Rethink personalised sudden cardiac death risk assessment in non-dilated left ventricular cardiomyopathy: a case report

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This article was published on 14 Apr 2025 at www.hkmj.org.

This version may differ from the print version.

Hong Kong Med J 2025;31:Epub
https://doi.org/10.12809/hkmj2412128

Case presentation

A 56-year-old man was presented to the emergency department of our institution in June 2023 and has had been followed up in our medical clinic for 1 year prior to his current hospital admission. He had been diagnosed with frequent symptomatic premature ventricular complexes with an ectopic burden of 8.2% on extended ambulatory rhythm monitoring. There were also multiple recorded episodes of non-sustained ventricular tachycardia. Beta-blocker was initiated and uptitrated according to clinical symptoms. His family history was remarkable for the sudden cardiac death of his father at the age of 64 years. Subsequent transthoracic echocardiogram of the patient revealed a global hypokinetic left ventricle with a biplane-measured left ventricular ejection fraction (LVEF) of 45%. There was mild left atrial enlargement with a two-dimensional area of 25.7 cm^2 but no other structural abnormalities. Computed tomography coronary angiogram showed mild to moderate coronary artery disease in three vessels and guideline-directed medical treatment was initiated. Cardiac magnetic resonance imaging (CMR) was scheduled to assess cardiac structures and function, as well as tissue characterisation for features of non-ischaemic cardiomyopathy. He had been scheduled to undergo catheter ablation for frequent symptomatic premature ventricular complexes.

The patient presented to our emergency department with out-of-hospital cardiac arrest. He had been found collapsed adjacent to a swimming pool and a bystander had initiated cardiopulmonary resuscitation. Spontaneous circulation was restored shortly after a single defibrillation delivered by an automated external defibrillator and he was transferred to our hospital immediately. On arrival at the emergency department, he was hemodynamically stable with a Glasgow Coma Scale score of 15. High-sensitive troponin I level was elevated at 44.9 ng/L. Electrocardiogram showed sinus rhythm of 71 beats/min with occasional premature ventricular complexes. There was no ST-segment elevation or significant conduction abnormalities. Bedside echocardiogram showed a similar biplane-measured LVEF of 43% with global hypokinesia. Urgent coronary angiogram showed non-occlusive moderate to severe coronary artery disease in three vessels. Given his current presentation, together with angiographic progression in coronary artery disease, complete revascularisation was performed uneventfully. He was then transferred to our cardiac care unit postoperatively for close monitoring. Inpatient CMR revealed a non-dilated left ventricle with mildly reduced LVEF of 43% with global hypokinesia. There was multifocal patchy mid-wall and subepicardial late gadolinium enhancement (LGE) at the mid-ventricular anterior, anteroseptal and anterolateral walls, as well as basal to mid-ventricular inferior and inferolateral walls (Fig 1). There was no evidence of myocardial infarct. Parametric mapping showed a mild increase in myocardial T1 with values up to 1067 ms to 1080 ms (native T1 values in healthy subjects obtained in our Aera 1.5T magnetic resonance imaging scanner [Siemens, Munich, Germany] is 996±26 ms for males), suggestive of mild diffuse interstitial fibrosis (Fig 2). Prior to hospital discharge, a transvenous implantable cardioverter defibrillator (ICD) was implanted for secondary prevention. Subsequent genetic testing identified a heterozygous pathogenic truncating variant NM_001458.5(FLNC):c.3279del p.(Gly1094Alafs*4) in the filamin-C gene. The final clinical diagnosis was sudden cardiac arrest secondary to filamin-C variant–associated cardiomyopathy in a patient with non-dilated left ventricular cardiomyopathy (NDLVC) and mid-range ejection fraction.

Discussion

The filamin-C gene encodes the filamin-C protein that plays essential roles in the sarcomere stability in cardiac muscles. Filamin-C variants have been increasingly recognised as an important cause

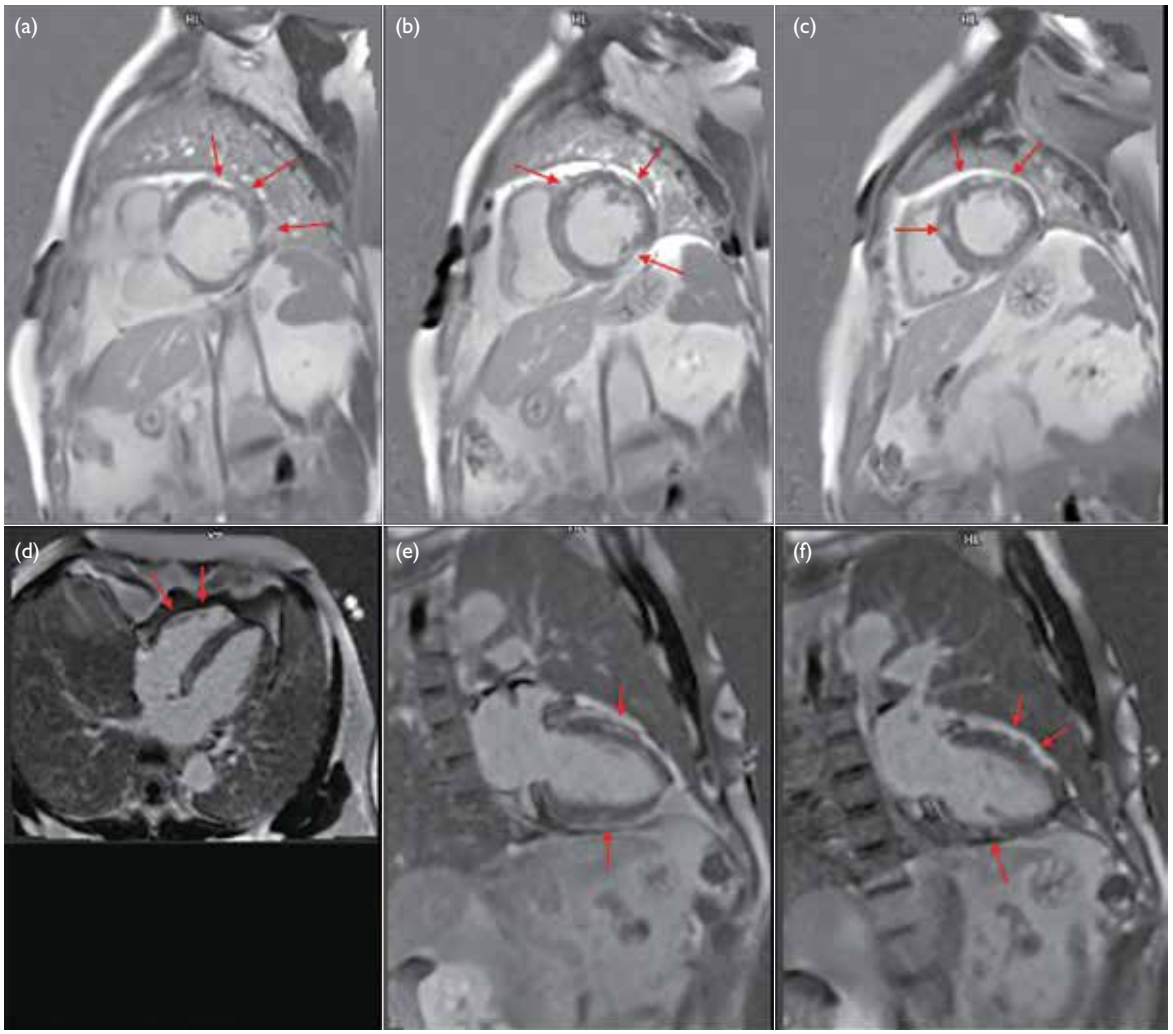

FIG 1. Multifocal patchy mid-wall and subepicardial late gadolinium enhancement at mid-ventricular anterior, anteroseptal and anterolateral walls, as well as basal to mid-ventricular inferior and inferolateral walls (arrows). (a-c) Short axis views of the left ventricle. (d) Apical four-chamber view of the left ventricle. (e, f) Apical two-chamber view of the left ventricle

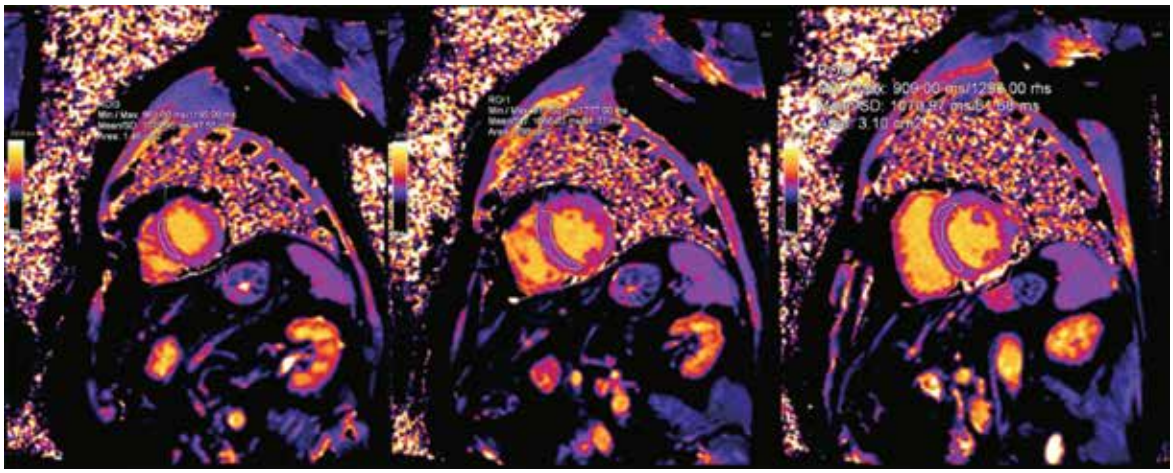

FIG 2. T1 mapping of the left ventricle. Parametric mapping shows mildly increased myocardial T1 values up to 1067 ms to 1080 ms, suggestive of mild diffuse interstitial fibrosis

of cardiomyopathy. It has been identified in approximately 3% to 4% of patients with dilated cardiomyopathy and commonly presents in early-to-mid adulthood with high arrhythmic risks.[1]

According to the 2021 European Society of Cardiology (ESC) Guidelines for the diagnosis and treatment of acute and chronic heart failure,[2] primary prevention ICD is indicated in patients with symptomatic heart failure with an LVEF ≤35% despite optimal medical treatment and a reasonable quality of life. Such recommendation is supported by numerous landmark trials including MADIT (Multicenter Automatic Defibrillator Implantation Trial),[3] DEFINITE (DEFibrillators In Non-Ischemic Cardiomyopathy Treatment Evaluation),[4] and SCD-HeFT (the Sudden Cardiac Death in Heart Failure Trial).[5] In addition, several additional clinical risk factors should also be considered in sudden cardiac death risk assessment, especially in patients with non-ischaemic cardiomyopathy.[2] These risk factors include significant LGE on CMR, younger age, and specific genotypes. Nonetheless these recommendations are ambiguous, and the guideline has not defined, for example, the burden of LGE and variant mechanisms in several high-risk genes that would warrant ICD implantation. Moreover, there are limited recommendations for primary prevention ICD in patients with heart failure with mid-range or preserved ejection fraction.

In the updated 2023 ESC Guidelines for the management of cardiomyopathies,[6] a new entity of NDLVC is introduced. An algorithm for consideration of primary prevention ICD similar to that for patients with dilated cardiomyopathy is recommended in this patient population. Patient genotype and imaging features on CMR have been proposed in the early sudden cardiac death risk assessment for patients with NDLVC. A previous study has demonstrated a higher rate of malignant arrhythmic events in patients who are genotype-positive, compared with their genotype-negative counterparts.[7] Such association has been observed irrespective of LVEF. Variants in certain genes including lamin A/C, phospholamban, filamin-C, RNA-binding motif protein 20, desmoplakin and plakophilin-2 are associated with a high risk of malignant ventricular arrhythmias and sudden cardiac death. Apart from genotype information, the presence and distribution of LGE on CMR, such as a ring-like pattern of LGE, has also been shown to be a strong risk marker for ventricular arrhythmias.[8] Hence, based on the current ESC Guidelines,[6] primary prevention ICD should be considered in patients with NDLVC and high-risk genotype and in the presence of additional risk factors such as syncope and LGE on CMR, irrespective of LVEF.

Our case highlights the need to incorporate a patient's genotype and imaging features on CMR into the personalised risk assessment for sudden cardiac death in patients with NDLVC. This will facilitate a more comprehensive and informative discussion about the indication for primary prevention ICD and improve the clinical outcome for patients with cardiomyopathy.

Author contributions

Concept or design: KWC Lun, DPH Lee.
Acquisition of data: All authors.
Analysis or interpretation of data: KWC Lun, DPH Lee.
Drafting of the manuscript: KWC Lun, DPH Lee.
Critical revision of the manuscript for important intellectual content: All authors.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

Funding/support

This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethics approval

The patient was treated in accordance with the Declaration of Helsinki. The patient provided consent for all treatments and procedures, and consent for publication of the case report.

References

1. Agarwal R, Paulo JA, Toepfer CN, et al. Filamin C cardiomyopathy variants cause protein and lysosome accumulation. Circ Res 2021;129:751-66.
2. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J 2021;42:3599-726.
3. Moss AJ, Zareba W, Hall WJ, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med 2002;346:877-83.
4. Kadish A, Dyer A, Daubert JP, et al. Prophylactic defibrillator implantation in patients with nonischemic dilated cardiomyopathy. N Engl J Med 2004;350:2151-8.
5. Bardy GH, Lee KL, Mark DB, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Engl J Med 2005;352:225-37.
6. Arbelo E, Protonotarios A, Gimeno JR, et al. 2023 ESC Guidelines for the management of cardiomyopathies. Eur Heart J 2023;44:3503-626.
7. Escobar-Lopez L, Ochoa JP, Mirelis JG, et al. Association of genetic variants with outcomes in patients with nonischemic dilated cardiomyopathy. J Am Coll Cardiol 2021;78:1682-99.
8. Meier C, Eisenblätter M, Gielen S. Myocardial late gadolinium enhancement (LGE) in cardiac magnetic resonance imaging (CMR)—an important risk marker for cardiac disease. J Cardiovasc Dev Dis 2024;11:40.

