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Effective myocardial perfusion and concomitant haemodynamic status determine the clinical diversity of anomalous left coronary artery from the pulmonary artery

Amr A. Matoq[1] and Takeshi Tsuda[1,2]

[1]Nemours Cardiac Center, Alfred I. duPont Hospital for Children, Wilmington, DE 19803, USA and [2]Department of Pediatrics, Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA 19107, USA

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Author for correspondence:
T. Tsuda, MD, FAAP, FACC, Nemours Cardiac Center, Nemours/Alfred I. duPont Hospital for Children, 1600 Rockland Rd, Wilmington, DE 19803, USA. Tel: (302) 651-6677; Fax: (302) 651-6601; E-mail: ttsuda@nemours.org

Abstract

Background: Anomalous left coronary artery from the pulmonary artery is a rare congenital heart disease (CHD) with diverse clinical presentations despite the same anatomy. Factors determining this heterogeneous presentation are not well understood. *Method and Results:* We retrospectively investigated 14 patients (12 females) who underwent surgical repair of anomalous left coronary artery from the pulmonary artery. These patients were divided into three groups based upon the severity of initial presentation: (1) severe, life-threatening condition (n = 5), (2) mild-to-moderate distress (n = 6), and (3) asymptomatic (n = 3). All patients presented with left ventricular dilation and retrograde flow in left coronary artery by echocardiogram. Eight patients in (1) and (2) presented with severe left ventricular dysfunction. All but one showed abnormal ECG consistent with myocardial ischemia or infarction. Asymptomatic patients had preserved left ventricular systolic function despite ischemic findings on ECG. In 13 patients after surgical repair, all but one normalised left ventricular geometry and systolic function, suggesting nearly full myocardial recovery upon improvement of myocardial perfusion; 8 patients had residual echogenic papillary muscle with variable degree of mitral regurgitation. *Conclusions* Evidence of myocardial ischemic injury was present in all patients with anomalous left coronary artery from the pulmonary artery regardless of their initial presentation. Retrograde flow in left coronary artery, implying collateral vessel development from right coronary artery to left coronary artery, was noted in all patients, yet only few patients had preserved systolic function at the time of diagnosis. The balance between effective myocardial perfusion and a deleterious fistulous flow provided by these collaterals and the simultaneous haemodynamic status are what determine the clinical diversity of anomalous left coronary artery from the pulmonary artery.

Anomalous left coronary artery from the pulmonary artery is a rare congenital coronary artery anomaly that can cause lethal myocardial infarction in the first year of life if untreated.[1–4] It was first reported in 1885 by Brooks in two cardiac specimens demonstrating a left coronary artery originating from the pulmonary sinus of Valsalva that anastomosed distally with the branches of the aortic coronary arteries.[5] Reported prevalence is approximately 1 in 300,000 live births,[2] which represents 0.25–0.5% of congenital heart disease (CHD).[2,3] Usually, anomalous left coronary artery from the pulmonary artery is an isolated congenital abnormality, but it is occasionally associated with other CHD, including secundum atrial septal defect, primum atrial septal defect, bicuspid aortic valve, patent ductus arteriosus, tetralogy of Fallot, and coarctation of the aorta.[6,7]

The clinical presentation of isolated anomalous left coronary artery from the pulmonary artery is variable. The classic infantile angina first described by Bland et al. consists of paroxysmal attacks of discomfort, tachypnea, and sweating precipitated by nursing.[8] Such symptoms might be misdiagnosed as colic, failure-to-thrive, feeding intolerance, or asthma.[9] Patients with anomalous left coronary artery from the pulmonary artery frequently present with congestive heart failure or cardiogenic shock in early infancy.[3,4,10] On the other hand, some patients with anomalous left coronary artery from the pulmonary artery may be totally asymptomatic during childhood often with an audible heart murmur,[3,11] whereas others present with exercise intolerance, palpitation, anginal chest pain, or even sudden death during adulthood.[11–14] Thus, anomalous left coronary artery from the pulmonary artery encompasses a diverse clinical spectrum from lethal myocardial infarction in early infancy to heart murmur in otherwise asymptomatic children and adults. However, the underlying pathophysiology in which the same anatomical abnormality results in such a diverse clinical spectrum remains poorly understood. The degree of direct myocardial injury and subsequent haemodynamic deterioration may be influenced by certain physiological parameters.

Here, we have studied a series of anomalous left coronary artery from the pulmonary artery patients we experienced in our centre and investigated the possible mechanisms that may be responsible for its clinical diversity.

Patients and methods

Retrospective chart review was conducted for patients with the diagnosis of anomalous left coronary artery from the pulmonary artery at Nemours Cardiac Center, Alfred I. duPont Hospital for Children in Wilmington, DE, from January 1998 to August 2019. The study was approved by the Nemours Institutional Review Board. We obtained demographic and clinical data from the electronic medical record, including the age at initial encounter, sex, signs and symptoms at presentation, initial clinical assessment, chest radiograph, ECG, and echocardiogram. Cardiac catheterisation with coronary angiography was performed in selected cases. Initial hospital management, either in the emergency department or cardiac ICU, was also reviewed.

The ECG was analysed for cardiac rhythm (arrhythmias and conduction abnormalities), myocardial injury (ST-T depression/elevation and abnormal Q waves), and left ventricular hypertrophy. Chest radiograph was examined for the presence of cardiomegaly (cardiothoracic ratio ≥ 0.55) and increased pulmonary vascular and/or interstitial markings. Echocardiogram was examined to assess (1) presence of retrograde filling of left coronary artery into main pulmonary artery, (2) Z score of left ventricular internal diameter in diastole, (3) left ventricular systolic function by fractional shortening, (4) degree of mitral regurgitation, and (5) presence of echogenic papillary muscle. Left ventricular dimension was graded as mild (left ventricular internal diameter in diastole Z score: >2 and ≤4), moderate (>4 and ≤6), or severe (>6). Left ventricular systolic function was graded as normal (fractional shortening ≥ 30%), mildly decreased (≥25% and <30%), moderately decreased (≥20% and <25%), or severely decreased (<20%). The degree of mitral regurgitation was graded based upon % area of colour Doppler-generated mitral regurgitation central jet over total LA area in apical four-chamber view: mild (<20%), moderate (≥20% and <40%), or severe (≥40%).

Results

Seventeen patients with anomalous left coronary artery from the pulmonary artery were identified in our clinical database. Three patients were excluded because of lack of sufficient pre-operative and operative records. Clinical data of 14 patients are summarised in Table 1. The age of diagnosis ranged from 1.5 months to 16 years (median age: 2 months) with female predominance (86%; 12/14). We divided our 14 patients into 3 groups based upon the clinical severity at the time of diagnosis: (1) severe, life-threatening condition (n = 5), (2) mild-to-moderate distress (n = 6), and (3) asymptomatic (n = 3).

In group 1, all five patients required pre-operative intravenous inotropic infusion for cardiogenic shock and mechanical ventilation via endotracheal tube for respiratory failure. Two had cardiopulmonary resuscitation for cardiac arrest at home; one was successfully defibrillated by automated external defibrillator with documented ventricular fibrillation. Patient #3 presented with simultaneous group B streptococcal meningitis and septic shock and died on post-operative day 39 after surgical repair of anomalous left coronary artery from the pulmonary artery. All patients in this group had prominent cardiomegaly and increased pulmonary interstitial markings consistent with pulmonary edema on chest radiograph as well as ST-T segment depression and/or abnormal Q waves in lead I and aVL indicating myocardial ischemic insults. Echocardiogram showed moderate or severe left ventricular systolic dysfunction and severe left ventricular dilation in all cases.

All patents in group 2 (ages ranging from 1.3 months to 16 years; median age of 2.5 months) had respiratory symptoms and/or feeding difficulties at the time of diagnosis, except the patient #11, who had mitral valve surgery at 7 years of age (with unrecognised anomalous left coronary artery from the pulmonary artery) and who developed exercise intolerance at age 16 years; she was misdiagnosed as having cardiomyopathy. Patient #10 was in the process of diagnostic workup by gastroenterology for conjugated hyperbilirubinemia when he presented to the emergency department with irritability and fussiness. At the emergency department, his chest radiograph showed cardiomegaly, which triggered cardiac evaluation, and subsequently, the diagnosis of anomalous left coronary artery from the pulmonary artery was made. Post-operatively, genetic workup confirmed Alagille syndrome (JAG1 mutation). All patients in this group had cardiomegaly on chest radiograph, abnormal ECG findings, and mild-to-severe left ventricular systolic dysfunction by an echocardiogram. All patients presented with varying degrees of left ventricular dilation (Table 1) except patient #11, which might be explained by the fact that she had mitral stenosis at the time of anomalous left coronary artery from the pulmonary artery diagnosis secondary to her previous mitral valve surgery.

Group 3 included three asymptomatic patients (ages of 9 months, 14 months, and 3.4 years) referred to the cardiology clinic for evaluation of heart murmur. The diagnosis of anomalous left coronary artery from the pulmonary artery was made by an echocardiogram with retrograde main pulmonary artery filling through anomalous left coronary artery. All had cardiomegaly on pre-operative chest radiograph. Two patients had abnormal ECG (abnormal Q wave in I and aVL) suggestive of previous ischemic myocardial insults and left ventricular dilation by echocardiogram. However, all three patients showed preserved left ventricular systolic function by echocardiogram.

The diagnosis of anomalous left coronary artery from the pulmonary artery was made solely by echocardiogram in 10 cases. All patients, regardless of the clinical severity, showed retrograde filling of anomalous left coronary artery into main pulmonary artery and variable degree of left ventricular dilation, whereas only asymptomatic patients had normal left ventricular systolic function. Mitral regurgitation was present in 12 patients, the degree of which did not well correlate with the clinical severity. Four patients in groups 1 and 2 underwent pre-operative cardiac catheterisation with coronary angiogram to confirm the diagnosis (Table 2). All four patients showed a dilated right coronary artery with collateral connections to the left coronary artery system filling retrograde into the main pulmonary artery. The degree of opacification of main pulmonary artery was variable. The left ventricular end-diastolic pressure was elevated in three patients.

All our patients underwent surgical correction of anomalous left coronary artery from the pulmonary artery; three patients underwent creation of an aortopulmonary window and an intrapulmonary baffle reconstruction (Takeuchi procedure), one underwent subclavian turn-down anastomosis to left coronary artery, and the rest had direct left coronary artery reimplantation to aortic position. None underwent ligation of anomalous left coronary artery from the pulmonary artery. There was no post-operative mortality except for one patient who died of intractable

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Table 1. Initial clinical presentation of 13 patients with anomalous left coronary artery from the pulmonary artery

						Echocardiogram			
Pt	Age (mo)	Sex	Clinical presentation	CXR¶	ECG	LV dilatation	LV dysfunction	MR	Echogenic PM
1	2	F	Cardiogenic shock Respiratory failure, intubation	Cardiomegaly Pulmonary oedema	ST-T abnormality T wave inversion, LVH	Moderate to severe‡	Severe‡	Moderate	Y
2	2	F	Cardiogenic shock Apnea, CPR at home Respiratory failure, intubation	Cardiomegaly Pulmonary oedema	Abnormal Q wave: I and aVL T wave inversion NSVT (started on lidocaine)	Severe 7.4†	Severe 15%*	Mod to severe	Y
3	2	F	Cardiogenic shock Respiratory failure, intubation Sepsis/GBS meningitis	Cardiomegaly Pulmonary oedema	ST-T abnormality T wave inversion: inferior leads LVH	Severe 8.4†	Severe 11%*	None	N
4	1.5	F	Cardiogenic shock cardiac arrest (VF) Respiratory failure, intubation	Cardiomegaly Pulmonary oedema	Abnormal Q wave: I and aVL T wave inversion: V5 and V6 VF/cardiac arrest PVCs (started on lidocaine)	Severe 9.4†	Severe 9%*	Mild to mod	Y
5	3	F	H/O feeding difficulty Respiratory failure, intubation	Cardiomegaly	LVH/RVH T wave inversion in V5, V6 Left atrial enlargement	Severe 11.9†	Severe 11.9%*	Mild to mod	Y
6	3	F	Cough, retractions Feeding difficulty	Cardiomegaly	T wave inversion LVH	Moderate‡	Moderate‡	Moderate	Y
7	2	M	Wheezes, respiratory distress Gallop rhythm	Cardiomegaly	T wave inversion LVH	Mild 3.5†	Severe 19%*	Mild	N
8	1.3	F	Wheezes, respiratory distress	Cardiomegaly Pulmonary oedema	Abnormal Q wave: aVL T wave inversion: V5 and V6	Moderate 4.9†	Severe 17%*	Mild to mod	N
9	18	F	Colic, feeding intolerance Heart murmur	Cardiomegaly	Abnormal Q wave: aVL T wave inversion: I and aVL LAD	None 1.8†	None 38.5%*	Moderate	Y
10	1.6	F	Irritability, fussiness, jaundice Heart murmur	Cardiomegaly	Abnormal Q wave: aVL Non-specific ST-T abnormality LAD	Mild 3.2†	Severe 18%*	<Mild	Y
11	203	F	Exercise intolerance, chest pain Misdiagnosed as cardiomyopathy MV surgery at 7 years of age	Cardiomegaly	T wave inversion: V5 and V6 Ectopic atrial rhythm	None 1.4†	<Mild 29%	N/A (MS after MV surgery)	N
12	41	F	Heart murmur	Cardiomegaly	Normal	None 1.8†	None 35%*	Mild	Y
13	14	F	Heart murmur	Cardiomegaly	Abnormal Q wave: I, aVL LVH	Mild 2.2†	None 36.5%*	Moderate	N
14	9	M	Heart murmur	Cardiomegaly	Abnormal Q wave: I, aVL LVH, RVH	Severe 7†	None 39%*	severe	Y

CPR = cardiopulmonary resuscitation; CXR = chest radiograph; LAD = left axis deviation; GBS = group B streptococcal; LV = left ventricular; LVH = left ventricular hypertrophy; MR = mitral regurgitation; MS = mitral stenosis; MV = mitral valve; NSVT = non-sustained ventricular tachycardia; PM = papillary muscle; PVCs = premature ventricular contractions; RVH = right ventricular hypertrophy; VF = ventricular fibrillation.
¶Cardiomegaly is defined as cardiothoracic ratio of >0.55. Pulmonary oedema is defined as increased pulmonary interstitial marking.
‡Quantitative value not available.
†LV end-diastolic diameter Z scores (<2: normal, ≥2 and <4: mild, ≥4 and <6: moderate, and ≥6: severe).
*Assessed by LV fractional shortening (≥30%: normal, <30% and ≥25: mild, <25% and ≥20: moderate, and <20%: severe).

Table 2. Cardiac catheterisation and coronary angiography

Pt	Indications	Haemodynamics			Angiographic findings
		LVEDP*	Qp/Qs	pMPA*	
3	Confirm coronary anatomy Assess LV dysfunction	21			Mildly dilated RCA, small collaterals to LCA, and incomplete opacification of MPA
8	Confirm coronary anatomy	18			Dilated RCA, collateral flow into LCA, and retrograde filling of MPA
9	Confirm coronary anatomy	15	1.2	27/12 (19)	Dilated RCA with extensive collateral to the LCA and retrograde filling into MPA with complete opacification of MPA
10	Confirm coronary anatomy				Dilated RCA with retrograde filling of the LCA from collaterals from the RCA with faint contrast flow into MPA. No LCA seen originating from the aortic root

LCA = left coronary artery; LVEDP = left ventricular end-diastolic pressure; MPA = main pulmonary artery; pMPA = main pulmonary arterial pressure (mmHg); Pt = patient; Qp/Qs = pulmonary blood flow/systemic blood flow; RCA = right coronary artery.
*presented as mmHg.

Table 3. Follow-up of symptoms, ECG, and echocardiogram after surgical repair

Pt	Years*	Symptoms	ECG	Echocardiogram				
				LVIDd (cm)	Z score	%FS	MR	Echogenic PM
1	12.8	Asymptomatic	Normal	4.9	0.86†	34†	Trivial†	N†
2	16.4	Asymptomatic	RAD; Otherwise normal	5.6	2.6†	38.7†	Mild†	Y
3	0.1	Death§	N/A					
4	1	Asymptomatic**	RAE, Non-specific T wave changes; Otherwise normal	2.9	2.3†	40.9†	Moderate†	Y
5	0.5	L-VAD/Listed***	LVH; Q wave in aVL, T wave inversion.	4.6	11	9.3	Trivial	Y
6	14.6	Asymptomatic	LAE; Otherwise normal	4.6	0.65†	37.7†	Mild†	Y
7	15.6	Asymptomatic	LAD; Otherwise normal	5.1	−0.04	43.9†	None†	N
8	18.5	Asymptomatic	LAE; Otherwise normal	4.8	0.03†	36.2	Trivial†	N
9	2.3	Asymptomatic	LAE; LAD; Otherwise normal	3.7	1.5	45.7†	Mild to mod†	Y
10	3.8	Asymptomatic	RVH, Otherwise normal	3.5	1.2†	34.4†	Trivial	Y
11	N/A	N/A‡						
12	6.7	Asymptomatic	Normal	4.8	0.53†	34.3	Trivial†	Y
13	0.03	Asymptomatic	Normal	3.1	1.5†	32.6	Moderate	Y¶
14	0.2	Asymptomatic	LVH/RVH/BAE	3.3	2†	35.2	Moderate†	Y

%FS = % fractional shortening; BAE = biatrial enlargement; GBS = group B streptococcal; LAD = left axis deviation; LAE = left atrial enlargement; LVH = left ventricular hypertrophy; L-VAD = left ventricular assist device; LVIDd = left ventricular internal diameter in diastole; MR = mitral regurgitation; PM = papillary muscle; Pt = patient; RAE = right atrial enlargement; RVH = right ventricular hypertrophy.
N/A = not available.
*Years after surgery.
†Improvement from the initial presentation.
§Presented with GBS meningitis.
**Had mitral valvuloplasty 6 month after initial repair for MR with preserved LV function.
***Required L-VAD at 2 months post-operatively as a bridge to transplant.
‡Transferred back to the referring institution after the discharge.
¶Not notified at the initial presentation.

group B streptococcal sepsis (as described earlier). One patient (patient #5) had persistent left ventricular systolic dysfunction and dilatation despite continuous inotrope support who was listed for heart transplant and required left ventricular assist device as a bridge to transplant. The patient with Alagille syndrome (patient #10) underwent surgical pulmonary arterioplasty 2 years after the initial surgical repair. Patient #4 underwent mitral valve repair for worsening mitral regurgitation and congestive heart failure at 6 months from the original surgery despite full recovery of left ventricular systolic function.

Follow-up data were not available on patient #11. Twelve patients had follow-up ECG and echocardiogram after surgical repair of anomalous left coronary artery from the pulmonary artery (0.7–18.5 years after surgery, median 6.7 years) (Table 3). Except patient #5 who is on left ventricular assist device awaiting heart transplant, all other 11 patients showed normal left ventricular systolic function with no focal left ventricular wall motion abnormality or abnormal Q waves in ECG, suggesting high plasticity of the young ventricular myocardium against initial myocardial ischemic injury. Ten patients showed distinct reduction in left

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ventricular chamber size (83%) from the initial presentation (Table 1). Spontaneous improvement of mitral regurgitation was noted in nine patients (75%), whereas nine patients continued to have echogenic papillary muscles indicating myocardial scar formation.

Discussion

Variable clinical presentation of anomalous left coronary artery from the pulmonary artery

In our 14 anomalous left coronary artery from the pulmonary artery patients, we encountered the following 3 major findings. First, regardless of the severity of clinical presentation, all patients presented with cardiomegaly on chest radiograph as well as variable degree of left ventricular dilation, as was reported previously.[4,10,15,16] Cardiomegaly primarily represents left ventricular dilatation due to direct myocardial ischemic injury, compensatory response to left ventricular systolic dysfunction, and/or increased volume overload due to left-to-right shunt via collateral vessels and mitral regurgitation. Second, all patients except one (patient #12) initially presented with clinical evidence of myocardial ischemic injury regardless of the severity. An ECG abnormality was noted even in two asymptomatic patients (group 3). Third, all three asymptomatic patients revealed preserved left ventricular systolic function at the time of diagnosis. Nevertheless, they all had retrograde filling of left coronary artery by echocardiogram, suggesting that collateral flow to left coronary artery in these cases provided more effective myocardial perfusion evident by preserved left ventricular systolic function rather than fistulous shunt flow responsible for "coronary steal". Abnormal Q waves were noted in two of these three patients with preserved left ventricular systolic function, which may indicate a coexisting process of myocardial ischemic insults with simultaneous myocardial regeneration.

Based upon these findings, all anomalous left coronary artery from the pulmonary artery patients developed variable degrees of ischemic myocardial injury with consequent left ventricular dysfunction and dilatation but demonstrated improved left ventricular systolic function with normalised left ventricular volume and recovered ventricular wall thickness after recanalisation surgery in majority of cases, suggesting a favourable myocardial regeneration that reverses myocardial loss without significant scar formation.[17,18]

What factors may affect the extent of initial myocardial ischemic injury?

Collateral vessel formation or arteriogenesis is a natural postnatal developmental process in anomalous left coronary artery from the pulmonary artery, as collateral vessel development depends on a pure shear stress-induced phenomenon and is not a result of myocardial ischemia.[19–21] Although a lack of collateral development causes poor prognosis in cases of anomalous left coronary artery from the pulmonary artery,[22] intercoronary collaterals between right coronary artery and left coronary artery induce both positive and negative effects on anomalous left coronary artery from the pulmonary artery, a true myocardial perfusion from collateral vessels to myocardial capillary network into coronary sinus and a fistulous flow via collateral vessels draining into main pulmonary artery responsible for coronary steal phenomenon, respectively.[4] Effective angiogenesis sprouting from the collateral vessels to the ischemic myocardium is necessary to enhance the former process.[23] In newborn hearts, circulating macrophages are known to contribute to myocardial regeneration by promoting angiogenesis rather than inducing scar formation.[24,25]

Providing effective coronary blood flow is a critical determinant in protecting and recovering ischemic myocardium from further insults. Main pulmonary arterial pressure is one important factor that influences the clinical presentation of anomalous left coronary artery from the pulmonary artery. As pulmonary vascular resistance falls, main pulmonary artery pressure decreases, and the augmented coronary blood flow via collateral vessels favours draining into left coronary artery as an ineffective fistulous flow rather than providing effective myocardial perfusion. Surgical left coronary artery ligation used to be a treatment option for anomalous left coronary artery from the pulmonary artery in the past as it worked simply by eliminating this coronary steal.[4] Pulmonary arterial pressure is also influenced by associated cardiovascular conditions including patent ductus arteriosus, ventricular septal defect, pulmonary hypertension, and branch pulmonary stenosis, which have been reported to alter the presentation.[15,26–28] Demonstration of this theory is clear when anomalous left coronary artery from the pulmonary artery is associated with patent ductus arteriosus that is responsible for persistent elevation of main pulmonary artery pressure and subsequently for higher anomalous left coronary artery perfusion pressure. Surgical ligation of patent ductus arteriosus suddenly decreased main pulmonary artery pressure, unmasking the undiagnosed anomalous left coronary artery from the pulmonary artery.[26,27] After patent ductus arteriosus ligation, the transient left ventricular dysfunction due to increased afterload[29,30] can increase myocardial oxygen demand and thus lead to acute ischemic myocardial injury in combination with reduced effective myocardial perfusion.[26,27]

Underlying pathophysiology of anomalous left coronary artery from the pulmonary artery

Factors that increase myocardial oxygen demand may have a role in the onset of presentation. Increased left ventricular wall stress by ventricular dilation and wall thinning increases myocardial oxygen demand.[31] Mitral regurgitation induced by ischemic injury of papillary muscle (evident by increased echogenicity) increases left ventricular volume overload but simultaneously reduces pressure overload. The degree of mitral regurgitation did not correlate well with the clinical severity in our cases. Because myocardial oxygen supply is at risk in anomalous left coronary artery from the pulmonary artery patients, even subtle increase in myocardial oxygen demand may induce supply–demand mismatch, responsible for progressive clinical deterioration. Other factors that may increase myocardial oxygen demand include fever, infection, anemia, and crying and its associated tachycardia. Patients presenting with upper and lower respiratory tract infection have been reported in cases of anomalous left coronary artery from the pulmonary artery.[9,10]

Ischemic myocardial injury is inevitable in anomalous left coronary artery from the pulmonary artery, as all our symptomatic patients (groups 1 and 2) and two asymptomatic patients (group 3) presented with ECG abnormality suggestive of ischemic myocardial injury. However, the majority of patients who presented with myocardial infarction and severe dilated cardiomyopathy completely recover left ventricular systolic function after coronary revascularisation surgery,[17,18,32–35] consistent with our current findings (Table 3). Myocardial regeneration after coronary revascularisation surgery is evident by normalisation of left ventricular dilatation, systolic dysfunction, and ECG findings of myocardial infarction. Recovered ventricular wall thickness and systolic

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function by enhanced myocardial regeneration may reduce ventricular wall stress and thus ameliorate negative myocardial oxygen balance, which promotes further tissue replenishment from the initial ischemic injury. It is possible that myocardial regeneration starts even before surgical repair, and that the regeneration and ongoing ischemia may coexist. This is supported by the evidence of ischemia on the ECG of older asymptomatic patients with preserved left ventricular systolic function.

The balance between myocardial oxygen supply and demand in left ventricular myocardium determines the overall clinical presentation of anomalous left coronary artery from the pulmonary artery. An effective coronary flow distribution to left ventricular myocardium is determined by collateral vessel formation (arteriogenesis), angiogenesis, and main pulmonary artery pressure in anomalous left coronary artery from the pulmonary artery, not merely by the presence of retrograde flow in left coronary artery. Concomitant haemodynamic status is another important determinant that not only influences myocardial oxygen supply through effective myocardial perfusion by modulating main pulmonary artery pressure, but also alters myocardial oxygen demand by affecting left ventricular volume loading status and heart rate.

This study is limited by its retrospective nature and the small sample size in a single centre. In addition, we have not demonstrated the difference between effective myocardial perfusion and ineffective fistulous flow via collateral vessels, but left ventricular systolic function can be used as a surrogate for adequate myocardial perfusion. We were not able to show the direct evidence of cardiomyocyte proliferation or angiogenesis in our patients, but it is almost impossible (and not ethical) to obtain myocardial samples from critically sick infants. However, we did observe spontaneous improvement of left ventricular dimension, wall thickness, and systolic function in most of the anomalous left coronary artery from the pulmonary artery patients as indirect evidence of myocardial regeneration. Lastly, the underlying mechanism of collateral vessel formation (arteriogenesis) in anomalous left coronary artery from the pulmonary artery has not been established, which is a different condition from a conventional coronary steal model of vascular stenosis/obstruction.[36,37]

Conclusion

A wide clinical spectrum is expected in patients with anomalous left coronary artery from the pulmonary artery. The mere presence of intercoronary collaterals does not determine the severity of anomalous left coronary artery from the pulmonary artery, but rather the net balance between effective perfusion and fistulous shunt flow is primarily responsible for the pathophysiology of anomalous left coronary artery from the pulmonary artery. The coexisting increased haemodynamic workload has a negative impact on ischemic left ventricular myocardium by further exacerbating this balance. Myocardial regeneration may help recover the initial myocardial ischemic injury by reducing the negative oxygen supply–demand balance in the damaged myocardium, which is unique in anomalous left coronary artery from the pulmonary artery when compared with other coronary artery diseases.

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Conflicts of Interest. None.

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