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Case Report

Concurrent Arrhythmogenic Right Ventricular Cardiomyopathy and Hypertrophic Cardiomyopathy: A Rare Phenotypic Overlap

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Abstract

Background: Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) and Hypertrophic Cardiomyopathy (HCM) are distinct inherited cardiac disorders that represent leading causes of sudden cardiac death, particularly in young adults. While both conditions display autosomal dominant inheritance patterns, they typically involve different genetic mutations and pathophysiological mechanisms. Case report: We present a rare case of a 45-year-old male with ventricular tachycardia who demonstrated concurrent phenotypic features of both ARVC and HCM on comprehensive cardiac evaluation. Electrocardiography showed epsilon waves characteristic of ARVC, while cardiac magnetic resonance imaging (CMR) revealed right ventricular dilatation consistent with ARVC alongside mid-ventricular hypertrophic obstructive cardiomyopathy (HOCM). This unusual phenotypic overlap highlights the importance of comprehensive multimodality cardiac imaging and raises intriguing questions about potential genetic and molecular intersections between these cardiomyopathies. Conclusion: This case highlights the importance of comprehensive multimodality cardiac imaging in identifying complex structural abnormalities and raises questions about potential genetic and molecular intersections between ARVC and HCM. Our case also adds to the extremely limited literature documenting the co-occurrence of these conditions and underscores the value of CMR in identifying complex structural cardiac abnormalities. Management of patients with this rare phenotypic overlap presents unique challenges, requiring careful consideration of risk stratification and medical therapy. Further research may provide valuable insights into the pathophysiology and optimal management strategies for patients with overlapping cardiomyopathic phenotypes.

Keywords

Arrhythmogenic Right Ventricular Cardiomyopathy, Hypertrophic Cardiomyopathy, Mid-ventricular Obstruction, Ventricular Tachycardia, Epsilon Wave, Cardiac Magnetic Resonance Imaging

1. Introduction

Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) and Hypertrophic Cardiomyopathy (HCM) represent distinct inherited cardiac disorders with characteristic genetic, pathophysiological, and phenotypic profiles. ARVC is characterized by progressive fibrofatty replacement of right ventricular myocardium, leading to electrical instability and right ventricular dysfunction [1]. In contrast, HCM is defined by unexplained left ventricular hypertrophy, myocardial disarray,

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and fibrosis, typically affecting the interventricular septum [2].

Both conditions pose significant risk for sudden cardiac death (SCD), particularly in young adults and athletes [3]. ARVC has an estimated prevalence of 1: 1000 to 1: 5000, with regional variations [4], while HCM affects approximately 1: 500 individuals in the general population [5]. Despite their distinction as separate disease entities, rare case reports have documented phenotypic overlap or concurrent presentation of these cardiomyopathies [6-8].

We present a unique case of a middle-aged male with a history of ventricular tachycardia who demonstrated concurrent phenotypic features of both ARVC and mid-ventricular HOCM on comprehensive cardiac evaluation, including electrocardiography and cardiac magnetic resonance imaging (CMR).

2. Case Presentation

A 45-year-old male with no significant past medical history presented to our cardiology department following an episode of palpitations, dizziness, and pre-syncope. There was no family history of sudden cardiac death or known cardiomyopathy. His physical examination was notable for an irregular pulse and a grade 3/6 mid-systolic murmur best heard at the left sternal border. Blood pressure was 128/78 mmHg with a heart rate of 92 beats per minute.

A 12-lead electrocardiogram (ECG) showed sinus rhythm with T-wave inversions in leads V1-V3 and the presence of an epsilon wave in lead V1, raising suspicion for ARVC (Figure 1). A 24-hour Holter monitor captured multiple episodes of non-sustained ventricular tachycardia.

Transthoracic echocardiography demonstrated right ventricular enlargement with regional wall motion abnormalities.

Cardiac magnetic resonance imaging (CMR) confirmed the presence of a dilated right ventricle (right ventricular end-diastolic volume index of 107 ml/m²) with reduced RVEF of 29% with multiple areas of dyskinesia and aneurysmal dilatation in the right ventricular free wall and outflow tract, consistent with ARVC. Strain analysis showed reduced systolic global circumferential strain of Left and right ventricle of -7.8% and 4% with reduced diastolic strain rates of 54% and 24% Additionally, CMR revealed asymmetric mid-ventricular septal hypertrophy with a maximum wall thickness of 30 mm confirming mid-ventricular HOCM (Figure 2). Late gadolinium enhancement (LGE) was present in both ventricles, with patchy enhancement in the right ventricular free wall and more diffuse enhancement in the hypertrophied mid-ventricular septum. The Extracellular volume (ECV) was moderately increased in left ventricle myocardium -34% and markedly increased in Right ventricle- 60% (Figure 3). Genetic assessment could not be done as the patient refused consent for the same.

The patient underwent electrophysiology study with inducible monomorphic ventricular tachycardia originating from the right ventricle. Given his risk profile for sudden cardiac death due to the dual pathology, he received an implantable cardioverter-defibrillator (ICD) and was started on beta-blocker therapy. First follow up visit after six weeks showed no arrhythmogenic activity on ECG.

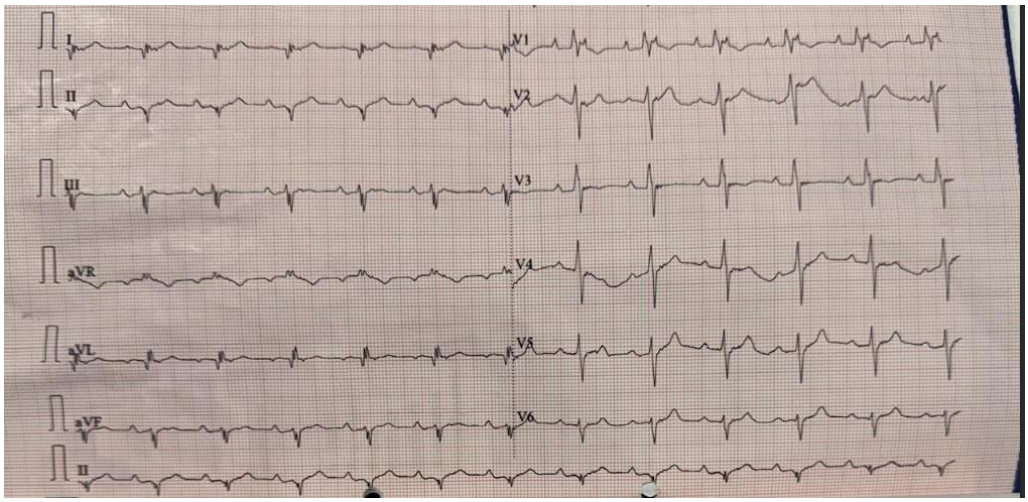

Figure 1. *Electrocardiogram showing presence of epsilon waves in I-III and aVL, avF leads.*

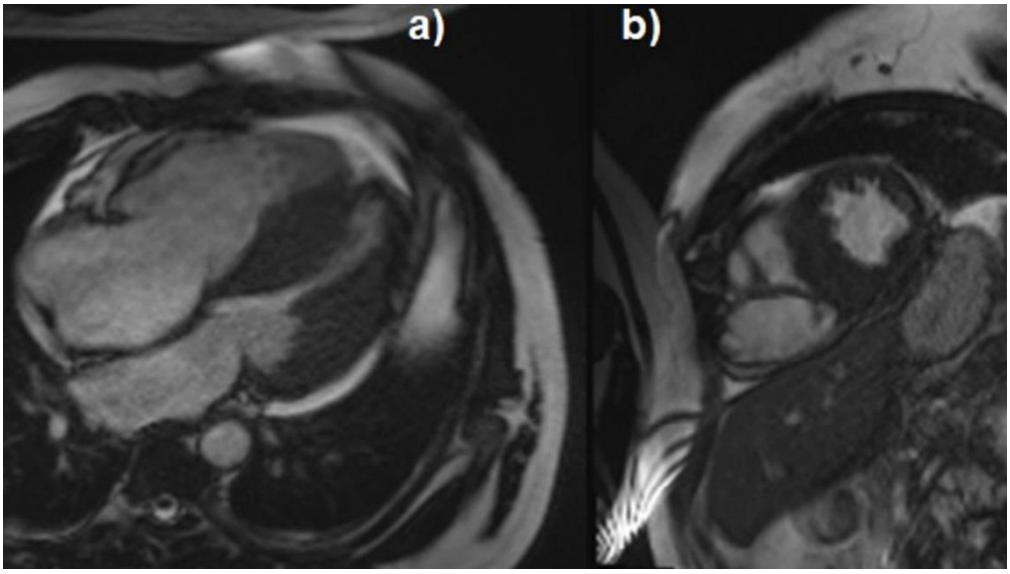

Figure 2. *a) Cine CMR 4 chamber view showing asymmetric mid left ventricle wall thickening with reduced cavity size along with dilated right ventricle b) Short axis view confirming the above findings with 29 mm end diastolic wall thickening of septum and posterior inferior walls with dilated hypokinetic right ventricle.*

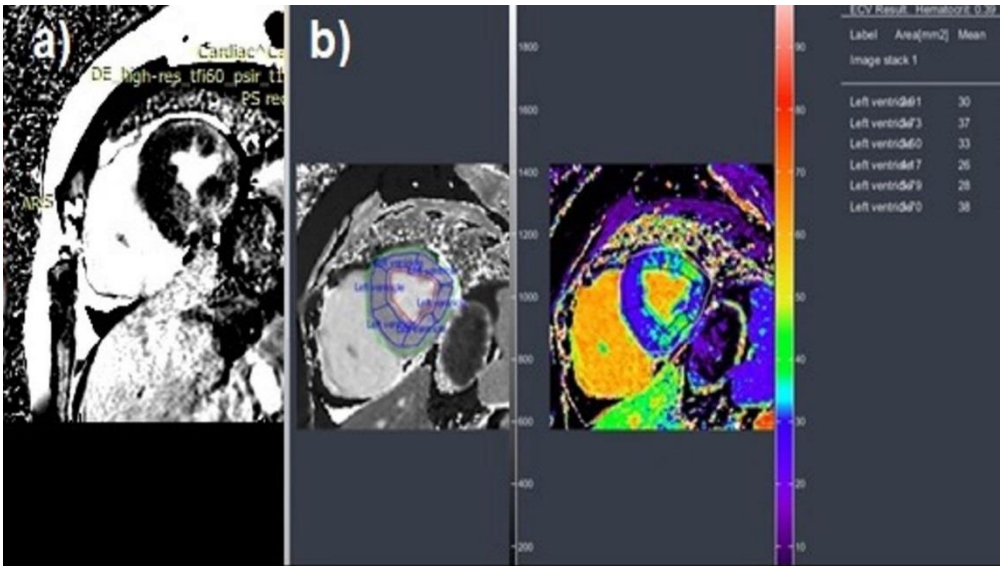

Figure 3. *a) Post contrast late enhancement phase short axis view showing intramural areas of. Late enhancement in the inferior septal, posterior and anterior walls in left ventricle. b) ECV analysis image showing increased ECV of left ventricle.*

3. Discussion

This case presents an extremely rare concurrent manifestation of two distinct inherited cardiomyopathies: ARVC and HCM. While both conditions share an autosomal dominant inheritance pattern, they typically involve mutations in different genes affecting different components of the cardiomyocyte [9].

ARVC predominantly involves mutations in genes encoding desmosomal proteins (PKP2, DSP, DSG2, DSC2, and JUP), which are crucial for cell-to-cell adhesion [10]. In contrast, HCM is primarily associated with mutations in sarcomeric protein genes, most commonly MYH7 and MYBPC3, which encode components of the cardiac contractile apparatus [11]. This genetic distinction typically results in separate and distinguishable cardiac phenotypes.

However, our case demonstrates that these conditions can coexist, creating a unique and potentially high-risk cardiac phenotype. The presence of an epsilon wave on ECG—a specific marker for ARVC—alongside mid-ventricular hypertrophy is particularly unusual. Mid-ventricular obstruction represents a relatively uncommon variant of HCM, occurring in approximately 10% of HCM cases [12]. The combination of right ventricular pathology from ARVC and mid-ventricular

obstruction from HCM creates a complex hemodynamic situation with potential for both right and left ventricular dysfunction.

Several potential explanations exist for this rare phenotypic overlap. First, it may represent the coincidental occurrence of two separate genetic cardiomyopathies in one individual. Second, it could result from a single genetic mutation with pleiotropic effects affecting both ventricular myocardium and intercellular junctions. Third, it might represent an advanced stage of either condition with secondary changes mimicking features of the other cardiomyopathy [13].

Recent research has identified potential molecular intersections between these cardiomyopathies. For instance, mutations in the desmosomal protein plakoglobin (JUP) have been associated with both ARVC and left ventricular hypertrophy in some cases [14]. Additionally, disruption of the Wnt/β-catenin signaling pathway has been implicated in both the fibrofatty replacement characteristic of ARVC and the myocyte hypertrophy seen in HCM [15].

The case described by Mashego and Nethononda [8] shares striking similarities with our patient, though in their case, a younger female presented during pregnancy with heart failure. Both cases highlight the importance of comprehensive multimodality cardiac imaging, particularly CMR, in identifying complex structural cardiac abnormalities that may not be fully appreciated on echocardiography alone.

CMR has emerged as the gold standard for non-invasive assessment of both ARVC and HCM, offering superior tissue characterization, precise quantification of ventricular volumes and function, and detection of myocardial fibrosis through LGE [16]. In our case, CMR was pivotal in establishing the dual diagnosis by demonstrating both the right ventricular abnormalities typical of ARVC and the asymmetric septal hypertrophy with obstruction characteristic of HCM.

Management of patients with this rare phenotypic overlap presents unique challenges. Both conditions carry an elevated risk of sudden cardiac death, with arrhythmogenic potential from both ventricles [17]. Risk stratification is complicated by the lack of specific guidelines for this dual pathology. In our case, the presence of non-sustained ventricular tachycardia, significant myocardial fibrosis on LGE imaging, and the concurrent presentation of two SCD-associated cardiomyopathies warranted ICD implantation for primary prevention.

Medical therapy similarly requires careful consideration. Beta-blockers represent first-line therapy for both conditions, addressing ventricular arrhythmias in ARVC and reducing outflow obstruction in HCM [18]. However, negative inotropic agents used for obstruction in HCM must be used cautiously in the setting of right ventricular dysfunction from ARVC.

4. Conclusion

Our case highlights an extremely rare phenotypic overlap of ARVC and mid-ventricular HOCM in a middle-aged male presenting with ventricular arrhythmias. This unusual combination of pathologies underscores the importance of comprehensive cardiac assessment, including CMR imaging, in patients with suspected cardiomyopathy. The coexistence of these conditions raises intriguing questions about potential genetic and molecular intersections between distinct cardiomyopathies. Further research, including genetic studies and long-term clinical follow-up of similar cases, may provide valuable insights into the complex pathophysiology and optimal management strategies for patients with overlapping cardiomyopathic phenotypes.

Abbreviations

ARVC	Arrhythmogenic Right Ventricular Cardiomyopathy
HCM	Hypertrophic Cardiomyopathy
SCD	Sudden Cardiac Death
LGE	Late Gadolinium Enhancement
CMR	Cardiac Magnetic Resonance
HOCM	Hypertrophic Obstructive Cardiomyopathy
ECV	Extracellular Volume

Conflicts of Interest

The authors declare no conflicts of interest.

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