

Hypoplastic coronary artery disease and hypertension in a child: a case report

Yuji Doi *, Kenji Waki, Kayo Ogino , and Tomohiro Hayashi

Department of Pediatrics, Kurashiki Central Hospital, 1-1-1 Miwa Kurashiki-City, Okayama 710-8602, Japan

Received 13 May 2021; first decision 17 June 2021; accepted 22 December 2021; online publish-ahead-of-print 28 December 2021

Background

Hypoplastic coronary artery disease (HCAD) is an extremely rare disease associated with a risk of sudden cardiac death. It is rarely recognized in a live paediatric patient.

Case summary

We report a case of HCAD in a patient who first presented with vomiting and poor feeding, suggestive of acute heart failure due to cardiomyopathy or acute myocarditis in infancy. Hypertension and signs of ischaemia became evident on electrocardiography and scintigraphy after his cardiac function fully recovered, and he was diagnosed with HCAD by angiography performed at the age of 8 years. He has remained under close observation with anti-hypertensives, aspirin, and exercise restriction.

Discussion

Although HCAD is a rare disease, it may not only cause ischaemia but may also result in heart failure and sudden cardiac death. It should be considered in any paediatric patient with heart failure. Mid-term follow-up visits might be necessary to detect signs of ischaemia in paediatric patients presenting with features of heart failure.

Keywords

Hypoplastic coronary artery disease • Acute myocarditis • Myocardial ischaemia • Coronary artery disease • Case report

ESC Curriculum

3.4 Coronary angiography • 6.1 Symptoms and signs of heart failure • 3.2 Acute coronary syndrome

Learning points

- Hypoplastic coronary artery disease should be considered when seeing an infant or a child with heart failure.
- Signs of ischaemia may only be present later on, thus requiring mid-term follow-up.

Introduction

Hypoplastic coronary artery disease (HCAD) is a rare coronary artery anomaly with a guarded prognosis due to the risk of sudden cardiac death.¹ It is defined as the underdevelopment of one or more coronary arteries with markedly diminished lumina.² With an increase in the number of reported cases, both congenital and acquired factors that affect coronary artery flow are considered to play roles in this rare entity.³ Herein, we report a paediatric case of HCAD who first presented with symptoms of acute heart failure, which mimicked acute myocarditis. The patient later presented with hypertension and signs of ischaemia, leading to the diagnosis of HCAD.

* Corresponding author. Email: yd16549@kchnet.or.jp; fools.gold.712@gmail.com

Handling Editor: Sylvia Krupickova

Peer-reviewers: Luis Antonio Moreno-Ruiz and Filippo Puricelli

Compliance Editor: Nikolaos Spinthakis

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-NonCommercial License (<https://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

Timeline

10 months old	Patient presented with poor feeding and vomiting. Echocardiogram showed left ventricular ejection fraction (LVEF) of 64.8% and left ventricular diastolic diameter (LVDD) of 32.3 mm (117.9% of normal) with mild to moderate mitral regurgitation.
1 year 8 months old	Mitral regurgitation became trivial while LVEF declined to 45.4% and left ventricular dilatation (132.3% of normal) was observed. Patient was started on diuretics.
1 year 9 months old	First catheter was performed to perform myocardial biopsy, which was unsuccessful. Aortography showed hypoplastic left coronary, yet this was left unnoticed. As the aortic pressure was high, he was started with anti-hypertensive medication. No apparent renal artery stenosis was observed, but plasma renin levels were high.
1 year 10 months old	Left ventricular ejection fraction recovered to 77.2% with LVDD of 128.0% of normal. Mitral regurgitation was trivial at this point and remained stable thereafter. Diuretics were gradually weaned off.
4 years old	Left ventricular diastolic diameter nearly normalized to 38.0 mm (112.4% of normal), and remained stable thereafter. Mitral regurgitation was trivial and did not deteriorate.
6 years old	Second catheter was performed, which revealed no stenotic lesions in renal arteries.
7 years old	Features of ischaemia on electrocardiogram were observed and confirmed with scintigraphy.
8 years	Coronary angiogram clearly depicted hypoplastic left coronary artery. Left main trunk was 3.1 mm (Z-value 0.94), anterior descending artery was 0.40 mm (Z-value -6.58), and left circumflex artery was 0.57 mm (Z-value -6.19).
9 years	Follow-up angiogram with nitrates excluded coronary vasospasm.

Case presentation

An 11-month-old male infant with no prior medical history was admitted to our hospital for vomiting and poor feeding. He was lethargic, but his skin colour was normal and his capillary refill time was about 2 s. Physical examination revealed a systolic murmur at the left lower sternal border, and subsequent echocardiography revealed mild to moderate mitral regurgitation (MR). There was no papillary muscle rupture, short chordae, or any other anomaly of the mitral valve. The left ventricular diastolic diameter (LVDD) was 32.3 mm (118% of normal value), and left ventricular ejection fraction (LVEF) was 64.8% (cube method). No apparent congestion on chest X-ray could be seen, and his brain natriuretic peptide (BNP) level was only

17.2 pg/mL. Electrocardiography (ECG) showed normal sinus rhythm without ST-segment changes or abnormal Q waves. Mitral regurgitation was gradually ameliorated and was mild at 1 year and 8 months. However, the LVDD was 39.7 mm (132.3% of normal value), LVEF declined to 45.4% without any locality, and the BNP level rose to 413.7 pg/mL; therefore, he was started on diuretics. When he was 1 year and 9 months old, he underwent his first cardiac catheterization for myocardial biopsy in a bid to exclude cardiomyopathy, but the procedure was not successful as he only weighed 11.8 kg. Aortography showed normal orifices of the left and right coronary arteries. Aortic pressure revealed hypertension above the 97th percentile for an age-matched Japanese male infant. Although renal artery stenosis was not evident on angiography, he was diagnosed with high renin hypertension because his plasma renin activity was as high as 19 ng/mL/h (normal value: 0.2–4.1 ng/mL/h) and extensive evaluation excluded most common secondary causes. He was started on enalapril and carvedilol sequentially. His left ventricular (LV) function improved gradually by 1 year and 10 months of age, and the BNP level decreased to 20.0 pg/mL. His LVDD nearly normalized to 112.4% of normal by 4 years of age, so the diuretics were stopped. Renal vein renin sampling performed when he was 6 years old showed that the left renal vein renin level was more than twice as high as the right renal vein renin level (17.0 and 8.3 ng/mL/h, respectively). However, renal artery stenosis or any other anomalies such as branch stenosis was not observed.

He remained stable on anti-hypertensive medication for years until his ECG showed features of ischaemia and was confirmed with scintigraphy when he was 7 years old (Figure 1). His echocardiogram showed normal ventricular function, and he was clinically stable, without any symptoms of acute coronary syndrome. He underwent catheterization with selective angiography at the age of 8 years, which showed an extremely hypoplastic left coronary artery (LCA) (Figure 2). Left main trunk was 3.1 mm (Z-value 0.94), anterior descending artery was 0.40 mm (Z-value -6.58), and left circumflex artery was 0.57 mm (Z-value -6.19). A careful review of the first angiogram that was performed years earlier showed that the hypoplastic LCA was present but unnoticed. He underwent another coronary angiography when he was 9 years old to check for disease progression. Nitrates were infused during the 2nd session, which ruled out vasospasm and confirmed the diagnosis of HCAD. He has remained on aspirin and anti-hypertensive medication with exercise restriction to prevent ischaemic or arrhythmic events. He is fairly stable and under close observation, with future consideration for implantable cardioverter-defibrillator (ICD) implantation.

Discussion

Congenital anomalies of the coronary arteries affect nearly 1% of the total population.⁴ Although the incidence of HCAD has been reported to be 0.22% in a necropsy study of 224 cases with congenital variations of the coronary arteries,⁵ the true incidence of HCAD in the general population is unknown. Despite its rarity, it is important to suspect HCAD when signs of myocardial ischaemia are present, as the risk of myocardial infarction and sudden cardiac death is high.¹

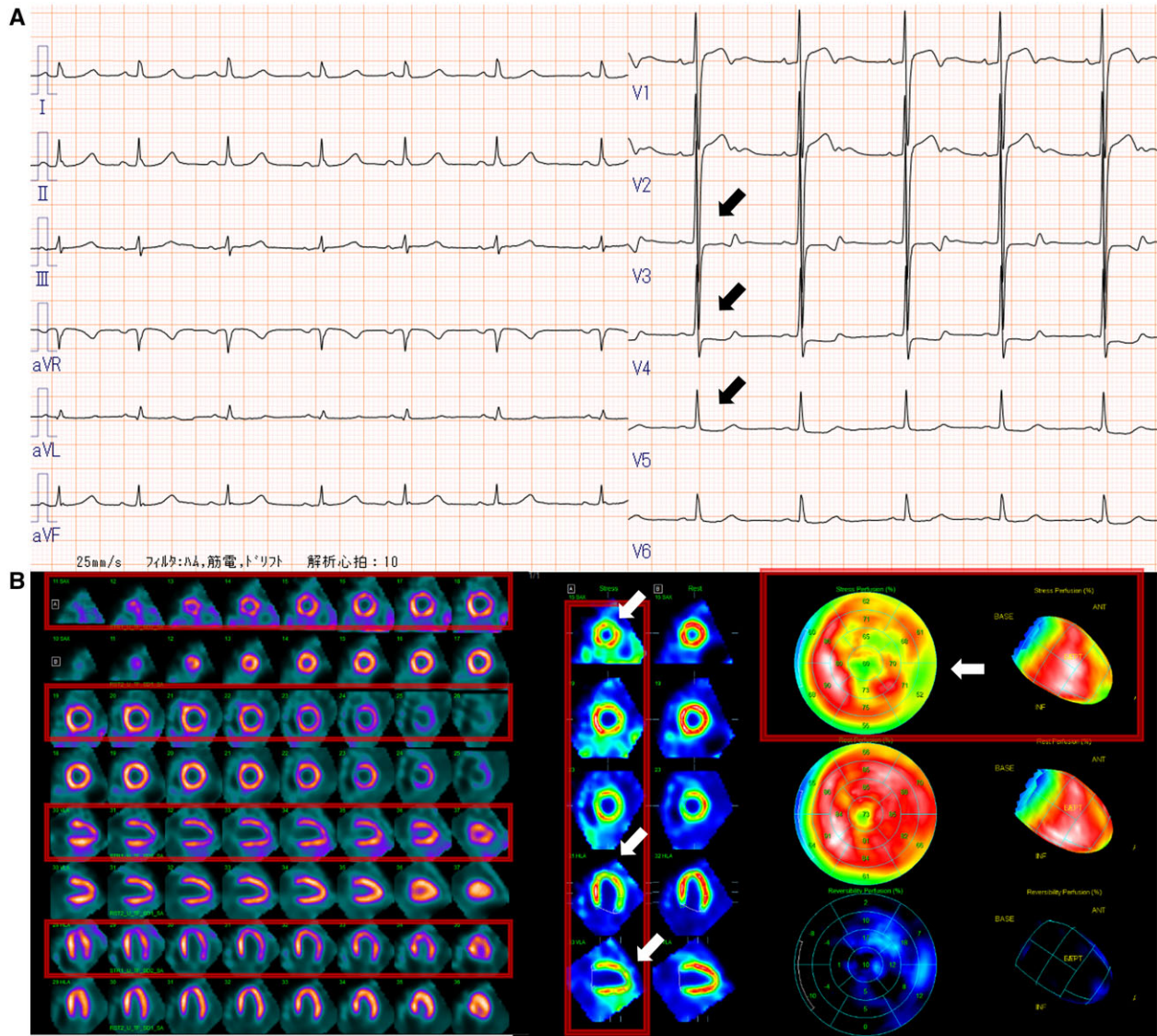


Figure 1 (A) A 12-lead electrocardiogram at rest performed when the patient was 7 years of age showing ST depression on leads V3 to V5. (B) Subsequent scintigraphy showed signs of ischaemia of the left anterior lateral wall and the apex (white arrow). The illustration surrounded in red is the scan performed at stress.

The present case first presented with symptoms of acute cardiac failure in infancy without signs of ischaemia. His first angiogram performed when he was 1 year and 9 months old revealed a hypoplastic LCA, but it was unnoticed because he had a normal coronary artery orifice, and there was no suspicion of coronary artery disease at the time. The initial episode of decreased cardiac function may have resulted from the HCAD, but there were no ST changes on ECG. Despite the ischaemic changes on ECG and scintigraphy, his cardiac function was preserved and no regional wall motion abnormality was observed when he was diagnosed with HCAD at the age of 8 years. We were not able to determine why LVEF decreased when MR was ameliorated. Decrease of LVEF may have been caused by the presence of hypertension. Spontaneous resolution of MR may have affected LVEF by appearance (emptying of LV by MR may result in

better LVEF). As for the coronary artery, there were no obvious collateral arteries from right coronary artery. There is a possibility that some patients with HCAD may not have collateral arteries as in patients with anomalous LCA from the pulmonary artery (ALCAPA).⁶ Unlike patients with ALCAPA, patients with HCAD will have saturated blood perfusion, though they are insufficient. Patients without collateral arteries still may not present symptoms of ischaemia until they reach childhood when their exercise capacity increases. This may explain why our case did not present signs of ischaemia until he became 7 years old.

Hypoplastic coronary artery disease is a form of coronary artery anomaly, but some environmental factors such as hypercholesterolaemia and diet may also be implicated in the obstruction of coronary artery blood flow.³ As the initial presentation was somewhat similar

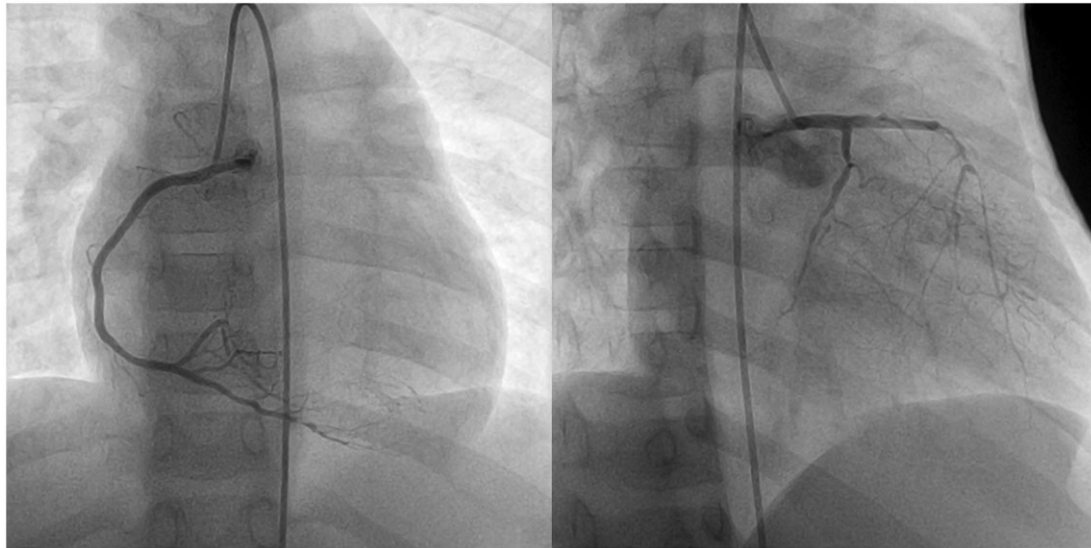


Figure 2 Selective angiography at the age of 8 years revealed extremely hypoplastic left coronary artery while right coronary artery was intact with a mild stenosis at the distal portion. There were no obvious collateral arteries from the right coronary artery to left coronary artery. Left main trunk was 3.1 mm (Z-value 0.94), anterior descending artery was 0.40 mm (Z-value -6.58), and left circumflex artery was 0.57 mm (Z-value -6.19).

to acute myocarditis, the LV dilation and MR may have resulted from myocarditis; however, he was afebrile and no pathological test was conducted to confirm this. Since acute myocarditis has direct and immune-mediated inflammatory effects on the coronary arteries,⁷ it can worsen the coronary artery lesion of HCAD. This may explain the decline in his LV function and its subsequent recovery.

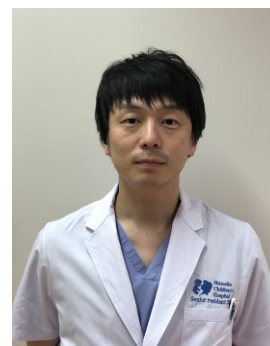
We could not confirm an association between hypertension and HCAD. A review of previous cases reported 17 paediatric cases of HCAD, and only two had concomitant hypertension.³ We considered that it may be a compensatory mechanism to maintain coronary perfusion, similar to hypertension occurring after acute ischaemic stroke⁸; however, this is unlikely because there are barely any reports of this phenomenon in adult patients with acute myocardial ischaemia or other coronary artery anomalies including HCAD. Further studies are warranted to determine if there is any association between HCAD and hypertension. As hypertension is a well-known risk factor for atherosclerosis, our patient received anti-hypertensive medication to maintain his blood pressure below the 90th percentile for age-matched Japanese males. He also received aspirin as recommended for chronic coronary artery syndrome, although lifelong use may be considered at some point.⁹ Although coronary artery bypass is an option for selected patients with HCAD,¹⁰ cardiac transplantation, an extremely limited option in Japan, is the only cure for HCAD. Thus, it is important to avoid factors that can worsen HCAD. In this regard, it is important to restrict physical activity as sudden cardiac death during rigorous exercise has been reported.¹¹ Implantable cardioverter-defibrillator is an option worth considering, although we deferred their placement as paediatric patients may experience inappropriate shocks,¹² and our patient never experienced ventricular arrhythmias. Although ICD is an option, restriction of physical activity may be sufficient for compliant patients. Other conditions such as hypertension and hyperlipidaemia, which can have

additional negative effects on coronary arteries, warrant attention as well.

Conclusion

Although rare, HCAD should be considered when signs of heart failure or myocardial ischaemia are detected; however, signs of ischaemia may not be present initially, and this may mimic acute myocarditis or cardiomyopathy. Close observation and physical activity restriction are necessary to ensure the patient's safety.

Lead author biography



Yuji Doi graduated from Osaka University School of Medicine in 2011. After residency, he trained as a general paediatrician and later as a paediatric cardiologist at Shizuoka Children's Hospital until March 2019. He is currently working at Kurashiki Central Hospital as a board-certified paediatric cardiologist. He has particular interest in arrhythmias and electrophysiology.

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 guidance.

Conflict of interest: None declared.

Funding: None declared.

References

- De Giorgio F, Abbate A, Stigliano E, Capelli A, Arena V. Hypoplastic coronary artery disease causing sudden death. Report of two cases and review of the literature. *Cardiovasc Pathol* 2010;**19**:e107–e111.
- Zugibe FT, Zugibe FT Jr, Costello JT, Breithaupt MK. Hypoplastic coronary artery disease within the spectrum of sudden unexpected death in young and middle age adults. *Am J Forensic Med Pathol* 1993;**14**:276–283.
- Morales R, Bokowski J, Aljemmal S, Murphy J, Bharati S, Abdulla RI. A rare report of hypoplastic coronary arteries and pulmonary veins: a case report and review of the literature. *Pediatr Cardiol* 2020;**41**:1231–1237.
- Villa AD, Sammut E, Nair A, Rajani R, Bonamini R, Chiribiri A. Coronary artery anomalies overview: the normal and the abnormal. *World J Radiol* 2016;**8**:537–555.
- Ogden JA. Congenital anomalies of the coronary arteries. *Am J Cardiol* 1970;**25**:474–479.
- Peña E, Nguyen ET, Merchant N, Dennie C. ALCAPA syndrome: not just a pediatric disease. *Radiographics* 2009;**29**:553–565.
- Woudstra L, Juffermans LJM, van Rossum AC, Niessen HWM, Krijnen PAJ. Infectious myocarditis: the role of the cardiac vasculature. *Heart Fail Rev* 2018;**23**:583–595.
- Semplicini A, Maresca A, Boscolo G, Sartori M, Rocchi R, Giantin V et al. Hypertension in acute ischemic stroke: a compensatory mechanism or an additional damaging factor? *Arch Intern Med* 2003;**163**:211–216.
- Jacobsen AP, Raber I, McCarthy CP, Blumenthal RS, Bhatt DL, Cusack RW et al. Lifelong aspirin for all in the secondary prevention of chronic coronary syndrome: still sacrosanct or is reappraisal warranted? *Circulation* 2020;**142**:1579–1590.
- Casta A. Hypoplasia of the left coronary artery complicated by reversible myocardial ischemia in a newborn. *Am Heart J* 1987;**114**:1238–1241.
- Amabile N, Fraise A, Quilici J. Hypoplastic coronary artery disease: report of one case. *Heart* 2005;**91**:e12.
- Garnreiter JM, Pilcher TA, Etheridge SP, Saarel EV. Inappropriate ICD shocks in pediatrics and congenital heart disease patients: risk factors and programming strategies. *Heart Rhythm* 2015;**12**:937–942.