holter monitoring (high-grade ventricular ectopy) preceded detectable structural abnormalities in ARVC mutation carriers. However, sustained ventricular arrhythmias occurred exclusively in patients with both electrical abnormalities and abnormal CMR. The same group evaluated a large cohort of ARVC relatives and found that both abnormal electrical and structural substrates were present in all patients at the time of sustained ventricular arrhythmias.

In our present case, during documentation of the two episodes of LBBB-VT and the first episode of RBBB-VT, no echocardiographic or CMR anomalies were observed in the right ventricle and LV, respectively. Moreover, ECG changes occurred as the latest manifestation. This case highlights that a normal CMR does not exclude underlying AC contrary to the perceptions of many clinicians. Re-evaluation with CMR 1–2 years later is strongly advised where the clinical suspicion for AC is very high.

Lead author biography

Prof. Bernard Belhassen graduated at University Paris VII (France) and completed his training in cardiac electrophysiology in Femand Widal Hospital (Paris) under the direction of Prof. Gilbert Motte. Between 1978 and 2015, he directed the cardiac electrophysiology laboratory at Tel Aviv Medical Center. In 1983–1984, he was visiting Professor at Hahnemann University, Philadelphia. He is presently working at the Heart Institute, Hadassah University Hospital, Jerusalem, and serving as Professor Emeritus at Tel Aviv University. He is the author of over 230 medical publications in leading journals including those on SABRUS with the outstanding cooperation of Drs Anat Milman, Yoav Michowitz, and all other co-authors.

Supplementary material

Supplementary material is available at European Heart Journal - Case Reports online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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