Apical hypertrophic cardiomyopathy associated with circumflex to left ventricular fistulae: a case report of two rare subtypes of rare conditions occurring together

Samuel Conway 1*, Anna S. Herrey1,2, and Roby D. Rakhit1,3

1Department of Cardiology, Royal Free Hospital, Pond Street, Hampstead, London, NW3 2QG, UK; 2Barts Heart Centre, St. Bartholomew’s Hospital, West Smithfield, London EC1A 7BE, UK; and 3Institute of Cardiovascular Science, University College London, 62 Huntley Street, Fitzrovia, London WC1E 6DD, UK

Background
Coronary arterial fistulae are rare yet have been associated with hypertrophic cardiomyopathy (HCM). We present a patient who was found to have a left circumflex (LCx) to left ventricular (LV) fistula in combination with apical HCM.

Case summary
A 72-year-old female presented with syncope after exercise. She sustained facial injuries including fracture of her nasal bones. There were no previous episodes, no cardiac history, and she denied chest pain or anginal symptoms. Electrocardiogram showed sinus rhythm with T-wave inversion throughout the chest leads. Echocardiography suggested apical HCM with hypertrophy of the LV apex but good systolic function. This was confirmed on cardiac magnetic resonance imaging with a characteristically spade-shaped LV cavity. Coronary angiography demonstrated a distal LCx to LV fistula from the apical hypertrophy but no coronary artery disease. She was started on beta-blockers and has had no further episodes, remaining well.

Discussion
Coronary fistulae are present in 0.002% of the population but clinical outcomes are poorly understood. The majority are asymptomatic but anginal chest pains can occur through the ‘coronary steal’ phenomenon. Apical HCM is a subtype of HCM characterized by spade-shaped LV cavity obliteration. It is unclear whether the association between fistulae and HCM occur because of the increased vascularization and fibrosis associated with HCM or whether congenital malformation leads to hypertrophy. Both can produce a constellation of cardiac symptoms. Our patient has the previously unreported combination of apical HCM and an LCx fistula; two rarer subtypes of rare conditions appearing together.

Keywords
Apical • Hypertrophic • Cardiomyopathy • Circumflex • Fistula • Congenital • Case report

* Corresponding author. Tel: (+44) 0207 794 0500 Ext. 34469, Email: samuel.conway@nhs.net
Handling Editor: Richard Alexander Brown
Peer-reviewers: Inga Voges and Piotr Nikodem Rudzinski
Compliance Editor: Alexander Tindale
Supplementary Material Editor: Elhosseyn Guella
© The Author(s) 2021. Published by Oxford University Press on behalf of the European Society of Cardiology.
This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com
Learning points

- Fistulae between the coronary arteries and the chambers of the heart or major vessels are rare (present in 0.002% of the population) and differ widely in their appearance and presentation, but often produce angina-like pain through the ‘coronary steal’ phenomenon.
- Apical hypertrophic cardiomyopathy (HCM) is a subtype of HCM characterized by spade-shaped left ventricular cavity obliteration and once considered benign, it is now known to have outcomes equivalent to other subtypes and is managed similarly.
- Hypertrophic cardiomyopathy and coronary artery-ventricular fistulae have a known association, but it remains unclear whether fistulae occur because of the increased vascularization and fibrosis associated with apical HCM or whether congenital fistula formation leads to hypertrophy.

Introduction

We describe a left circumflex (LCx) coronary artery to left ventricular (LV) fistula associated with apical hypertrophic cardiomyopathy (HCM) in a 72-year-old patient who presented with syncope. Coronary arterial fistulae are rare, yet have been associated with HCM. We outline of the common features of both and discuss the clinical relevance and pathophysiology of fistulae in the context of HCM.

Timeline

| Date       | Event                                                                 |
|------------|----------------------------------------------------------------------|
| 26 April 2017 | Presented to emergency department after syncopal episode when walking to her car, after 30 min of water aerobics and a hot shower. |
| 28 April 2017 | Discharged by medical team after negative troponins and 48 h inpatient monitoring. Placed for outpatient echo and 24-h Holter monitor, with referral to cardiology. |
| Early May 2017 | Echo suggestive of apical hypertrophic cardiomyopathy and negative 24 h tape. |
| 26 May 2017  | Cardiac magnetic resonance imaging confirming apical HCM with apical systolic cavity obliteration but no aneurysm, systolic anterior motion of the mitral valve or resting left ventricular outflow tract obstruction. |
| 17 June 2017 | Coronary angiography undertaken as outpatient showing left circumflex artery to left ventricular fistula but otherwise normal coronary arteries. |
| March 2019   | No significant changes on further echo and repeat 24 h tape, and no further symptoms. |
| March 2020   | Remains well at most recent follow-up appointment, with no further episodes of syncope or other symptoms. |

Case presentation

A 72-year-old Caucasian female presented with syncope after 30 min of water aerobics. After having a hot shower and when walking to her car, she described momentary pre-syncopal symptoms before losing consciousness, rousing to passers-by assisting her seconds later. She felt well prior with no palpitations or chest pain. She sustained facial injuries including nasal bone fracture but no injury to the hands. There were no previous episodes and no cardiac history. Her medical history includes asthma, dyslipidaemia, and osteoporosis, all receiving satisfactory treatment. She is a non-smoker and does not drink alcohol. Her older brother (77 years) has a history of HCM and is well. She was admitted by the medical team for further assessment.

Examination was normal except for lacerations around her right eye and nose, with no murmurs or neurological lesions. Her blood pressure was 151/71 on arrival (but normalized after analgesia).

Electrocardiogram (ECG) showed sinus rhythm with T-wave inversion throughout the chest leads (deepest V3–V5) and inferiorly, with positive voltage criteria for left ventricular hypertrophy (Figure 1). Serial troponins were not significantly raised (initially 12 ng/L and 15 ng/L 4 h later, normal <15 ng/L) and no arrhythmias were seen on inpatient monitoring. Other investigations including routine bloods and chest X-ray were unremarkable. She was discharged after 48 h (unfortunately before any further inpatient investigations were completed) and referred for outpatient cardiology assessment.

She underwent investigations a few weeks later following a cardiology outpatient appointment. Echocardiography suggested apical HCM, showing hypertrophy of the LV apex with apical wall thickness of 1.7–2.0 cm but good systolic function (Video 1). No LV pressure gradients were detected but tissue Doppler suggested diastolic dysfunction with raised LV filling pressures and severe left atrial (LA) dilation (90.5 mL). A 24-h ECG monitor showed normal sinus rhythm with no bradycardia or arrhythmias.

Cardiac magnetic resonance imaging (MRI) (1-month post-presentation) confirmed the diagnosis of apical HCM (Video 2). She had a small, characteristically spade-shaped LV cavity (Figure 2) with a maximum wall thickness of 14 mm circumferentially at the apex (9 mm at basal-septal level). There was a supra-normal ejection fraction and 22 mm apical systolic cavity obliteration (Figure 3). Papillary muscles were displaced but there was no systolic anterior motion of the mitral valve or LV outflow tract obstruction. The right ventricle and atrium had normal structure and function and the LA was mildly dilated (27 cm²). There was no late gadolinium enhancement and...
valves were normal. There was an inducible perfusion defect in the apex. Coronary angiography was undertaken 3 weeks later to assess inducible ischaemia seen on MRI. This demonstrated unobstructed coronary arteries but a stream of contrast into the left ventricle from the apex (Video 3). This distal LCx to LV fistula emerged from a bed of increased vascularity, corresponding to the apical hypertrophy. The interpretation of the perfusion defect

**Video 1** Transthoracic echocardiogram loops. Apical four-chamber, left ventricular-focused four-chamber, and three-chamber views show the apical thickening of the left ventricle with preservation of systolic function.

**Video 2** Cardiac magnetic resonance cine videos in two-chamber, three-chamber, and four-chamber views confirming the diagnosis and highlighting the left ventricular cavity obliteration.
**Figure 2** Cardiac magnetic resonance imaging cine two-chamber views in diastole (A) and systole (B) with where the apical hypertrophy clearly contrasts with the normal wall thickness seen throughout the rest of the left ventricle. Also note the left atrial enlargement.

**Figure 3** Cardiac magnetic resonance imaging cine three-chamber (A and B) and four-chamber views (C and D). Obliteration of the left ventricular cavity during systole (B and D) is demonstrated with the ‘spade shape’ appearance of the left ventricular cavity typical of the condition in diastole (A and C).
Although these features are not deemed ‘high-risk’ in themselves,3 cardiac MRI. Our patient presented with such ECG abnormalities and trophic voltage criteria and confirmed with echocardiography and ECG changes including deep T-wave inversion and positive LV hypertrophy. It can be suggested by the anatomical region affected. It can be implied by the site of coexistence and presence with varying degrees of success.11

Discussion

Hypertrophic cardiomyopathy is the most common heritable cardiomyopathy, presenting as asymmetrical LV hypertrophy without secondary cause.1 Genetic mutations (frequently encoding sarcomeric proteins) underlie the pathology2 but a broad range of affected genes produce a phenotypically diverse condition with several subtypes categorized by the anatomical region affected. It can be suggested by ECG changes including deep T-wave inversion and positive LV hypertrophy voltage criteria and confirmed with echocardiography and cardiac MRI. Our patient presented with such ECG abnormalities and although these features are not deemed ‘high-risk’ in themselves,3 ESC syncope guidelines recommend further inpatient investigation when combined with a brief (or no) prodromal period prior to collapse.3 Inpatient echocardiography would have provided the initial diagnosis of apical HCM before discharge.

Apical HCM is a subtype (3% of HCM in the USA, but 15% in Japan where first described4) characterized by a spade-shaped LV cavity with apical systolic obliteration and sometimes aneurysm formation. Once considered benign it is now known to have outcomes equivalent to other subtypes.1 It has been misdiagnosed as other pathologies including LV thrombus, tumours, or non-compaction cardiomyopathy. Hypertrophic cardiomyopathies produce symptoms from arrhythmias (including atrial fibrillation), heart failure, syncope/ presyncope, and chest pain to sudden cardiac death but many patients are asymptomatic. Management is through family/genetic screening, symptom alleviation (through lifestyle modification, pharmacological, or interventional strategies), and risk stratification for sudden death (with ICD insertion in high-risk individuals).1,2

Fistulae between the coronary arteries and the heart chambers or major vessels are present in 0.002%5 of the population and up to 0.2% of patients undergoing cardiac catheterization6 but differ widely in their appearance and presentation.7 Most are congenital (and up to 20% have other congenital malformations8) but acquired causes exist including iatrogenic, traumatic, and disease-related. They most commonly affect the right coronary or left anterior descending arteries, with the circumflex being the least common. 5% of patients have involvement of two arteries or more.6

Long-term outcomes are poorly understood.8 Although the vast majority are asymptomatic, the most common symptom is anginal chest pain through the ‘coronary steal’ phenomenon in patients who have no/minimal coronary artery disease. Ischaemia is produced in areas of myocardium distal to the fistula origin as blood is shunted in diastole to the lower-pressure LV cavity from the coronary arteries via the low resistance tract. Other manifestations include thrombosis, embolism, cardiac failure, atrial fibrillation, rupture, endocarditis/endarteritis, and arrhythmia.9

Management is mostly conservative with anti-anginal agents to control symptoms (usually beta-blockade/nicorandil), lessening the demand-supply imbalance by reducing oxygen demand. If signs of failure, significant left-to-right shunt or other coronary/cardiac lesions then surgical closure can be successful10 but was not indicated here. Catheter-based treatments using coils for embolization are also available with varying degrees of success.11

There is an association between coronary fistulae and hypertrophic cardiomyopathies.12 Most cases are found during investigations for angina where first-line investigations of echocardiography and coronary angiography find both conditions concurrently. The reduced oxygen supply due to coronary steal and the increased oxygen requirements of the hypertrophic myocardial tissue may exacerbate ischaemia. There are, however, no reported cases of myocardial infarction due to the combination. A number of cases specifically show an association with apical HCM13,14 yet no cases appear to show a fistula to the LV arising from the LCx artery.15

It remains unclear whether fistulae occur because of the increased vascularization and fibrosis associated with HCM or whether congenital malformation leads to hypertrophy as a compensatory response to chronic volume overload caused by the shunt between artery and ventricle. Conversely, microfistulae may be produced due to disarray of myocardial cells and abnormal vascularity supplying the areas of hypertrophy.

Hypertrophic cardiomyopathy and coronary artery-ventricular fistulae are rare conditions with a known association. Both produce a constellation of cardiac symptoms including chest pain. Our case is of interest due to the previously unreported combination of apical HCM and an LCx artery fistula; two rarer subtypes of rare conditions...
occurring together. Our patient denied prior symptoms and the abnormalities were unexpected findings after an episode of syncope. Her risk has been deemed low and she has had no requirement for an ICD. She remains well on medical therapy and has experienced no further syncope 3 years after her initial presentation. She continues to be followed up in clinic with annual echocardiography.

**Lead author biography**

Dr Samuel Conway is Senior Clinical Fellow in Heart Failure at the Royal Free Hospital. He graduated from UCL Medical School in 2015 and has continued his training in hospitals across London. He has previously held cardiology posts at the Hammersmith Hospital and the Royal London Hospital.

**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 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 guidelines.

**Conflict of interest:** none declared.

**Funding:** none declared.

**References**

1. Geske JB, Ömmen SR, Gersh BJ. Hypertrophic cardiomyopathy: clinical update. *JACC Hear Fail* 2018;6:364–375.
2. Zannorono JL, Anastassakis A, Borger MA, Borggreve M, Cecchi F, Charron P et al. 2014 ESC guidelines on diagnosis and management of hypertrophic cardiomyopathy: the task force for the diagnosis and management of hypertrophic cardiomyopathy of the European Society of Cardiology (ESC). *Eur Heart J* 2014;35:2733–2779.
3. Brignole M, Moya A, De Lange FJ, Deharo JC, Elliott PM, Fanciulli A, ESC Scientific Document Group et al. 2018 ESC Guidelines for the diagnosis and management of syncope. *Eur Heart J* 2018;39:1983–1948.
4. Kitao S, Doi Y, Casey SA, Hitomi N, Furuno T, Maron BJ. Comparison of prevalence of apical hypertrophic cardiomyopathy in Japan and the United States. *Am J Cardiol* 2003;92:1183–1186.
5. Ogden JA. Congenital anomalies of the coronary arteries. *Am J Cardiol* 1970;25:474–479.
6. Yamanaka O, Hobbs RE. Coronary artery anomalies in 126,595 patients undergoing coronary arteriography. *Cathet Cardiovasc Diagn* 1990;21:28–40.
7. Challoumas D, Pericleous A, Dimitrakaki IA, Danelatos C, Dimitrakakis G. Coronary arteriovenous fistulae: a review. *Int J Angiol* 2014;23:1–10.
8. Waterhouse DF, Murphy TM, McCreery C, O’Hanlon R. Hypertrophic cardiomyopathy and coronary fistulae. *Br J Cardiol* 2017;24:118–119.
9. Qureshi SA. Coronary arterial fistulas. *Orphanet J Rare Dis* 2006;1:51.
10. Tirilomis T, Aleksic I, Busch T, Zenker D, Ruschewski W, Dalichau H. Congenital coronary artery fistulas in adults: surgical treatment and outcome. *Int J Cardiol* 2005;98:57–59.
11. Gowda RM, Vasavada BC, Khan IA. Coronary artery fistulas: clinical and therapeutic considerations. *Int J Cardiol* 2006;107:7–10.
12. Chung T, Yiannikas J, Freedman SB, Thruchesides L. Unusual features of apical hypertrophic cardiomyopathy. *Am J Cardiol* 2010;105:879–883.
13. Hong OR, Choi SH, Kang SM, Lee MH, Rim SJ, Jang YE et al. Multiple coronary artery-left ventricular microfistulae in a patient with apical hypertrophic cardiomyopathy: a demonstration by transthoracic color Doppler echocardiography. *Yonsei Med J* 2003;44:710–714.
14. Alyan O, Ozek O, Golkasi Z. Coronary artery-left ventricular fistulae associated with apical hypertrophic cardiomyopathy. *Eur J Echocardiogr* 2006;7:326–329.
15. Dresios C, Apostolakis S, Tsartzis S, Lazaridis K, Gardikis A. Apical hypertrophic cardiomyopathy associated with multiple coronary artery-left ventricular fistulae: a report of a case and review of the literature. *Eur Hear J Cardiovasc Imaging* 2010;11:E9.