

Against all odds—late repair of multiple shunt lesions in a patient with Down syndrome: a case report

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Background

Children with congenital heart defects (CHD) usually undergo elective surgical repair of haemodynamically relevant shunt lesions within the first year of life. Due to susceptibility for pulmonary arterial hypertension (PAH) in patients with Down syndrome, repair is usually aimed for no later than 6 months of life. However, with rising immigration from developing countries to Europe, more patients with unrepaired CHD are diagnosed at a later age. Anatomical repair may be precluded, when advanced pulmonary vascular disease has been established.

Case summary

We report a 39-month-old male patient with Down syndrome with a large non-restrictive perimembranous ventricular septal defect, a large patent ductus arteriosus, and a secundum-type atrial septal defect with a prominent left-to-right shunting. Haemodynamic assessment revealed only a mild increase of pulmonary artery pressures (mPAP) with low pulmonary vascular resistance index (PVRi). Vasodilator testing led to a further increase of the left-to-right shunt and decrease of PVRi, suggesting operability. After careful consideration, the patient underwent complete surgical repair with a good post-operative clinical outcome. Cardiac catheterization 6 months after corrective repair showed a normal mPAP. No signs of PAH have been detected in the medium-term follow-up.

Discussion

Expertise, increased physician awareness, and a thorough pre-operative multidisciplinary evaluation are paramount to determine the best treatment approach for patients, who may present late with multiple shunts, and—in our case—underlying Down syndrome. Long-term close post-surgical follow-up in an expert centre is warranted to promptly diagnose and treat a possible late presentation of PAH appropriately.

Keywords

Case report • Multiple congenital heart defects • Down syndrome • Pulmonary arterial hypertension • Late diagnosis • Haemodynamic evaluation • Surgical repair

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Learning points

- Late referral and diagnosis of paediatric patients with congenital heart defects is increasing with rising immigration from underserved countries.
- Careful clinical, echocardiographic, and haemodynamic assessment is warranted to assess patients' operability as irreversible pulmonary vascular disease may already have been established.
- In case of a surgical approach, close long-term follow-up in expert centres is advised, as the risk for post-operative pulmonary arterial hypertension persists even for decades after surgery.

Introduction

Depending on clinical presentation, children with congenital heart defects (CHD) and haemodynamically relevant shunt lesions usually undergo elective surgical repair within the first year of life, to avoid the development of progressive pulmonary vascular disease (PVD).^{1,2} An even earlier timing for repair and shunt closure is recommended in those patients with associated Down syndrome, as irreversible PVD is thought to develop earlier in life and is often multifactorial.³ However, late referral and diagnosis is still a problem, mainly in underserved countries, which may preclude anatomical repair, when advanced PVD has usually been established.⁴

Pulmonary arterial hypertension (PAH)–CHD patients are at high risk for serious post-operative complications, including right heart failure and death.⁵ Despite successful technical repair of their shunt lesion, survival prospects in those patients who develop severe progressive post-operative PAH is often worse compared to their natural course and the long-term development of an Eisenmenger physiology.⁵ Even survivors with no immediate obvious PVD remain at risk for PAH, which is sometimes diagnosed years after repair.^{2,6} Thus, it is critically important to decide whether a patient, who presents beyond infancy with a haemodynamically significant left-to-right shunt, should undergo complete defect repair, with acceptable (peri-)operative risk and a favourable long-term outcome, with a low chance of developing late PVD. Herein, we highlight an unusual case of late presentation of a patient with intra- and extracardiac shunts and PAH, who successfully underwent corrective repair.

Timeline

Time	Events
38 months old	First evaluation abroad No documents available
Initial presentation and pre-operative evaluation	
Day 1 (39 months old)	Outpatient clinical and echocardiographic evaluation Confirmation of diagnosis
Day 30 (40 months old)	Inpatient invasive evaluation Left- and right heart catheterization with acute vasoreactivity testing

Continued

Continued

Time	Events
	Confirmation of operability
Operation	
Day 40 (41 months old)	Open heart surgery Ventricular septal defect–atrial septal defect and patent ductus arteriosus closure
Post-operative clinical course	
Day 1–Day 5	Intensive care unit Stable clinical course without post-surgical complications
Day 5–Day 15	Post-operative care on normal ward
Day 15	Hospital discharge
Day 30	1st outpatient follow-up Stable clinical condition
Day 90	2nd outpatient follow-up
Day 180 (47 months old)	3rd follow-up Invasive re-assessment (right heart catheterization) No signs of post-operative pulmonary arterial hypertension (PAH)/pulmonary vascular disease
Year 2 (4 years old)	4th outpatient follow-up No clinical or echocardiographic signs of PAH
Year 3 (5 years old)	5th outpatient follow-up No clinical or echocardiographic signs of PAH

Case presentation

A 39-month-old refugee boy with Down syndrome presented with a large perimembranous ventricular septal defect (VSD), a secundum-type atrial septal defect (ASD II), and a patent ductus arteriosus (PDA). The diagnosis was made a month before his first consultation in our hospital. He presented with dyspnoea on exertion, being asymptomatic at rest (functional class: Panama II*, WHO II).⁷ Adenoid and tonsillar hypertrophy have been noted. No previous surgery was reported. Cardiac auscultation revealed a mild systolic murmur at the left upper sternal border and a variable splitting of the second heart sound (S2) with an accentuated pulmonary component.

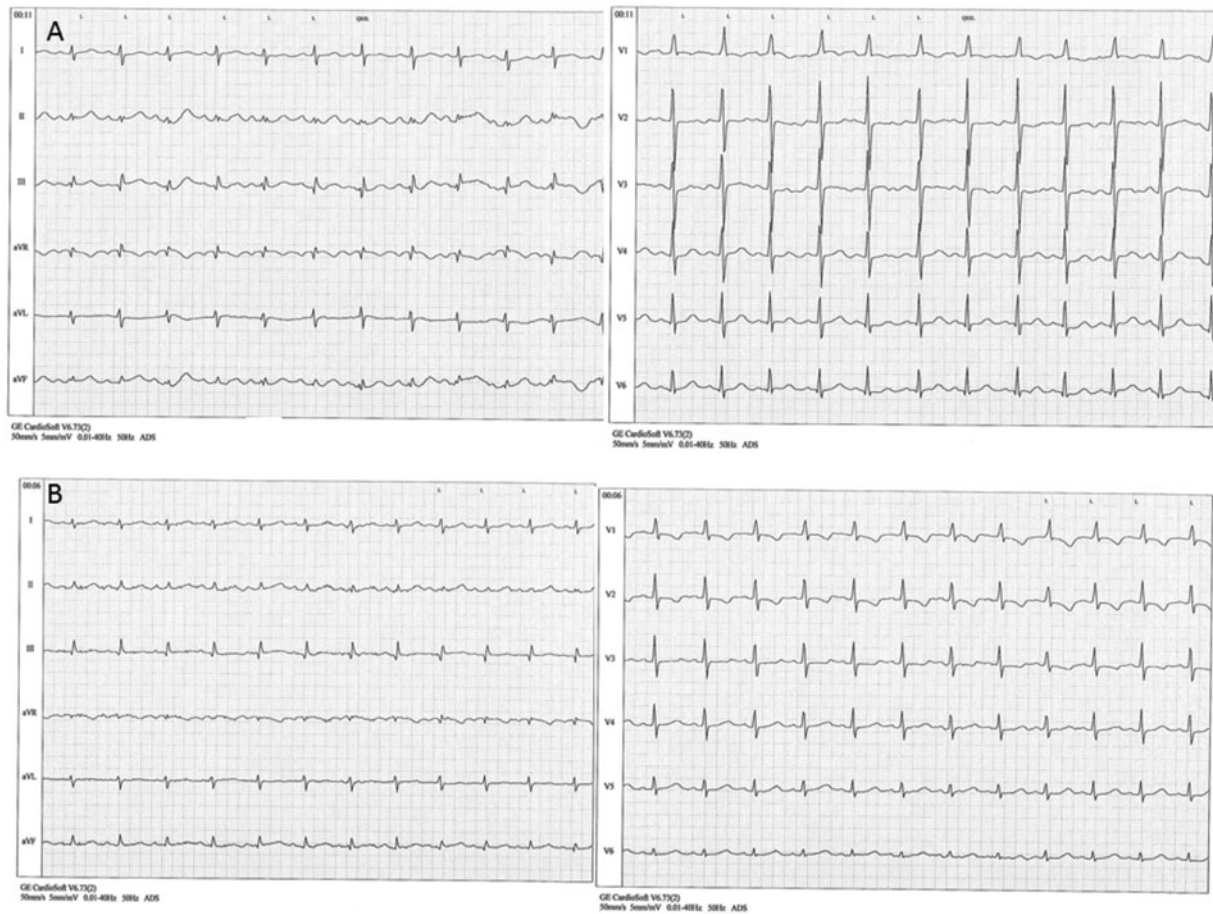


Figure 1 Twelve-lead electrocardiogram (5 mm/mV) at presentation (A) shows sinus rhythm (75 b.p.m.), with slight rightward QRS-axis deviation and signs of right ventricular hypertrophy. Although pulmonary vascular resistance index (PVRI) was not significantly increased, chronic right ventricular volume overload has been present, as demonstrated by the increased pulmonary flow (Q_p), which may have led to the maintenance of right ventricular foetal hypertrophy; 6 months post-surgery (B) QRS axis has shifted more to the right and T inversions have become prominent in V1 and V2 with reduced left ventricular forces in the precordial leads. This change could be explained by the haemodynamic change due to shunt closure and abolishment of pulmonary overcirculation and relief of strain from the overloaded left ventricle by the ventricular septal defect.

His baseline transcutaneous oxygen saturation at rest was 96%. His weight at presentation was 10.6 kg (<25th Down's centile) with a height of 83 cm (<25th Down's centile).

Electrocardiogram (ECG) showed sinus rhythm with a slight rightward axis deviation and signs of right ventricular (RV) hypertrophy (Figure 1A). Chest X-ray revealed biventricular dilatation and enlargement of the main pulmonary artery (Figure 2). His transthoracic echocardiogram demonstrated a large non-restrictive perimembranous VSD, 12 mm in diameter, in addition to a smaller muscular VSD, both of which revealed left-to-right shunting (Figure 3C and D and Video 1). Furthermore, a large PDA with a predominant left-to-right shunting in colour Doppler (Video 2) and an ASD II (Figure 3A and B and Video 3) were depicted. Biventricular dilatation [left ventricular (LV) end-diastolic diameter 35 mm, z-score +2.95; RV end-diastolic diameter 17 mm, z-score +3.5] was present. Biventricular function (LV fractional shortening 52%, tricuspid annular plane systolic excursion 22 mm, z-score +3.3) was well preserved.

Cardiac catheterization was performed under general anaesthesia to assess the patient's operability. It revealed a mildly elevated mean pulmonary arterial pressure (mPAP 30 mmHg) with normal pulmonary vascular resistance index (PVRI $1.9 \text{ WU} \cdot \text{m}^2$) and a pulmonary to systemic flow ratio (Q_p/Q_s) of 2.9. Acute vasoreactivity testing with inhaled nitric oxide (20 ppm) showed a further increase in left-to-right shunting (Q_p/Q_s : 3.8/1) with a >20% decrease in PVRI ($1.2 \text{ WU} \cdot \text{m}^2$) and a low indexed pulmonary vascular resistance to systemic vascular resistance (SVRI) ratio (PVRI/SVRI < 0.3), suggesting suitability for repair (Table 1).

The patient was discussed in the multidisciplinary team meeting. Given the favourable haemodynamic results, complete surgical repair, without leaving an atrial fenestration, was opted for. Eventually, the VSD was closed with an autologous pericardial patch and a direct suture of the ASD and PDA was performed at 3.5 years of age. Patient's post-operative course was uncomplicated. There were no echocardiographic evidence of any residual left-to-right shunt or signs



Figure 2 Chest radiograph at presentation. There is an increased cardio-thoracic ratio with evidence of biventricular dilatation and enlargement of the main pulmonary artery. The hilar pulmonary vessels are also noted.

of persistent PAH (Figure 4A and B). In the absence of a sufficient tricuspid insufficiency to accurately estimate mPAP and the potential high risk for the development of post-operative PAH, in view of his late presentation and associated Down syndrome, it was decided to re-evaluate the patient invasively, in order not to miss a post-operative increase in the pulmonary vascular resistance (PVR). Invasive re-assessment 6 months after surgical repair revealed a normal mPAP with a relative increase in PVRi (Table 1). One explanation might be an increase of pulmonary flow (Qp) due to the abolished left-to-right shunting. However, it deserves further attention and close follow-up. In addition, a rightward shift of his QRS axis in the ECG has been noted (Figure 1B), that could be explained by the haemodynamic change attributed to the shunt closure, abolishment of the pulmonary overcirculation and relief of strain from the overloaded LV. However, if right axis deviation persists or shifts even more to the right, it could be a sign of increasing RV pressure and strain with an increasing PVRi.

The patient remains asymptomatic on further follow-up with no clinical signs for pulmonary hypertension. In addition, he now shows catch-up growth, as his latest weight assessment was between 75th and 95th centile (before surgery <25th centile) for patients with Down syndrome and his height was between the 25th and 50th centile (before surgery <25th centile).

Discussion

The present case demonstrates that even among older children, with a susceptibility to develop PVD, multiple defect closure may still be feasible, with a good post-operative outcome. With rising immigration from developing countries to Europe, more children with unrepaired CHD are seen in outpatient clinics and are diagnosed and evaluated at a later age.⁸ Careful clinical, echocardiographic, and haemodynamic

assessment is warranted to determine, if a shunt lesion is still amenable to repair. Although long-term data are lacking, recommendations exist about the probability of repair.⁹ Ruling out irreversible PVD plays a key role in the therapeutic decision-making process.

According to the latest update, PAH is haemodynamically defined as an increase in mPAP >20 mmHg and PVRi >3 WU*m², with a low pulmonary capillary wedge pressure (PCWP<15 mmHg).⁹ With a PVRi <6 WU*m² along with a PVRi/SVRi <0.3 a patient is deemed operable. Acute vasodilator testing is performed in patients with PAH-CHD to assess the significance and potential increase of a left-to-right shunt, PAH reversibility and thus, patients' operability. A ≥20% fall in both PVRi and PVRi/SVRi ratio is considered a positive response and a patient is thought to be operable with final PVRi below 6 WU*m² and PVRi/SVRi <0.3.¹⁰

The aetiology of PH in Down syndrome is often multifactorial. Although our patient had predisposing factors to develop irreversible PVD (post-tricuspid shunts, advanced age, and Down syndrome),¹¹ mPAP was only mildly elevated with an increased Qp and a considerably low PVRi. The baseline, Qp/Qs of 2.9 might have been overestimated under general anaesthesia. As our patient had adenoid and tonsillar hypertrophy, which is often associated with hypercapnia and additionally contributes to a higher PVRi, this finding may have prevented an even higher pulmonary blood flow and overcirculation. This reduction of shear stress may have prevented the onset of irreversible PVD. Sometimes an anatomically relevant VSD is partially functionally closed and flow diminishes via accessory tricuspid valve tissue, so the actual net flow via the VSD may have not been excessive. Moreover, unlike patients with a VSD and fixed PVR, in whom S2 often appears singular without any audible splitting, the variable splitting of S2 in our patient may be suggestive of reversible PAH.¹¹

Another hypothesis, why our patient has not developed PVD during the first years of life, is that he may have experienced a much slower postnatal adaptation and fall of his PVR. This would explain why our patient presented later in life, without expected symptoms of pulmonary overcirculation, like tachypnoea or failure to thrive. With a longer-standing increased Qp, as measured during cardiac catheterization, we would have expected him to be clinically more symptomatic. All these factors may have contributed to his relatively late clinical presentation, good tolerance, and benign haemodynamic findings.

PAH after surgical repair of shunt lesions has been reported in 7.4% of adult patients with CHD.⁶ Another recent study demonstrated a PAH prevalence of 3% among patients with corrected simple defects, with age at repair and age at follow-up being closely associated with the risk of PAH even decades after surgery.¹² Consequently, there is a need for a long-term regular follow-up of these patients in expert centres, in order to early diagnose and promptly treat any possible late PAH presentation. If there were any concerns of rising PAPs and development of PH, we would consider repeat cardiac catheterization and proactive treatment with advanced pulmonary vasodilatory agents.

Conclusion

A thorough work-up and assessment of patients with haemodynamically relevant shunt lesions—presenting even beyond infancy—is mandatory, like in our patient, in whom successful repair and

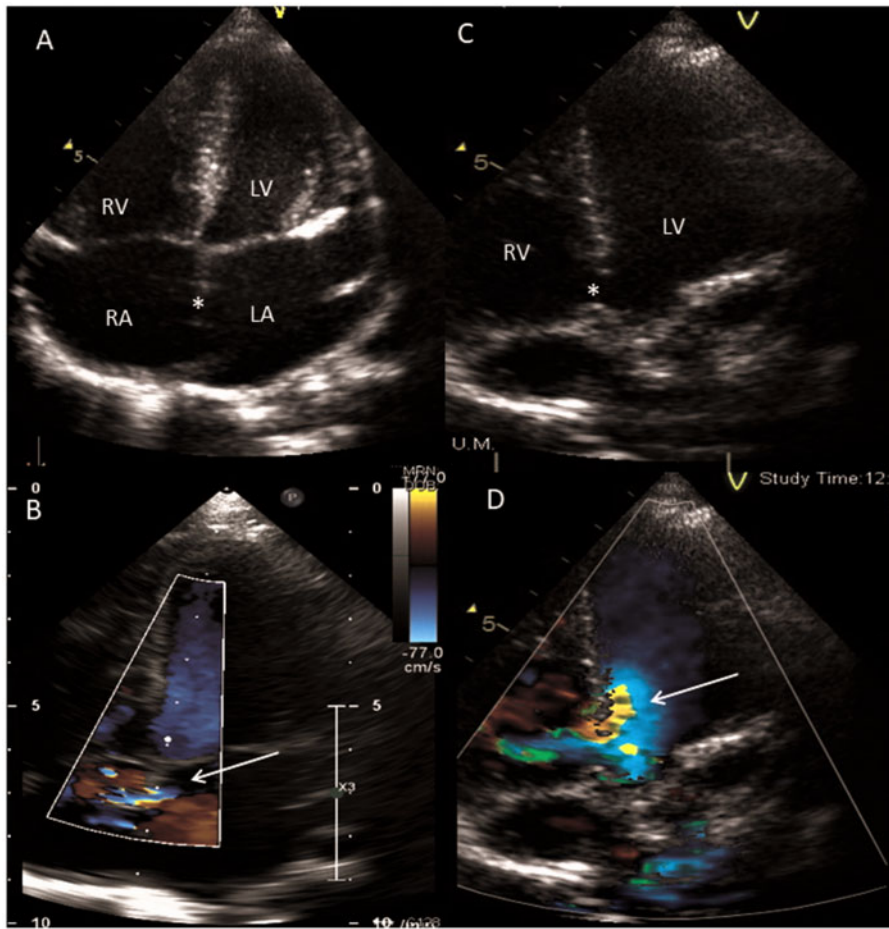
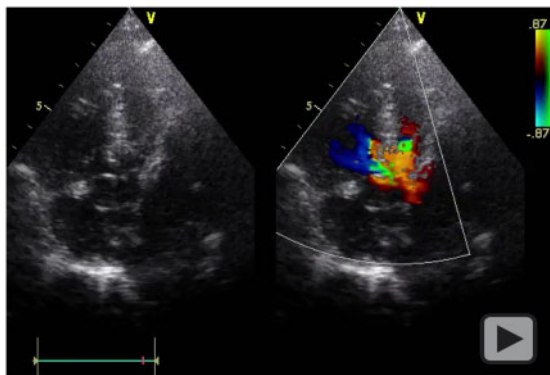
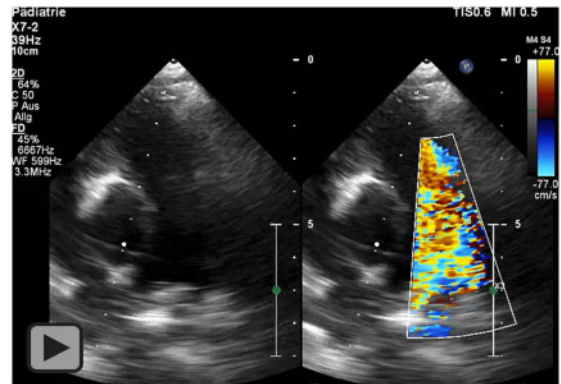


Figure 3 Transthoracic echocardiographic images at presentation reveal shunt lesions at atrial and ventricular level. (A) Four-chamber view shows mild biventricular dilatation and a secundum-type atrial septal defect (asterisk). (B) Colour Doppler demonstrated the predominant left-to-right shunt across the atrial septal defect in a four-chamber view (arrow). (C) Five-chamber view shows a perimembranous ventricular septal defect (asterisk) with left-to-right shunt (arrow) in colour Doppler (D). LA, left atrium; LV, left ventricular; RA, right atrium; RV, right ventricle.



Video 1 Transthoracic echocardiogram. Five-chamber view shows a perimembranous ventricular septal defect with a left-to-right shunt in colour Doppler.



Video 2 Transthoracic echocardiogram. Parasternal short-axis view at pulmonary valve level depicts a patent ductus arteriosus with a predominant left-to-right shunt in colour Doppler.

Table 1 Haemodynamic assessment before and after 6 months after surgical repair

	Pre-operative evaluation		Post-operative evaluation
	Baseline	Post-AVT	6 months post-repair
Height (cm)	80	80	91
Weight (kg)	10	10	14
BSA (m ²)	0.46	0.46	0.58
HR (b.p.m.)	85	87	82
BP (mmHg)	75/37	74/35	
mRAP (mmHg)	7	7	5
mPAP (mmHg)	30	32	15
PCWP (mmHg)	12	13	5
Qp (mL/min/m ²)	9.5	15.4	2.7
Qs (mL/min/m ²)	3.25	4	2.7
Qp/Qs	2.9	3.8	1
PVRi (WU*m ²)	1.9	1.2	3.7
SVRi (WU*m ²)	13.2	11.4	
PVRi/SVRi	0.14	0.10	
SaO ₂ %	98	98	98
SvO ₂ %	88	89	64

AVT, acute vasoreactivity testing; BSA, body surface area; HR, heart rate; BP, systolic and diastolic blood pressure in the ascending aorta; mRAP, mean right atrial pressure; mPAP, mean pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; Qp, pulmonary flow; Qs, systemic blood flow; Qp/Qs, pulmonary to systemic blood flow; PVRi, pulmonary vascular resistance index; SVRi, systemic vascular resistance index; PVRi/SVRi, indexed pulmonary vascular resistance to systemic vascular resistance ratio; SaO₂%, arterial oxygen saturation; SvO₂%, oxygen saturation in the pulmonary artery; WU, Wood Units.

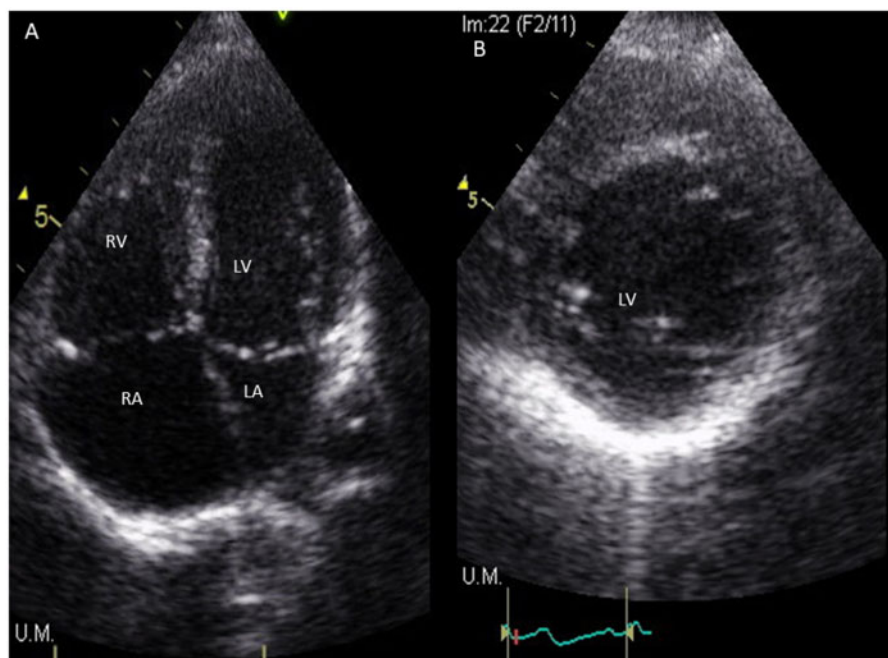
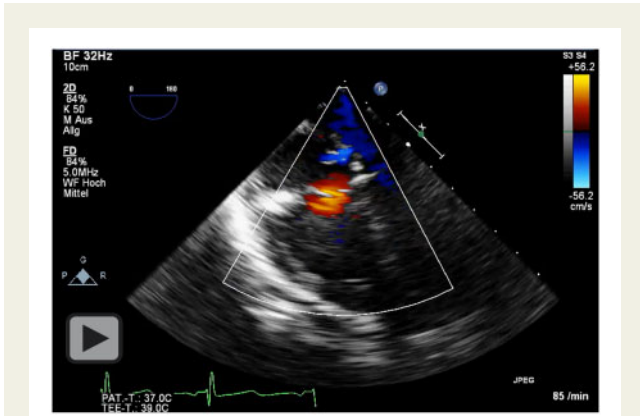


Figure 4 Transthoracic echocardiographic images 6 months post-operatively. (A) Four-chamber view shows no residual shunt at the atrial or ventricular level. (B) Short-axis view shows no significant interventricular septal flattening at diastole. LA, left atrium; LV, left ventricular; RA, right atrium; RV, right ventricle.



Video 3 Transoesophageal echocardiogram. Four-chamber mid oesophageal view 0° depicts a secundum atrial septal defect with significant left-to-right shunt in colour Doppler.

favourable outcome appeared against all odds. There may be patients with no significant increase in PVR, who benefit from surgical repair with a good long-term outcome. Long-term clinical follow-up is required, as PAH may even manifest decades after the operation.

Lead author biography



Astrid Elisabeth Lammers is a paediatric cardiologist and intensivist. From 2004 to 2013, she worked in the UK (Great Ormond Street Hospital and Royal Brompton Hospital). She has worked in the UK National Service for Paediatric Pulmonary Hypertension. Her UK-MD has been on 'Non-invasive evaluation, therapy, and transplantation in children with pulmonary arterial

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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's next of kin in line with COPE guidance.

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