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COMPETITION WINNER
Adult congenital heart disease

A case report of complex congenital heart disease co-existing with hypertrophic cardiomyopathy

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Background Myocardial abnormalities are sometimes overlooked in congenital heart disease (CHD). The co-existence of hypertrophic cardiomyopathy is so uncommon that it is assumed to be a coincidence rather than an association.

Case summary A 24-year-old gentleman, who was previously clinically well following a staged Fontan palliation for single-ventricle CHD, was transferred to our centre following an out-of-hospital cardiac arrest. He had return of spontaneous circulation after a period of cardiopulmonary resuscitation. Initial electrocardiogram showed sinus bradycardia. Computed tomography pulmonary angiography ruled out pulmonary embolism. Transthoracic echocardiography and cardiac magnetic resonance (CMR) demonstrated marked ventricular hypertrophy with no left ventricular outflow tract obstruction. Punctate areas of late gadolinium enhancement were noted in the basal septum, and T_1 values were consistent with fibrosis. Cardiac catheterization demonstrated low Fontan pressures and normal coronaries. Ventricular tachycardia rapidly degenerating into ventricular fibrillation was induced during electrophysiological studies. Genetic testing demonstrated a pathogenic cardiac myosin-binding protein C variant consistent with co-existent hypertrophic cardiomyopathy. Bisoprolol was initiated and a subcutaneous implantable cardiac defibrillator implanted 4 weeks after his initial presentation. Two years on, he remains well with no therapies from his defibrillator. As well as Fontan surveillance, cascade testing, exercise prescription, and pre-conception counselling were addressed during follow-up.

Discussion In CHD, ventricular hypertrophy may relate to congenital or acquired systemic outflow tract obstruction. Contemporary CMR techniques combined with genetic testing can be useful in differentiating between hypertrophy caused by congenital anomaly vs. concurrent cardiomyopathies. Multidisciplinary expertise is critical for accurate diagnosis and optimal care.

Keywords Congenital heart disease • Double-inlet left ventricle • Hypertrophic cardiomyopathy • Left ventricular hypertrophy • Fontan • Case report

ESC curriculum 6.5 Cardiomyopathy • 2.3 Cardiac magnetic resonance • 9.7 Adult congenital heart disease

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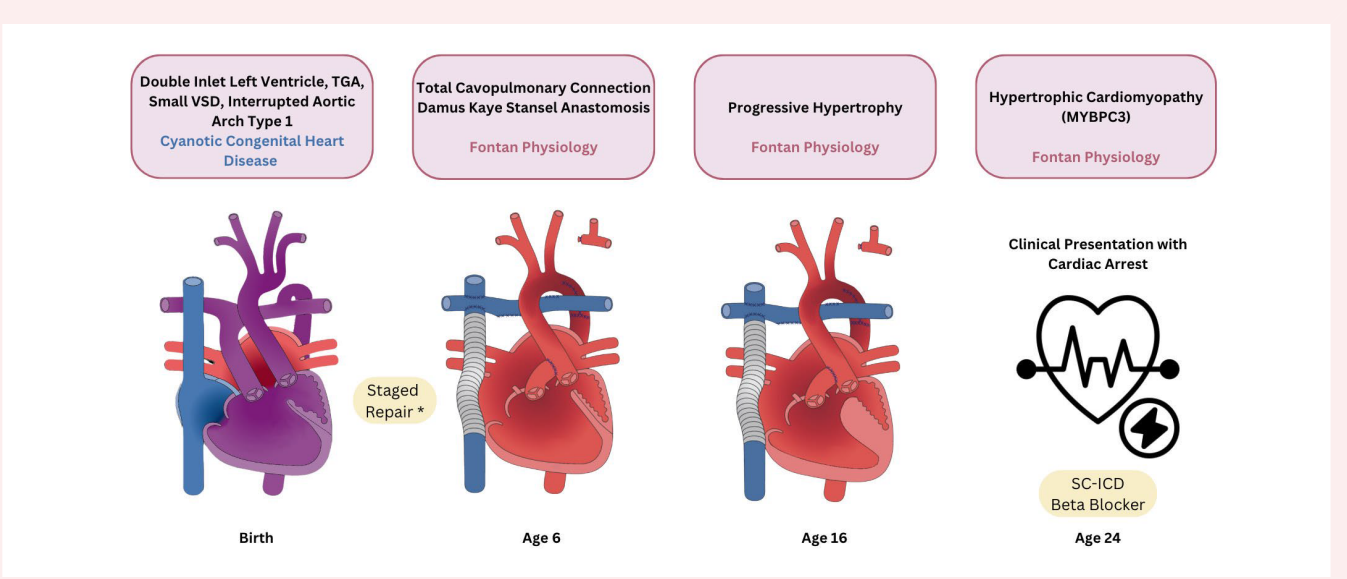
Learning points

- In patients with complex congenital heart disease (CHD), ventricular hypertrophy is often attributed to the haemodynamic consequences of the structural deformity or surgical repair. This may delay recognition of co-existent cardiomyopathies.
- It is important to suspect cardiomyopathies in CHD patients if the clinical picture and serial imaging do not fit with the expected description of the congenital anomaly.
- In complex cases where there is overlap between CHD and cardiomyopathy, management by a multidisciplinary team knowledgeable in multimodality imaging and genetic testing is crucial to secure the diagnosis and optimize patient care.

Introduction

Hypertrophic cardiomyopathy (HCM) is relatively common, with a prevalence of 1 in 500 adults.[1] Double-inlet left ventricle (DILV) is rare with an incidence of 0.05–0.1 per 1000 live births.[2] The co-existence of HCM and congenital cardiac malformations is so uncommon that it is thought to be co-incidental rather than an association.[3] We report a patient with a history of congenital heart disease (CHD) presenting with cardiac arrest and subsequently diagnosed with co-existent HCM.

Summary figure



Evolution in cardiac morphology and physiology from birth to clinical presentation with cardiac arrest. SC-ICD, subcutaneous implantable cardiac defibrillator; TGA, transposition of the great arteries; VSD, ventricular septal defect. *One week old: pulmonary artery band and arch repair; 10 months old: atrial septectomy, Damus–Kaye–Stansel anastomosis, and Glenn shunt; 6 years old: total cavopulmonary connection. Figure adapted from cardiac morphology images provided by http://www.chd-diagrams.com.

Case presentation

A 24-year-old gentleman with Fontan palliation for single-ventricle CHD (DILV, transposition of the great arteries, and interrupted aortic arch type A) was under clinical follow-up at our unit. During his annual cardiology outpatient reviews, he was clinically asymptomatic. He regularly exercised without restriction. On serial surveillance imaging, his Fontan pathways and Damus anastomosis were widely patent. There was no restriction to systemic outflow through the ventricular septal defect (VSD) noted at rest, and flow in the descending aorta was laminar. He had preserved ventricular function. He was, however, noted to have progressive asymmetric left ventricular hypertrophy (LVH) on serial transthoracic echocardiography since the age of 12 (*Table 1*). Cardiac magnetic resonance (CMR) was performed when he was 19 years old. This showed marked LVH with some focal regions of late gadolinium enhancement (LGE) in the septum of uncertain significance. Ejection fraction was 61%. The hypertrophy was felt to be unusual and other causes excluded including Fabry disease. Genetic testing was not performed at that point as it was felt it would unlikely alter management given the patient was asymptomatic.

Unfortunately, at the age of 24, he presented with an out-of-hospital cardiac arrest while jogging. Immediate bystander cardiopulmonary resuscitation (CPR) was performed. His estimated downtime was 22 min, and on paramedic arrival, he was found to be in pulseless electrical activity. Return of spontaneous circulation was achieved. He was intubated and transferred to critical care. Before the cardiac arrest, he had no prodromal symptoms and had cycled 15 km on the prior day without any limitations. Clinical examination revealed normal heart sounds and no signs of cardiac failure. A 12-lead electrocardiogram showed sinus bradycardia with voltage criteria for LVH, T-wave inversion, and Q-waves in inferior leads comparable with previous electrocardiograms (*Figure 1*). His high-sensitivity troponin I increased from 22 ng/L on admission (normal range 1–34) to 424 ng/L after 6 h in the context of CPR, but the troponin rise was not sustained after 12 h (246 ng/L) and 24 h (147 ng/L). Urgent computed tomography pulmonary angiography ruled out pulmonary embolism, which was considered in the context of the pro-thrombotic Fontan circulation.

Table 1 **Left ventricular wall measurements on serial transthoracic echocardiography including *Z*-scores**[4]

Age (years)	IVSd (cm)	*Z*-score	LVPWd (cm)	*Z*-score	LVIDd (cm)	*Z*-score
12	1.1	+2.26	1.1	+2.95	3.71	−1.55
13	1.0	+1.53	1.2	+3.08	3.80	−1.65
14	1.2	+2.01	1.4	+3.45	3.89	−2.05
16	2.6	+5.37	1.6	+3.84	3.67	−3.17
18	2.7	+5.33	1.6	+3.57	4.28	−2.18
19	2.7	+5.35	1.7	+3.90	4.30	−2.09
21	2.6	+5.05	1.7	+3.74	4.26	−2.53
22	2.8	+5.39	1.8	+4.03	4.24	−2.59
24	3.3	+6.33	1.9	+4.54	4.20	−2.20

IVSd, interventricular septum diameter at end-diastole; LVPWd, LV posterior wall diameter at end-diastole; LVIDd, LV end-diastolic diameter.

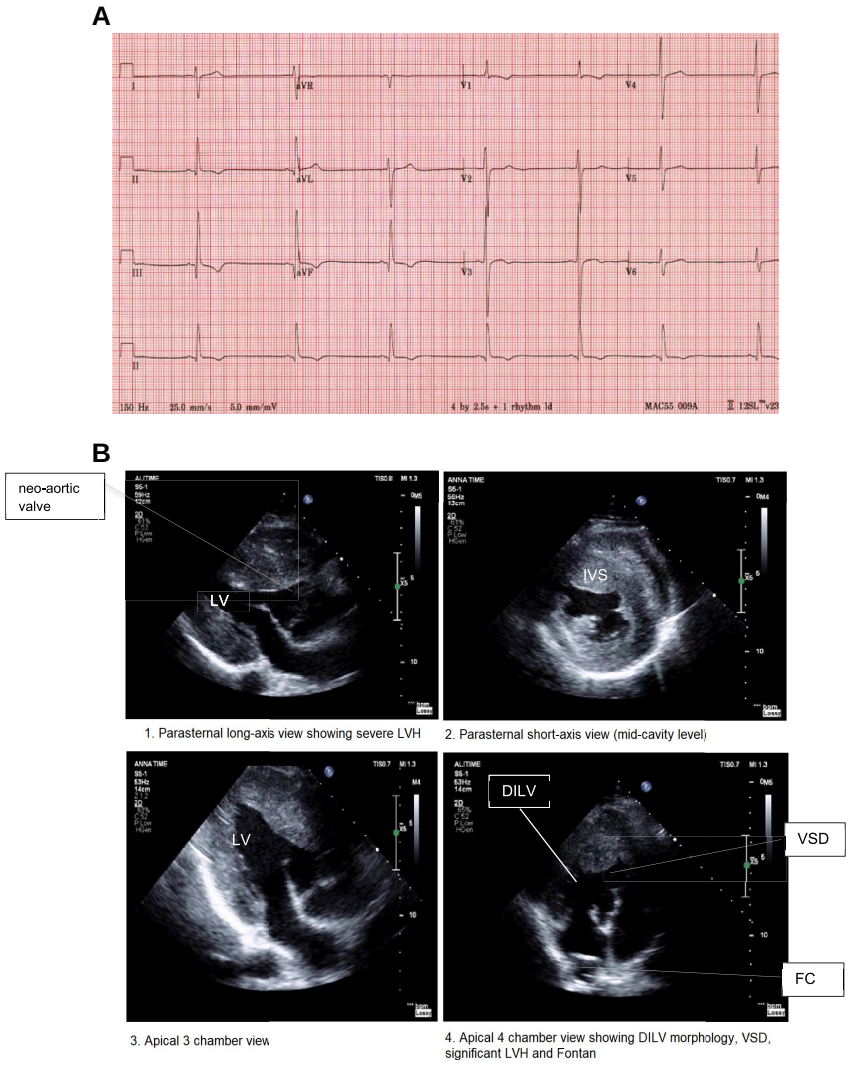


Figure 1 (*A*) Admission 12-lead electrocardiogram showing sinus bradycardia with voltage criteria for left ventricular hypertrophy, T-wave inversion, and Q-waves in inferior leads comparable with previous electrocardiograms. (*B*) Transthoracic echocardiogram demonstrating severe asymmetrical septal hypertrophy (interventricular septal diameter: 3.3 cm, left ventricular posterior wall diameter: 1.9 cm, interventricular septal diameter/posterior wall diameter ratio >1.5). There was also right ventricular hypertrophy (1.4 cm). DILV, double-inlet left ventricle; FC, Fontan circulation; IVS, interventricular septum; LV, left ventricle; LVH, left ventricular hypertrophy; VSD, ventricular septal defect.

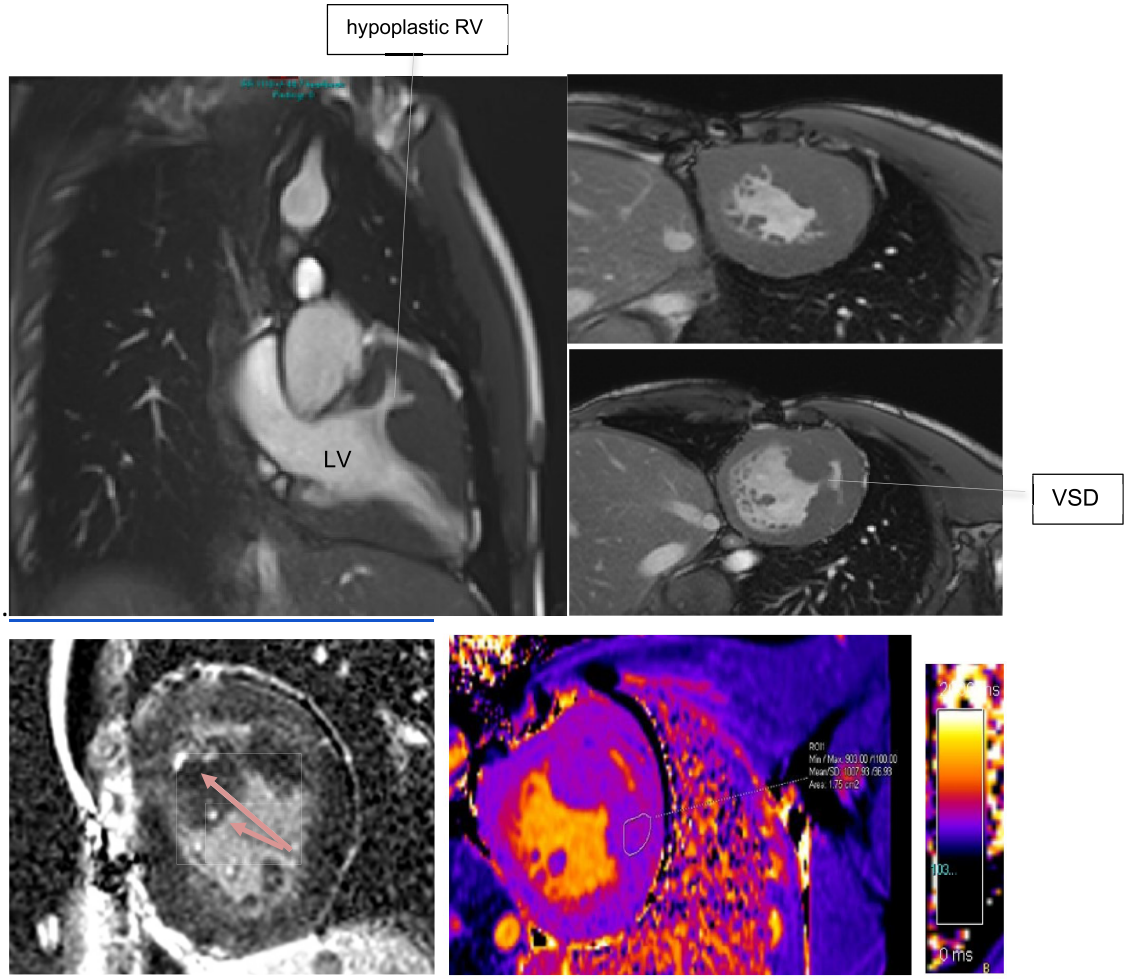


Figure 2 Cardiac magnetic resonance imaging images demonstrating asymmetric septal hypertrophy in the functional single left ventricle with sparing of the left ventricle apex. There were a few small focal areas of late gadolinium enhancement in the basal septum (denoted by arrows). Native T_1 values were 1000–1100 ms (reference range 0–2000 ms) in keeping with diffuse fibrosis rather than amyloid or Fabry's disease. LV, left ventricle; RV, right ventricle; VSD, ventricular septal defect.

Echocardiogram (*Figure 1*) showed severe ventricular hypertrophy. Left ventricular systolic function was borderline impaired with no outflow tract obstruction, and his Damus and Fontan pathways were patent. Cardiac catheterization demonstrated low Fontan pressure of 10 mmHg and unobstructed coronaries. Repeat CMR demonstrated marked ventricular hypertrophy with punctate areas of LGE in the basal septum, and T_1 values were consistent with fibrosis (*Figure 2*). In view of these findings, the patient was discussed at our cardiac genetics multidisciplinary team meeting. An extended gene panel was recommended, and a pathogenic variant (1504C>T) in exon 17 of *MYBPC3* encoding Arg502Trp was identified, confirming co-existent HCM.[1]

A primary arrhythmia cause was considered to be the most likely aetiology for his cardiac arrest. He subsequently underwent an electrophysiological study. Ventricular tachycardia was induced by incremental atrial pacing and rapidly degenerated into ventricular fibrillation requiring electrical cardioversion. No atrial arrhythmias were detected (*Figure 3*). Following discussion at the joint electrophysiology–CHD multidisciplinary team meeting, he was started on 2.5 mg of bisoprolol and a subcutaneous implantable cardiac defibrillator was implanted.

The patient was referred to a genetic counsellor to discuss the results and support cascade testing. His father, aged 58 years, was found to carry the same variant. His clinical phenotype is currently normal but is under surveillance for emergent cardiomyopathy (*Figure 4*). The patient also wished to start a family. Pre-implantation genetic testing was addressed as well as the emotional, psychological, and financial impact of a positive gene test.[5]

Two years on, the patient remains well on 2.5 mg of bisoprolol with no arrhythmia detections or therapies from his defibrillator. He has returned to moderate symptom-limited aerobic exercise. He remains under regular annual follow-up in the Fontan clinic.

Discussion

In complex CHD, ventricular hypertrophy can often be seen in association with congenital or acquired systemic outflow tract obstruction or

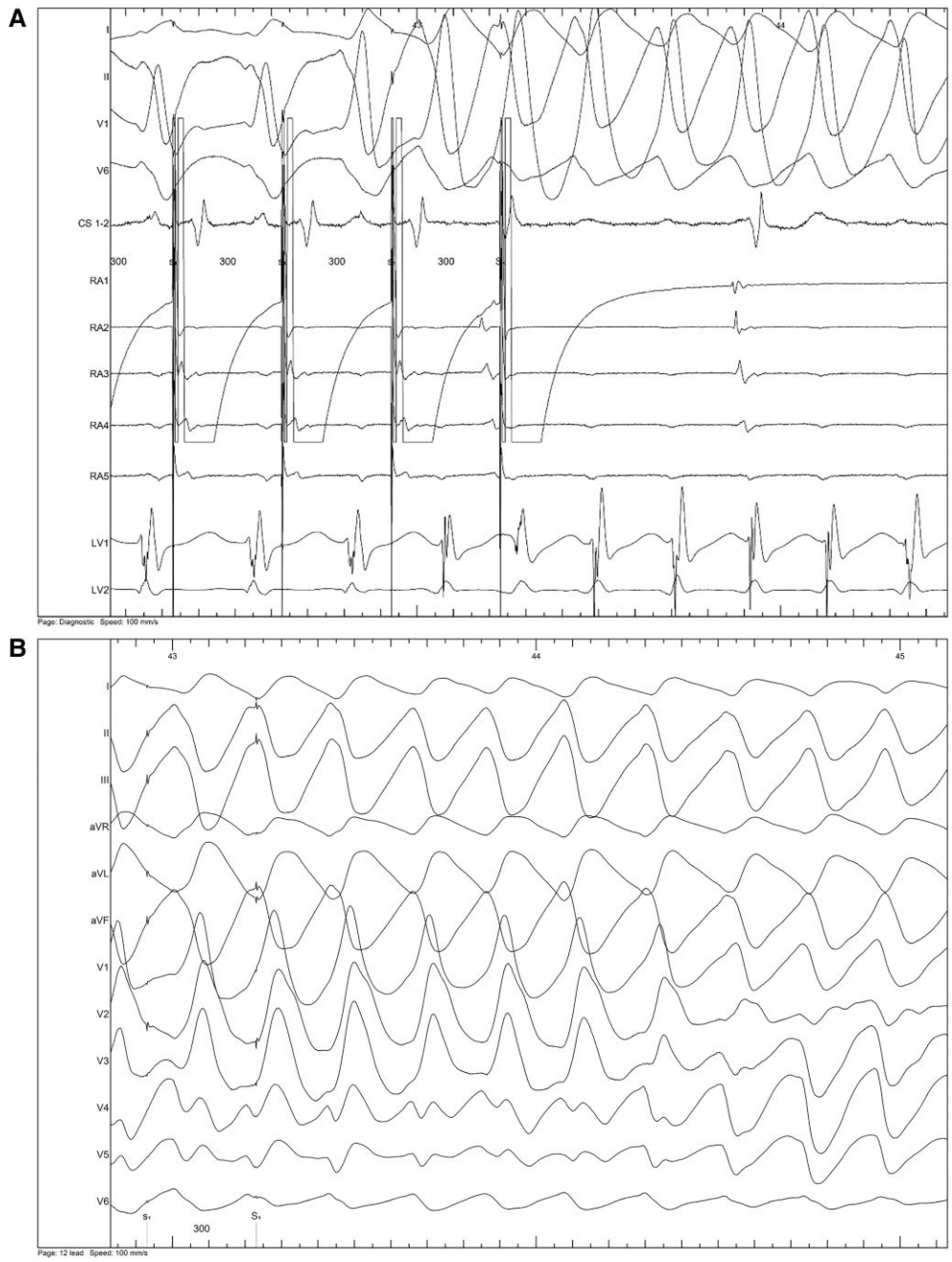


Figure 3 Intracardiac electrograms during electrophysiological study. (*A*) Induction of ventricular arrhythmia with atrial stimulation at 300 ms. (*B*) Surface 12-lead electrocardiogram demonstrating rapid degeneration into ventricular fibrillation.

associated hypertension.[6] For instance, interrupted aortic arch and a small VSD, which effectively guards the systemic outflow, can increase left ventricular afterload in the unrepaired state. This may be further exacerbated by the placement of the pulmonary artery band as the first element of the staged repair. Aortic arch repair increases aorta stiffness, is associated with hypertension, and can also increase left ventricular afterload.[7] Completion of the Fontan circulation results in passive cavopulmonary flow leading to impaired systemic ventricular filling and increased end-diastolic pressure, which may be further contributory.[8] Common electrocardiographic features (such as small R-waves and deep S-waves over right precordial leads and tall R-waves over left precordial leads) exist between DILV, interrupted arch, and HCM, which makes the diagnosis very challenging.[9] Contemporary CMR techniques can be useful in differentiating between LVH caused by CHD vs. cardiomyopathies. Myocardial fibrosis is the final common pathway in a variety of CHDs due to the multiple surgical procedures and haemodynamics to which these hearts are exposed but this is typically at surgical sites.[10] Late gadolinium enhancement in HCM is usually located at the insertion point of the ventricles or

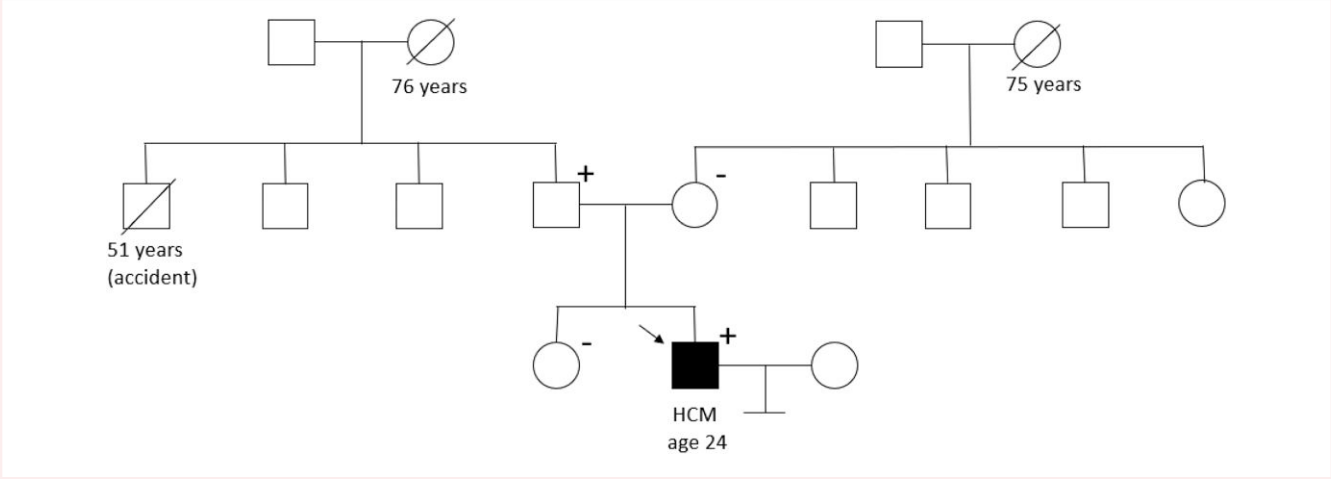


Figure 4 Family tree, obtained February 2022. The proband (arrow) was diagnosed with hypertrophic cardiomyopathy aged 24 following resuscitated cardiac arrest. Biological family relationships are denoted by squares (males) and circles (females). The age and cause of death of deceased relatives are shown by a scored symbol. The plus and minus symbols indicate presence or absence of the *MYBPC3* Arg502Trp variant identified in the proband. HCM, hypertrophic cardiomyopathy.

the most hypertrophied myocardial regions.[11] Late gadolinium enhancement has been associated with adverse ventricular mechanics, increased arrhythmic events, and time to death or transplant in both HCM and CHD.[10,11]

Patients with failing Fontan circulations are unable to augment pulmonary blood flow during exercise adequately due to absence of a sub-pulmonary ventricle, which can lead to substantially reduced stroke volume. They are also known to be at high risk for developing arrhythmias, which can cause rapid haemodynamic deterioration.[12] Fontan patients also have a higher risk of thromboembolism, occurring in up to 20% of patients, due to endothelial dysfunction associated with lack of pulsatility in the pulmonary circulaton.[12] The main differential diagnoses considered were therefore circulatory failure, arrhythmia, and thromboembolism. Electrophysiology studies should be considered in adults with CHD if arrhythmia is potentially related to cardiac arrest, and a defibrillator is indicated for survivors of an aborted cardiac arrest after evaluation for causality.[13] Many congenital patients will pass screening for subcutaneous implantable defibrillators despite abnormal cardiac anatomy and surface electrocardiogram axes. Subcutaneous devices avoid many of the risks of intracardiac leads, particularly in patients with intracardiac shunts, and should be considered.[13]

Patient perspective

A diagnosis of HCM with CHD has significant implications on various aspects of life including driving, exercise, occupation, family planning, and family screening. Good communication and liaison with multiple specialist teams within and outside cardiology such as clinical genetics, clinical psychology, and specialist nursing team were beneficial in helping the patient come to terms with his medical condition.

Conclusion

In such complex cases where CHD co-exists with cardiomyopathies, multidisciplinary expertise is critical for accurate diagnosis and ensuring optimal care of patients.

Lead author biography

Dr Kuldeepa Veeratterapillay graduated from Newcastle University with MBBS (Honours with distinction) in 2013. She is currently a higher specialty trainee in cardiology at the Freeman Hospital in Newcastle Upon Tyne, UK. Her subspecialty interests include adult congenital heart disease and advanced echocardiography. She was the recipient of the 2023 European Society of Cardiology Congress best clinical case award for this case presentation.

Supplementary material

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

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Consent: The authors confirm that written consent for submission and publication of this case report, including images and associated text, has been obtained from the patient in line with COPE guidance.

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Data availability

All data underlying this article are available as part of the article and in its online supplementary material. No additional source data are required.

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