Case Reports

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
50(2) 1–8

DOI: 10.1177/03000605221082882
journals.sagepub.com/home/imr
SAGE

Coronary artery–left ventricular multiple microfistulas, a rare disease that is easily missed: case report and literature review

Kaicong Chen, Zhihuan Zeng, Tudi Li, Rong Chen, Junqian Luo and Zihao Zhou

Abstract

Coronary artery–left ventricular multiple microfistulas (CALVMMFs) are a very rare type of coronary artery fistula. Because of their special anatomical structure and hemodynamics, CALVMMFs often result in no obvious symptoms and signs. Most patients are diagnosed by coronary angiography; however, as a routine noninvasive screening method, Doppler echocardiography is a potential first-choice diagnostic technique for patients with CALVMMFs. Although satisfactory results of CALVMMF closure are difficult to achieve, the clinical symptoms of these patients are not obvious, and drug therapy has a clear therapeutic effect on most patients. We herein introduce seven cases of CALVMMFs confirmed by our hospital and briefly review the related literature.

Keywords

Coronary artery fistula, microfistula, coronary vessel anomaly, case report, Doppler echocardiography, coronary angiography

Date received: 3 November 2021; accepted: 4 February 2022

Introduction

Most coronary artery fistulas (CAFs) are congenital, accounting for 0.2% to 0.4% of congenital heart diseases.[1] It is generally believed that the development of CAFs is related to incomplete degeneration of the

Cardiovascular Department, The First Affiliated Hospital of Guangdong Pharmaceutical University, Guangzhou, Guangdong Province, China

Corresponding author:
Zhihuan Zeng, Cardiovascular Department, The First Affiliated Hospital of Guangdong Pharmaceutical University, No. 19 Nonglinxia Road, Guangzhou, Guangdong 510080, People's Republic of China.
Email: gzzh@163.com

sinusoids.[2] Most CAFs are simple fistulas that drain to low-pressure structures such as the right ventricle and pulmonary artery.[3] However, complicated CAFs that drain to the left ventricle are extremely rare and exhibit a special anatomical structure and hemodynamics. We believe that such fistulas should be regarded as a special CAF type.

Case series

We herein describe seven patients who were diagnosed with coronary artery–left ventricular multiple microfistulas (CALVMMFs) in The First Affiliated Hospital of Guangdong Pharmaceutical University from 2020 to 2021 (Table 1). All patients were diagnosed by coronary angiography. The average age of the seven patients was 69.6 years (range, 52–91 years). All patients had obvious symptoms, among which chest pain and tightness were the most common (57.1%), followed by dyspnea, palpitation, dizziness, and fatigue. No obvious cardiac murmur was found in any patients. Nonspecific ST-T change was the most common electrocardiographic feature (85.7%); other electrocardiographic manifestations included atrial fibrillation and a prolonged QT interval (Table 2). Abnormal blood flow signals of the left ventricle during diastole were found by Doppler echocardiography in three patients (Figure 1). Coronary angiography showed no obvious abnormality in the branching and course of the coronary artery and no obvious fistula, but the contrast medium in the area of the distal microvascular fistula of the involved coronary artery directly diffused into the left ventricle in the diastolic phase, whereas the abnormal blood flow disappeared during systole (Figure 2). This is a characteristic manifestation of CALVMMFs. All patients underwent cardiac magnetic resonance imaging to rule out cardiomyopathies, such as left ventricular noncompaction. Because no effective surgical or interventional treatment is available for this microvascular fistula, we decided to treat the patients with β-receptor antagonists, and the patients agreed to our treatment plan. The patients were followed up for at least 6 months during treatment. All patients' clinical symptoms were significantly relieved, and Doppler echocardiography showed no deterioration of cardiac function. The reporting of this study conforms to the CARE guidelines.[4] All patients' personal information has been de-identified, and written informed consent for publication was obtained from all patients.

Discussion

The right ventricle and pulmonary artery are considered the most common drainage

Table 1. Basic information of patients.

Patient	Sex	Age (years)	Medical history	Symptoms	Cardiac murmur	Fistula
1	Female	83	—	Palpitations and dyspnea	—	LAD-LV
2	Female	67	—	Chest pain and dyspnea	—	LAD-LV
3	Male	52	—	Chest pain and tightness	—	LAD-LV
4	Male	64	Hypertension, coronary artery disease	Chest pain and tightness	—	LAD-LV
5	Female	68	—	Chest tightness	—	LAD-LV
6	Female	62	Atrial septal defect	Chest pain and tightness	—	D1-LV
7	Male	91	—	Dizziness and fatigue	—	D1-LV

LAD, left anterior descending coronary artery; D1, first diagonal branch; LV, left ventricle.

Table 2. Electrocardiogram and transthoracic echocardiography findings.

Patient	Electrocardiogram	Transthoracic echocardiography
1	Atrial fibrillation	Abnormal local blood flow signal at the papillary muscle of the left ventricle, increased left ventricular end-diastolic pressure, tricuspid regurgitation
2	Nonspecific ST-T changes	Abnormal blood flow signal at the apex of the left ventricle, tricuspid regurgitation
3	Nonspecific ST-T changes	Abnormal blood flow signal at the interventricular septum of the left ventricle
4	Nonspecific ST-T changes	Mitral and tricuspid regurgitation
5	Nonspecific ST-T changes	Ventricular septal thickening and mitral regurgitation
6	Nonspecific ST-T changes	Increased left atrial diameter, mitral and tricuspid regurgitation
7	QT interval prolongation, nonspecific ST-T changes	Left ventricular diastolic dysfunction, ventricular septal thickening

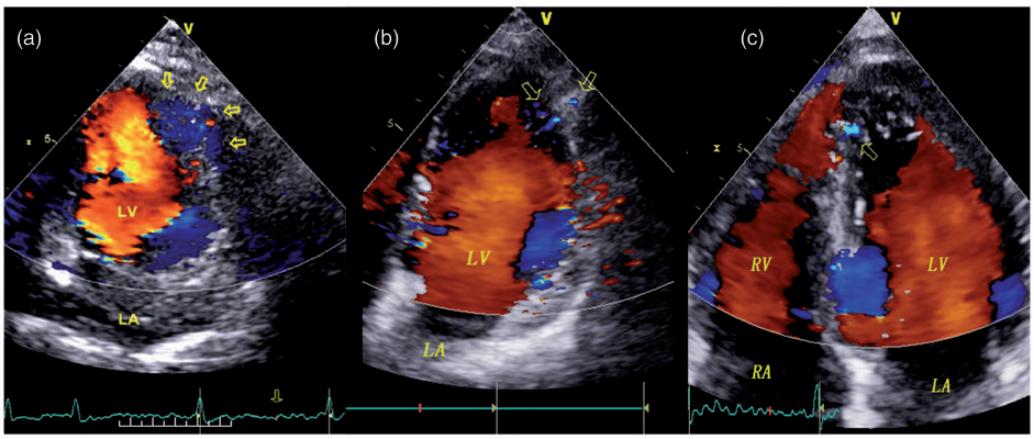

Figure 1. (a–c) Transthoracic echocardiography showed blue abnormal blood flow signals appearing at the papillary muscles and the apical and interventricular septum of the left ventricle during diastole.
RV, right ventricle; LV, left ventricle; RA, right atrium; LA, left atrium.

sites for CAFs,[3] whereas drainage of a CAF to the left ventricle is extremely rare. Ninety percent of CAFs are simple fistulas, and 10.7% to 16.0% are complex CAFs[2,5]; that is, multiple fistulas exist between the affected coronary artery and the drainage site. As a special complex type of CAF, a microvascular fistula is rarer and does not have a clear fistula structure. During coronary angiography, contrast medium can be observed to spread from the affected coronary artery through the plexiform vascular network to the drainage site. Like an ordinary CAF, a microvascular fistula can originate from any coronary artery. At the drainage site, however, it seems to only drain to the left ventricle, and there are no reported cases of a microvascular fistula

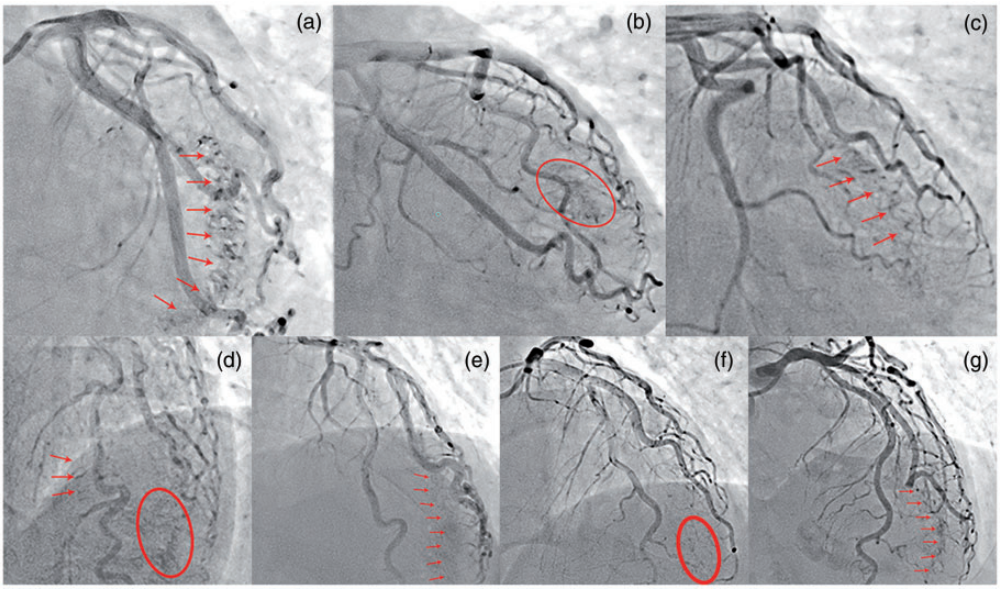

Figure 2. (a–e) Coronary angiography showed that the contrast medium diffused into the left ventricle, resembling smoke, from the left anterior descending coronary artery through the microvascular network. (f–g) The microvascular fistula originated from the first diagonal branch and drained to the left ventricle.

draining to other sites. Therefore, we believe that CALVMMFs should be regarded as a special subtype of CAF. The etiology of CALVMMFs remains unclear.

We believe that formation of these fistulas is related to the pressure and compliance of the drainage site. Because of the low compliance and high pressure of the left ventricle, a fistula with an obvious structure does not readily form even if the myocardium is normal, and the blood flow can only be diffused through the plexiform vascular network between the myocardium. Additionally, this special type of CAF may be associated with left ventricular noncompaction and can be caused by chromosomal abnormalities, such as 22q11.2 deletion.[6–8] We believe that left ventricular noncompaction may be one cause of CALVMMFs, but proving this etiology requires more evidence. Therefore, patients with CALVMMFs need routine echocardiography or cardiac magnetic resonance imaging to rule out the possibility of left ventricular noncompaction.

The coronary artery steal phenomenon is considered a main pathophysiological basis of CAFs[2,9,10] and is closely related to the symptoms and complications of CAFs. On one hand, the coronary artery steal phenomenon causes insufficient blood supply to the distal coronary artery, resulting in chest pain and even myocardial infarction.[11,12] On the other hand, continuous extra blood flow will increase the heart load, resulting in congestive heart failure and pulmonary hypertension, which will in turn lead to dyspnea, chest tightness, and other related symptoms.[2,5,13] The shunt flow through the fistula mainly depends on the size of the fistula and the pressure gradient between the coronary artery and the drainage site.[14] Because of the small fistula diameter and pressure gradient of CALVMMFs, the resultant hemodynamic changes are generally of little clinical

significance. In addition, our patients' coronary angiography results suggest that during systole, the microvascular fistulas close under pressure and the abnormal blood flow stops, which also reduces the degree of "coronary steal" to some extent. This special hemodynamic change means that the degree of myocardial ischemia and cardiac load increase in most patients with CALVMMFs may not be obvious,[11,14] and these patients may therefore have no obvious clinical symptoms or will require a long time to develop obvious symptoms. In our case series, the cardiac function of all except one patient with left ventricular diastolic dysfunction was not markedly decreased, indicating that these patients may have a good prognosis.

A cardiac murmur is considered to be a significant sign of a CAF. Studies have shown that more than 70% of patients with CAFs have an obvious cardiac murmur in the prethoracic area.[1,2,15] However, patients with CALVMMFs often do not have an obvious cardiac murmur because the blood flow is diffused along the microvessels to the left ventricle, and turbulence does not readily develop in the cardiac cavity.

The coexistence of coronary dilatation is a characteristic feature of CAFs, but in almost all cases of CALVMMFs, significant coronary dilatation is absent. This is consistent with our case series, and we believe that it may be due to the small shunt. Because of this special anatomical structure, coronary angiography is still the most meaningful detection method for the diagnosis of CALVMMFs. However, its application is limited by its invasiveness and radiation exposure, and most patients without obvious symptoms are not willing to undergo coronary angiography. Although computed tomography angiography has high temporal and spatial resolution, making it an important method to diagnose CAF at present,[16,17] no cases of CALVMMFs have been diagnosed by computed tomography angiography. As a routine noninvasive screening method, Doppler echocardiography can reveal abnormal diastolic blood flow signals in the ventricle or myocardium of patients with CALVMMFs.[6–8,18,19] However, the sensitivity of Doppler echocardiography for the diagnosis of CALVMMFs is low, mainly because the hemodynamics of most CALVMMFs have not changed significantly. The operator's experience and technical skill level are also important influencing factors. The use of higher-frequency transducers or transesophageal echocardiography can improve the diagnostic rate of CALVMMFs to a certain extent.[20] It is also necessary to improve operators' awareness of CALVMMFs.

In summary, the clinical symptoms and signs of patients with CALVMMFs are not obvious because of the special anatomical structure and hemodynamics of these fistulas, and it is difficult to identify these abnormalities by noninvasive methods. Therefore, CALVMMFs are difficult to find in the early stage, and most are diagnosed by coronary angiography after obvious complications and evidence of myocardial ischemia have developed. In our case series, the mean age at diagnosis was 69.6 years. In a retrospective study of CALVMMFs in Turkey, the mean age at diagnosis was 70.2 ± 10.8 years,[21] while in another retrospective study of 304 patients with CAFs, the mean age was 51.4 years; this is consistent with our speculation.[13]

Because of the increasing efficacy and safety of transcatheter closure and surgical treatment of CAFs, a consensus has been reached regarding percutaneous closure treatment for patients with large or symptomatic CAFs.[22] However, because of the special anatomical structure of CALVMMFs, it is difficult to achieve effective results by percutaneous closure.[23] Therefore, such treatment is not

recommended for these patients, even if they have obvious symptoms. Most case reports to date have shown that β-receptor antagonists and calcium channel blockers are effective in treating CALVMMF-related symptoms[7,12,24–26] and can improve the prognosis of patients. Therefore, conservative treatment with drugs should be regarded as the first choice for treating CALVMMFs.

Conclusion

Generally, CALVMMFs have a special anatomical structure and hemodynamics. We believe that they should be regarded as a rare subtype of CAFs and that they may have a good prognosis. Because of the lack of typical symptoms and signs, CALVMMFs are difficult to detect in the early stage. Although coronary angiography is still the gold standard for the diagnosis of CALVMMFs, Doppler echocardiography can also be used to diagnose CALVMMFs by revealing abnormal blood flow in the left ventricle or myocardium, and this imaging technique may become the first choice for the diagnosis of CALVMMFs. Because effective results of fistula closure are difficult to achieve, we recommend conservative drug treatment and regular follow-up for these patients.

Statement of ethics

Review board approval was not needed because of the nature of this study (case report). All patients provided written informed consent for publication of the manuscript.

Funding sources

The authors disclosed receipt of the following financial support for the research, authorship, and publication of this article: This work was supported by the Guangdong Provincial Innovation Team Project of Colleges and Universities (No. 2019KCXTD018).

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Author contributions

CKC designed the report and completed the manuscript. ZHZ and TDL operated on the patients and were responsible for their postoperative care. ZHZ revised the manuscript and supervised all the work. All authors read and approved the final manuscript.

ORCID iDs

Kaicong Chen https://orcid.org/0000-0002-5998-8426
Zhihuan Zeng https://orcid.org/0000-0002-2701-8556
Junqian Luo https://orcid.org/0000-0002-5005-220X

References

1. Huynh KT, Truong VT, Ngo TNM, et al. The clinical characteristics of coronary artery fistula anomalies in children and adults: a 24-year experience. *Congenit Heart Dis* 2019; 14: 772–777. doi: 10.1111/chd.12781.
2. Karazisi C, Eriksson P and Dellborg M. Coronary artery fistulas: case series and literature review. *Cardiology* 2017; 136: 93–101. doi: 10.1159/000447445.
3. Abdelmoneim SS, Mookadam F, Moustafa S, et al. Coronary artery fistula: single-center experience spanning 17 years. *J Interv Cardiol* 2007; 20: 265–274. doi: 10.1111/j.1540-8183.2007.00267.x.
4. Gagnier JJ, Kienle G, Altman DG, et al; CARE Group. The CARE guidelines: consensus-based clinical case reporting guideline development. *Headache* 2013; 53: 1541–1547.
5. Ali M, Kassem KM, Osei K, et al. Coronary artery fistulae. *J Thromb Thrombolysis* 2019; 48: 345–351. doi: 10.1007/s11239-019-01897-8.
6. Branton H, Warren AE and Penney LS. Left ventricular noncompaction and coronary artery fistula in an infant with deletion

22q11.2. *Pediatr Cardiol* 2011; 32: 208–210. doi: 10.1007/s00246-010-9837-z.
7. Hernández M, Carretero JM and Prada F. Propranolol as a treatment for multiple coronary artery micro-fistulas. *Cardiol Young* 2015; 25: 380–383. doi: 10.1017/S1047951114000249.
8. Gupta U and Makhija P. Left ventricular noncompaction cardiomyopathy in pediatric patients: a case series of a clinically heterogeneous disease. *Pediatr Cardiol* 2017; 38: 681–690. doi: 10.1007/s00246-016-1566-5.
9. Yun G, Nam TH and Chun EJ. Coronary artery fistulas: pathophysiology, imaging findings, and management. *Radiographics* 2018; 38: 688–703. doi: 10.1148/rg.2018170158.
10. Kahaly O and Boudoulas KD. Multiple small coronary artery fistulas emptying into the left ventricle: a rare but challenging problem. *Case Rep Med* 2016; 2016: 2406250. doi: 10.1155/2016/2406250.
11. Taha ME, Al-Khafaji J, Abdalla AO, et al. Coronary artery-left ventricular fistula and Takotsubo cardiomyopathy – an association or an incidental finding? A case report. *Am J Case Rep* 2018; 19: 614–618. doi: 10.12659/AJCR.908836.
12. Uyar IS, Akpinar B, Senarslan O, et al. Multiple coronary fistulae to left ventricle, with acute myocardial infarction. *Asian Cardiovasc Thorac Ann* 2015; 23: 561–563. doi: 10.1177/0218492314522045.
13. Said SA. Current characteristics of congenital coronary artery fistulas in adults: a decade of global experience. *World J Cardiol* 2011; 3: 267–277. doi: 10.4330/wjc.v3.i8.267.
14. Iyer P and Yelisetti R. Multiple left anterior descending coronary artery to left ventricular fistula – a case series and literature review. *J Community Hosp Intern Med Perspect* 2017; 7: 258–261. doi: 10.1080/20009666.2017.1369380.
15. Song G, Zhang J, Ren W, et al. Pediatric coronary artery fistula: echocardiographic case reports and literature review of treatment strategy. *Springerplus* 2016; 5: 1583. doi: 10.1186/s40064-016-3276-0.
16. Şişman SB, Doğan D, Şahin S, et al. The role of multislice computed tomography in the diagnosis of coronary artery fistulas. *Turk Gogus Kalp Damar Cerrahisi Derg* 2018; 26: 52–57. doi: 10.5606/tgkdc.dergisi.2018.14321.
17. Detorakis EE, Foukarakis E, Karavolias G, et al. Cardiovascular magnetic resonance and computed tomography in the evaluation of aneurysmal coronary-cameral fistula. *J Radiol Case Rep* 2015; 9: 10–21. doi: 10.3941/jrcr.v9i7.2305.
18. Hong GR, Choi SH, Kang SM, 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. doi: 10.3349/ymj.2003.44.4.710.
19. Nakashima M, Yunoki K, Miyaji K, et al. Multiple left and right coronary artery-left ventricular fistulas. *Intern Med* 2017; 56: 2535–2536. doi: 10.2169/internalmedicine.8843-17.
20. Vitarelli A, De Curtis G, Conde Y, et al. Assessment of congenital coronary artery fistulas by transesophageal color Doppler echocardiography. *Am J Med* 2002; 113: 127–133. doi: 10.1016/s0002-9343(02)01157-9.
21. Doğan M, Sunman H, Akyel A, et al. [Prevalence and clinical features of microfistulas between the coronary artery and left ventricle: single-center experience]. *Turk Kardiyol Dern Ars* 2014; 42: 332–338. Turkish. doi: 10.5543/tkda.2014.25936.
22. Warnes CA, Williams RG, Bashore TM, et al. ACC/AHA 2008 Guidelines for the Management of Adults with Congenital Heart Disease: Executive Summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to develop guidelines for the management of adults with congenital heart disease). *Circulation* 2008; 118: 2395–2451. doi: 10.1161/CIRCULATIONAHA.108.190811.
23. Meric M and Yuksel S. Diffuse coronary artery fistula leading to syncope and treated with transcatheter coil occlusion and a defibrillator: a case report. *Med Princ Pract* 2019; 28: 493–496. doi: 10.1159/000500309.
24. Arslan S, Gurlertop Y, Elbey MA, et al. Multiple coronary-cameral fistulae causing

angina pectoris. *Tex Heart Inst J* 2009; 36: 622–623.
25. Sambu N, Sharma R and Kalra PR. Multiple coronary to left ventricular fistulae. *Eur J Echocardiogr* 2009; 10: 352. doi: 10.1093/ejechocard/jen229.
26. Yildiz BS, Bilgin M, Alihanoglu YI, et al. A case of multiple coronary microfistulas to the left ventricle and apical myocardial hypertrophy coexisting with stable angina. *J Saudi Heart Assoc* 2013; 25: 209–211. doi: 10.1016/j.jsha.2013.02.002.