IMAGES in PAEDIATRIC CARDIOLOGY

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Abstract

Background

Infants with critical left sided obstructive lesions usually present with left ventricle dysfunction and pulmonary arterial hypertension (PAH). Left ventricular dysfunction and pulmonary artery pressures usually normalize after relief of obstruction.In some,PAH persists despite adequate relief of obstruction.

Patients and Methods

We retrospectively reviewed records of infants (less than 3 months) who underwent intervention for left sided obstruction (n=50) over four years (May 2012 –May 2016).

Result

We report four infants who had persistent of PAH despite relief of left sided obstruction. The causes of PAH were found to be high left ventricular end diastolic pressure(n=1), severe hypoplasia of pulmonary veins (n=1), stenosis of the lower branch of the right pulmonary artery (n=1) and non-regression of pulmonary vascular resistance (n=1).

Conclusion

That persistence of PAH after relief of obstruction should be investigated and other, less common causes should be sought.

MeSH: aortic stenosis, coarctation of aorta, LV dysfunction, pulmonary arterial hypertension

Introduction

The outcome for neonates born with critical left sided obstructive lesions has significantly improved over the last 2 decades, but long term data is not available due to high attrition rates.[1] In a study from 24 institutions ranging between 1994 to 2000 in neonates with critical aortic (AS) stenosis, data showed 77% survival at 3 months of age and 70% at 5 years after biventricular repair (n=116).[2] In a recently reported surgical series of 84 infants with aortic stenosis, the survival rate was 87% at 5 years and 85 % at 15 years. However this study had a high rate of re-intervention including aortic valve replacement, and consequently suggested reconsideration of balloon valvuloplasty as an initial strategy.[3] A study by Burch et al[1] found that persistence of PAH after relief of obstruction was one of the important causes of late morbidity and mortality.

Here we report four infants in whom PAH persisted after adequate relief of left sided obstruction and no significant aortic regurgitation. None of the patients had features of endocardial fibroelastosis.

Materials and Methods

We retrospectively reviewed clinical, echocardiography and cardiac catheterization data of neonates and small infants (n=50,age 2 days-3months, mean 30 days) who had undergone intervention for left ventricular outflow tract obstruction (LVOTO) over the last four years (May 2012 –May 2016) at our institute.

Various interventions done to relieve left ventricular outflow tract obstruction. These were:
1. Balloon aortic valvotomy n=11,
2. Balloon dilatation of aortic valve and coarctation of aorta n=2,
3. Balloon dilatation of coarctation of aorta n=7,
4. Surgical correction of coarctation of aorta n=30.

As per protocol, balloon dilatation is the preferred modality intervention in children with isolated severe valvular aortic stenosis. None of the infants underwent open surgical valvotomy, aortic valve replacement or a Ross procedure.

Definition of PAH: The definition of primary pulmonary hypertension in children is the same as for adult patients. It is defined as a mean pulmonary artery pressure ≥25 mmHg at rest or ≥30 mmHg during exercise, with a normal pulmonary artery wedge pressure and the absence of related or associated conditions.

In all infants, hemodyanamic assessment was initially done by echocardiography. In infants undergoing catheter intervention, pulmonary artery pressures were also documented by right heart catheterization. Post relief of LVOTO, pulmonary artery systolic pressure (by tricuspid regurgitation jet) of more than 75% of systemic arterial pressure was taken as severe PAH (n=4). All these infants except one underwent cardiac catheterization for hemodyanamic assessment. At the time of presentation, all babies had left ventricular dysfunction (ejection fraction 10-40%, mean 30%) and PAH (pulmonary artery systolic pressure 40-70 mmHg calculated by tricuspid regurgitation peak gradient).
After successful intervention, while left ventricular ejection fraction normalized in all, pulmonary artery pressure remained elevated in 4 of these infants (8%).

Persistence of PAH in these infants was found to be due to high left ventricular end-diastolic pressure (LVEDp) (n=1), stenosis of the lower branch of the right pulmonary artery (n=1), pulmonary vein hypoplasia (n=1) and nonregression of pulmonary vascular resistance (n=1).

Case descriptions:

Case 1: Forty-five day old male infant, presented with features of congestive cardiac failure. Echocardiography showed critical coarctation of the aorta (peak gradient across aortic arch 35 mmHg with pandiastolic spilling), severe left ventricular dysfunction (LVEF-25-30%), fossa ovalis ASD (5mm) with left to right shunt, mild TR with peak gradient of 70mmHg, normal connecting pulmonary veins and confluent and dilated pulmonary arteries. There was a bicuspid aortic valve and mild aortic stenosis (peak/mean gradient across aortic valve=23/15 mmHg). The child underwent balloon dilatation of coarctation of aorta successfully.

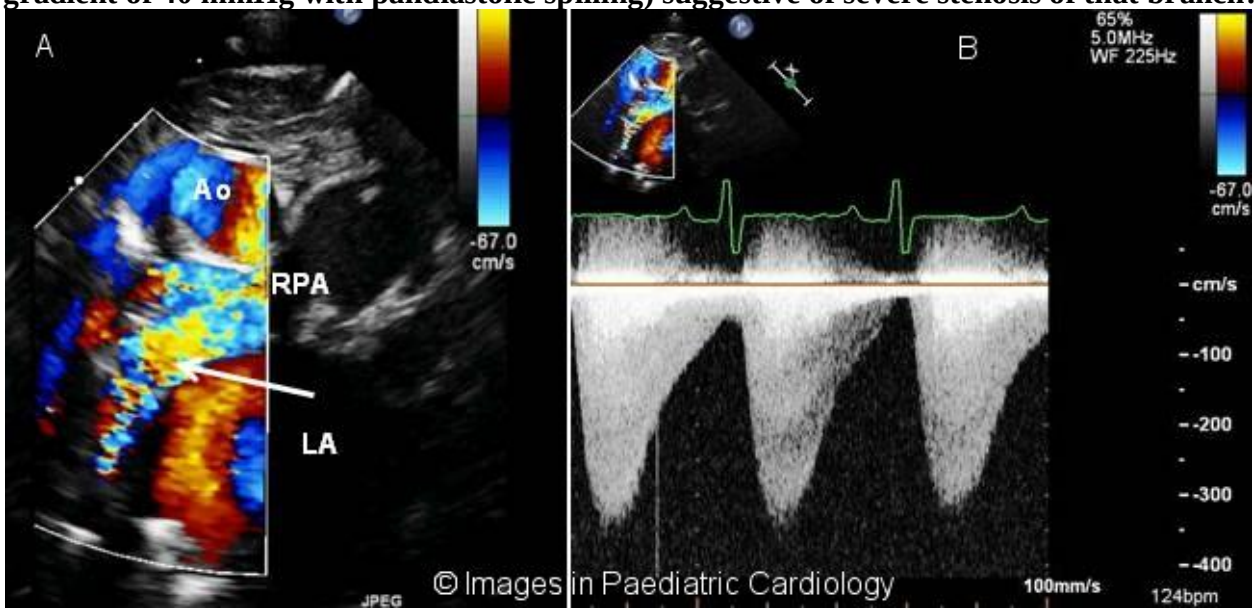
Post balloon dilatation of coarctation, catheterization data and echocardiography showed high right ventricular pressure despite the absence of significant gradient across the aortic valve and aortic arch (table 1), with improvement in left ventricular ejection fraction (LVEF 45%).

Table 1: Hemodynamic data of case 1. Data showed persistence of pulmonary arterial hypertension after relief of aortic stenosis

	Basal pressure(mmHg)			Post Balloon pressure(mmHg)		
Site	Systolic	Diastolic	Mean	Systolic	Diastolic	Mean
RA	a12	V8	8	a8	v6	5
RV	68	8		55	6	
PA	65	32	43	50	30	38
LV	120	22		104	15	
AAO	105			95	60	73
DAo	75	64	69	90	58	72

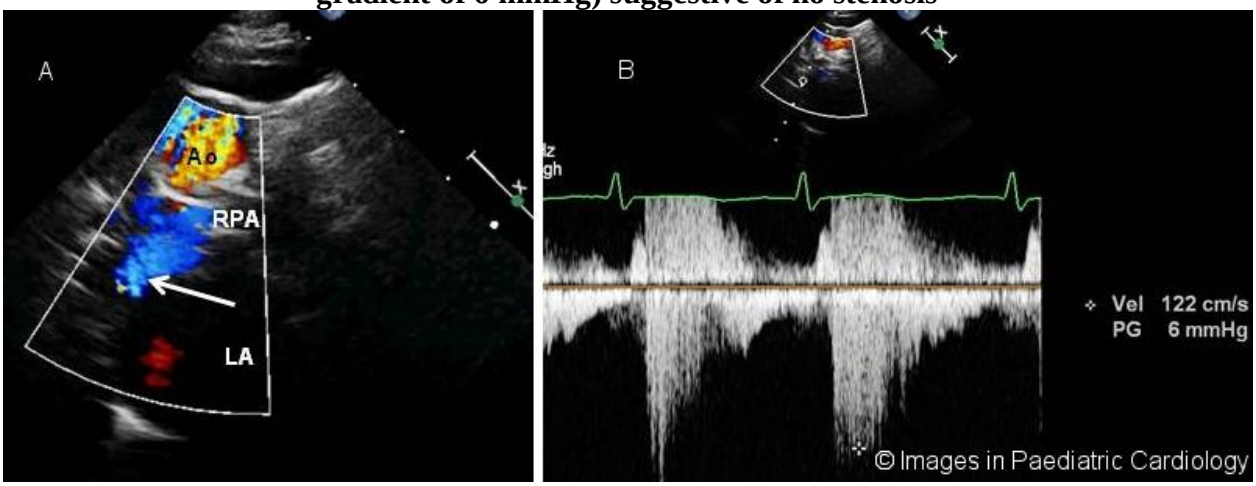
Echocardiography was reviewed again in detail and showed confluent and dilated central pulmonary arteries and stenosis of the lower branch of the right pulmonary artery (gradient 40mmHg with pandiastolic spilling - figure 1a,1b).

Figure 1a: Suprasternal short axis view with color Doppler interrogation showing mosaic flow in lower branch of right pulmonary artery (arrow) suggestive of stenosis. 1b: Continuous wave Doppler interrogation of lower branch of RPA showing velocity of 316 cm/sec (peak gradient of 40 mmHg with pandiastolic spilling) suggestive of severe stenosis of that branch.



Isolated branch pulmonary artery stenosis in isolation might not be responsible for severe PAH but was definitely contributing to high pulmonary artery pressures. The causes of persistence of PAH after relief of LVOTO could be a combination of pulmonary venous hypertension and branch pulmonary artery stenosis. As the child was clinically stable, he was discharged on a once on daily dose of diuretic (frusemide). Follow up after three months showed severe aortic valve stenosis and restenosis of a dilated coarctation segment. The child underwent balloon dilatation of the aortic valve, the coarctation and the lower branch of right pulmonary artery, with success. Post procedure echocardiography showed normalization of RV pressure (TR gradient 25 mmHg) with laminar flow in the right pulmonary artery branch (figure 2a,b). The child has been well since.

Figure 2a: Post balloon dilatation of lower branch of right pulmonary artery, color Doppler interrogation showing laminar flow (arrow) suggestive of normal pattern. 2b: Continuous wave Doppler interrogation of lower branch of RPA showing velocity of 122 cm/sec (peak gradient of 6 mmHg) suggestive of no stenosis



Case 2: Fifteen days old male neonate, birth weight of 2.8 Kg, was brought to emergency with severe respiratory distress and features of congestive cardiac failure. Echocardiography showed critical aortic stenosis, left ventricular hypertrophy, severe left ventricular dysfunction (EF 15%), and severe PAH (TR gradient 80 mmHg). The left ventricle was apex forming but the mitral valve annulus had a Z score of minus 2.34 (absolute value 8 mm).

Balloon dilatation of the aortic valve was done successfully. Post balloon dilatation echocardiography showed no significant gradient across the aortic valve (mean gradient 10mmHg), mild aortic regurgitation, normal LV systolic function (EF 58%), but persistence of PAH (TR gradient 75 mmHg). The baby was clinically stable and was discharged with regular cardiology follow up. In view of persistence of PAH, cardiac catheterization was done 6 months post balloon dilatation and this showed high LV end-diastolic pressure (LVEDP 18-20mmHg), high pulmonary capillary wedge pressure with no transmitral gradient (table 2).

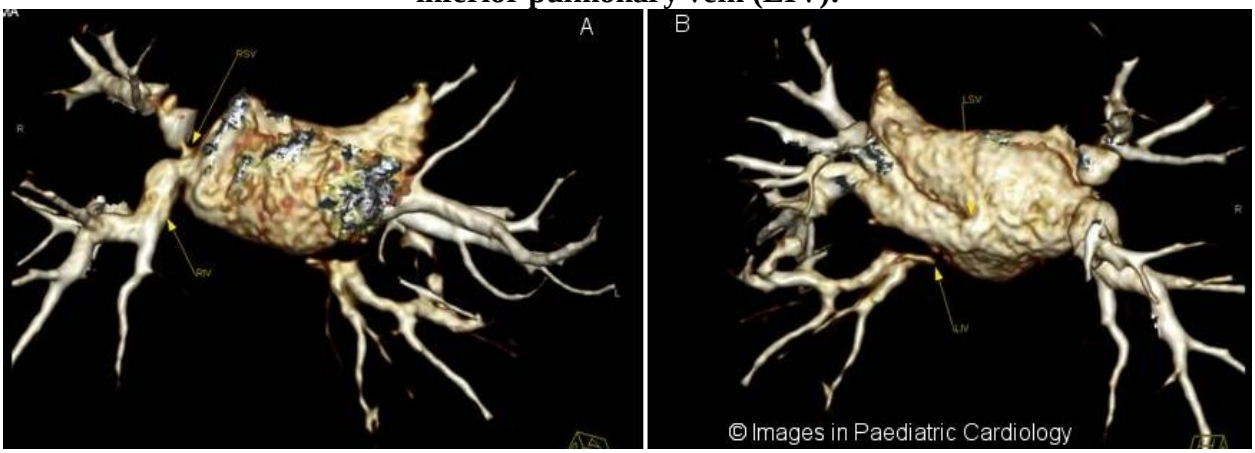
Table 2: Hemodyanamic data of case 2. Data showed no significant gradient across aortic valve, very high pulmonary capillary wedge and LVEDP.

Site	Systolic (mmHg)	Diastolic (mmHg)	Mean (mmHg)
Ao	84	48	60
RV	80	8	
PA	75	30	45
LV	98	18	
PCW	A20	V15	16

The child was started on oral diuretics and a pulmonary vasodilator (sildenafil). He is now 4 years old but failing to thrive (weight 15 kg, minus 2-3 standard deviation). On echocardiography, the right ventricle is dilated and apex forming, mitral annulus 13 mm (Z score minus 1.5) along with persistence of severe PAH and LV diastolic dysfunction.

Case 3: A one year old female child, weighing 6 kg, was brought to emergency with wheezing and respiratory distress. There was a history of multiple such episodes in the past. The child had undergone balloon dilatation of coarctation of the aorta in the neonatal period in another hospital and was on a pulmonary vasodilator (sildenafil) in view of persistence of PAH. After stabilization, echocardiography evaluation at our centre revealed a well opened dilated coarctation segment (gradient 12 mmHg, no diastolic spilling), tiny patent ductus arteriosus (PDA) with left to right shunt, normal left ventricular function and dimensions, dilated right atrium and ventricle, mild TR (gradient 73 mmHg), and turbulent flow in right and left pulmonary veins suggestive of stenosis. On continuous wave Doppler interrogation, there was continuous pattern with a mean gradient of 6 mmHg. CT pulmonary angiography was done to define the pulmonary veins. There was severe, long segment stenosis of the left lower pulmonary vein with hypoplasia, along with severe stenosis of the right upper pulmonary vein (figure 3a, b). Pulmonary veins stenosis was the factor responsible for persistence of PAH.

Figure 3: Three Dimensional reconstruction of CT angiography of pulmonary veins showing: A. Severe stenosis of right superior pulmonary vein (RSV) and B. Severe stenosis of left inferior pulmonary vein (LIV).



This stenosis of the pulmonary veins may be missed at the time of initial evaluation due to high LVEDP and venous hypertension with critical coarctation of aorta. The family was given the option of cardiac catheterization with high risk balloon dilatation/stenting of the pulmonary veins. The parents opted for medical management.

Case4: A 25 day old male baby born at full term gestation, with uneventful antenatal and perinatal period, birth weight of 3.1 kg, was brought to emergency with complaints of poor feeding and respiratory distress for one week. Chest radiograph showed cardiomegaly. Echocardiography revealed bicuspid aortic valve, critical aortic stenosis, small PDA (right to left shunt) and severe left ventricular dysfunction (LVEF 20%). The baby underwent balloon dilatation of the aortic valve successfully. Two days post balloon dilatation, repeat echocardiography while still on oxygen showed a mean gradient across the aortic valve of 18 mmHg, trivial aortic regurgitation, no flow across the PDA and mild tricuspid regurgitation (gradient 28 mmHg) with a left ventricular ejection fraction of 50%.

After 3 months, he was readmitted with features of congestive cardiac failure. Echocardiography showed a well opened aortic valve (mean gradient 20 mmHg), trivial aortic regurgitation, normal mitral valve, normal flow in the pulmonary veins and normal LV function. There was right ventricular dysfunction with severe PAH (TR peak gradient 86 mmHg). CT pulmonary angiography was done to profile pulmonary vein anatomy and to rule out any lung malformation contributing to PAH. The child was stabilized with diuretics and oxygen. Repeat echocardiography showed a TR gradient of 50 mmHg (on oxygen by nasal prongs 5 l /minute).

Cardiac catheterization was done for hemodynamic assessment. Hemodynamic data (taken on oxygen) is given in table 3. The data showed moderate pulmonary arterial hypertension, normal left ventricular filling pressure (5 mmHg) and no significant gradient across the aortic valve. The baby was stabilized on a pulmonary vasodilator (sildenafil) and oral diuretics (frusemide and aldactone). He was discharged in a clinically stable condition.

Table 3: Hemodyanamic data of case 4.Data shows no significant gradient across aortic valve. Left ventricular filling and pulmonary capillary wedge (PCW) pressures are normal while pulmonary artery pressure is 50% of systemic pressure.

	Pressure Data: On oxygen				
Site	Systolic (mmHg)	Diastolic (mmHg)	Mean (mmHg)	Saturation (%)	PO2 mmHg
FA	96	58	73	99	220
RV	48	5			
PA	49	14	30	65.2	
LV	98	5			
AAO	85	44	50		
PCW	a6	v2	4	99	
RA	a5	v2	2	67	

After two months the child returned with acute deterioration. Echocardiography showed severe pulmonary arterial hypertension with severe RV dysfunction. Despite all resuscitative measures, child could not be revived.

Discussion

PAH frequently develops in response to severe left sided obstructive lesions with LV dysfunction due to elevated pulmonary venous pressure. PAH secondary to LV dysfunction regresses after relief of outflow obstruction with normalization of LV function. In some patients, PAH persists despite adequate relief of obstruction. Restrictive left ventricular filling (especially in neonates and infants) is a known cause of persistence of PAH.[1] Chronic elevation in pulmonary artery pressure often leads to right ventricular pressure overload and subsequent right ventricular failure.[4]

Less common but treatable causes should also be sought as a cause of persistence of PAH. A review of the literature shows a series of lesions that range from diseases of the pulmonary veins, mechanical obstruction in the LA or at the mitral valve, or elevation in the left atrial and pulmonary venous pressure due to mitral regurgitation, and abnormal LA compliance as cause of persistence of PAH after adequate relief of LV outflow obstruction.[5-11]

Here we report four infants (< 3 months), who underwent adequate relief of left sided outflow tract obstruction (aortic valve stenosis and/or coarctation of aorta), with non-regression of PAH. Detailed evaluation showed following causes for persistence of high pulmonary artery pressure were, high LVED pressure (n=1), hypoplasia of pulmonary veins (n=1), stenosis of lower lobe branch of right

pulmonary artery (n=1) and non-regression of pulmonary arterial hypertension in one infant. Right ventricular pressure normalized in one 1 infant after balloon dilatation of right pulmonary artery lobar branch stenosis while severe PAH persisted is rest 3 infants. One baby with non-regression of PAH expired at 8 months of age despite pulmonary vasodilator therapy.

Conclusion

In the setting of PAH related to critical left-sided obstructive lesions, PA pressures commonly decrease significantly or return to normal after successful intervention. Unfortunately this does not occur in all. Some causes are correctable while others required early institution of medical therapy to reduce morbidity and mortality. The commonest cause for persistence of high pulmonary artery pressure is left ventricular diastolic dysfunction but less common causes are pulmonary vein stenosis or hypoplasia and distal branch pulmonary artery stenosis. Though results of catheter and surgical interventions for pulmonary veins stenosis are not encouraging pulmonary artery stenosis, if significant, can be relieved by catheter intervention.

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