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Peripheral Pulmonary Artery Growth in Alagille Syndrome after Central Pulmonary Artery Enlargement: A Case Report

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Abstract

Background: Peripheral pulmonary artery stenosis is a rare congenital defect that is frequently associated with Alagille syndrome and Williams syndrome. However, the optimal treatment of peripheral pulmonary artery stenosis is controversial. No reports have described central pulmonary artery enlargement in a patient with Alagille syndrome and peripheral pulmonary artery stenosis. We herein report a case in which central pulmonary artery enlargement enabled the peripheral pulmonary arteries, including the lobar and segmental arteries, to adequately grow.

Case Report: We treated an infant with Alagille syndrome, tetralogy of Fallot, and peripheral pulmonary artery stenosis. At 54 days of age, a central shunt was placed to encourage development of the pulmonary artery. However, no pulmonary artery growth was achieved. Because of worsening hypoxemia, enlargement of the central pulmonary arteries as well as total correction of the tetralogy of Fallot were performed. Although the peripheral pulmonary artery stenosis was not reconstructed at the segmental and lobar levels, growth of the diameter of the right and left pulmonary arteries and their first branches, and improvement of the Nakata index were seen at 5 years postoperatively.

Conclusion: Despite the difficulty of successfully surgically enlarging the peripheral pulmonary arteries in patients with Alagille syndrome, reconstruction of the central pulmonary arteries achieves sufficient enlargement of even the peripheral pulmonary arteries.

Keywords: Alagille syndrome; Peripheral pulmonary artery stenosis; Central pulmonary artery reconstruction

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Introduction

Peripheral Pulmonary Artery Stenosis (PPAS) is a relatively rare congenital heart defect that is found in fewer than 1% of patients with congenital heart disease [1]. Although rare, PPAS is frequently found in association with Alagille syndrome and is considered a phenotypic hallmark of this genetically mediated syndrome [2-4]. However, the optimal treatment of PPAS has not yet been established, with most institutions favoring catheter-based interventions. In contrast, we performed total correction of Tetralogy of Fallot (TOF) and surgical enlargement of the central pulmonary artery in a patient with TOF and PPAS. Consequently, growth of the peripheral pulmonary arteries was confirmed 5 years after total correction. This report shows that pulmonary artery growth can be expected by enlargement of the central pulmonary artery without surgical intervention to correct PPAS.

Case Presentation

The patient was born at 41 weeks 2 days of gestation with a birth weight of 2,716 g. She had been prenatally diagnosed with TOF on the basis of a fetal echocardiogram, which showed a large Ventricular Septal Defect (VSD) with overriding of the aorta, right ventricular hypertrophy, and sub-pulmonary and pulmonary stenosis. She was managed in a ventilator for 18 days after birth because her patent ductus arteriosus had almost closed, causing her oxygen saturation to be <60% on room air regardless of prostaglandin administration. Postnatal cardiac catheterization was performed 39 days after birth and confirmed PPAS. The patient was also diagnosed with Alagille syndrome. Her diagnosis was based on a family history of Alagille syndrome in her sister as well as the presence of characteristic features (elevated hepatic and biliary enzymes, a broad forehead,

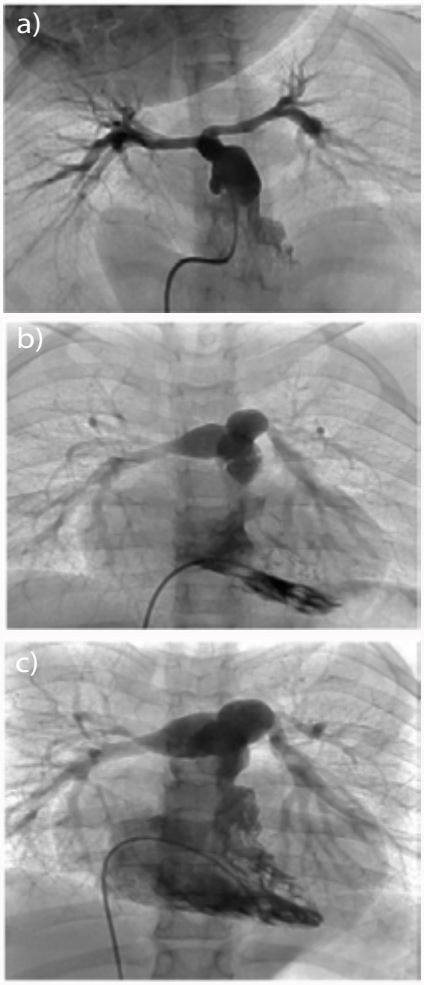

Figure 1: Angiographic images at various time points. (a) Angiography 8 months after central shunt placement (b) Angiography 1 year 6 months after total correction and central pulmonary artery enlargement (c) Angiography at 5 years after total correction.

and PPAS). Chromosome analysis was not performed. At 54 days of age (weight of 3.7 kg), central shunt placement was performed under beating-heart cardiopulmonary bypass to encourage development of the pulmonary artery. After the ascending aorta had been side-clamped, one side of a 3.5-mm expanded polytetrafluoroethylene graft (W.L. Gore & Associates Inc., Newark, DE, USA) was anastomosed to a punched-out hole in the aortic wall, while the other side of the graft was anastomosed to the main pulmonary artery. Because growth of the peripheral pulmonary arteries was not achieved, the pulmonary valve was percutaneously dilated by a 9-mm balloon (Tyshak II; TRYTECH Co., Ltd., Tokyo, Japan) about 8 months postoperatively. Although the main pulmonary artery to right ventricular pressure gradient improved from 50 mmHg to 39 mmHg after the pulmonary valve dilation, the right-to-left ventricular systolic pressure ratio remained at 0.98. Additionally, the pressure gradient from the main pulmonary artery to the right and left pulmonary arteries deteriorated from 32 and 31 mmHg to 46 mmHg and 42 mmHg, respectively (Figure 1a). The diameter of the first branch of the right and left pulmonary arteries was 2.8 and 3.0 mm, respectively, and the Nakata index was 58.7 mm^2/m^2 (Table 1). Although the hepatic and biliary enzyme concentrations did not become re-elevated, the oxygen saturation worsened; the left ventricular volume was 123%

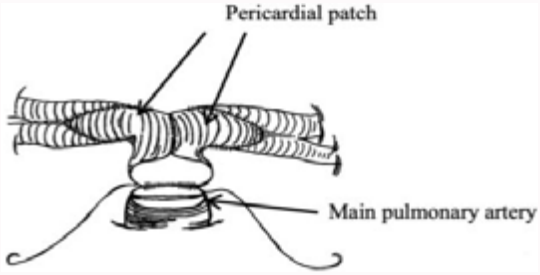

Figure 2: Operative schema showing enlargement of the central pulmonary artery wall by a pericardial patch.

of normal, the pulmonary-to-systemic blood flow ratio was 0.78, and the pulmonary vascular resistance was 0.79 Wood units. Therefore, surgical total correction and reconstruction of the pulmonary artery were performed when the patient was 27 months old and weighed 11.9 kg.

The central shunt was ligated, and the right and left pulmonary artery walls were incised longitudinally toward each PPAS until the first pulmonary artery branch was reached. The pulmonary arteries were enlarged by pericardial patches, but the PPAS was not reconstructed at the segmental and lobar levels. Under cardiac arrest with cardiopulmonary bypass, the VSD (16 mm × 12 mm) located in the outlet portion was closed with a Gore-Tex patch (W.L. Gore & Associates Inc.) with 3.0-mm holes. The main pulmonary artery was incised horizontally above the pulmonary valve, and the supravalvular stenosed portion of the pulmonary artery was removed. The condition of the pulmonary valve was normal. The main pulmonary artery trunk was then enlarged by a pericardial patch to achieve a pulmonary artery valve index of 2.2 cm^2/m^2 (Figure 2). The oxygen saturation recovered to 98% on room air. The postoperative course was uneventful, and the patient recovered well. Cardiac catheterization at 1 year 6 months postoperatively showed that the right-to-left ventricular systolic pressure ratio was 0.6; the diameter of the first branch of the right and left pulmonary arteries had grown to 6.2 and 5.9 mm, respectively; and the Nakata index had increased to 406.7 mm^2/m^2 (Figure 1b). At 5 years postoperatively, cardiac catheterization showed a right-to-left ventricular systolic pressure ratio of 0.50; diameter of the first branch of the right and left pulmonary arteries of 7.8 and 7.9 mm, respectively; and a Nakata index of 432.7 mm^2/m^2 (Figure 1c). In addition, the pressure gradient from the main pulmonary artery to the right and left pulmonary arteries improved from 30 and 29 mmHg, respectively, at 1 year 6 months postoperatively to 15 and 13 mmHg, respectively, at 5 years postoperatively (Table 1). Echocardiography revealed that the fenestration of the VSD patch was almost closed at 1 year 6 months postoperatively.

Discussion

Alagille syndrome with both TOF and PPAS is rare. About 70% of patients with Alagille syndrome have PPAS, while 9% have TOF [5]. Cardiac disease decreases the life expectancy of patients with Alagille syndrome and accounts for 34% of deaths among these patients [6]. Our patient required augmentation of her pulmonary blood flow to achieve pulmonary artery growth. However, a systemic–pulmonary shunt did not achieve satisfactory pulmonary vascular development. Therefore, the main, right, and left pulmonary arteries were enlarged during surgical repair of the TOF (Figure 2). The PPAS, including the lobar and segmental arteries, was not reconstructed because we

Table 1: Data at various time points.

	MPA diameter (mm)	RPA diameter (mm)	LPA diameter (mm)	1st branch diameter (mm)		NAKATA index (mm^2/m^2)	RVPLVP (mmHg) (RVP-LVP ratio)	AMPAP-RPAP	AMPAP-LPAP
				BPA	LPA				
Post-1st ope 8 months follow-up	5.1	3.4	4.3	2.8	3	58.7	98/100 (0.98)	46	42
Post-2nd ope 1 year and 6 months follow-up	12.6	12.6	12.5	6.2	5.9	406.7	70/117 (0.6)	30	29
Post-2nd ope 5 years follow-up	15.4	13.9	14.8	7.8	7.9	432.7	60/120 (0.50)	15	13

had little experience in surgical reconstruction of PPAS. Options for treating PPAS include balloon angioplasty and stenting of the peripheral pulmonary arteries, systemic–pulmonary shunt placement, and surgical reconstruction of the main and PPAS. Whereas transcatheter intervention for PPAS is reportedly safe and effective [7], some studies have shown that balloon angioplasty and stent implantation for PPAS are not successful and induce significant procedure-related complications and restenosis [8,9]. Furthermore, patients with Alagille syndrome who undergo placement of systemic–pulmonary shunts reportedly do not show evidence of pulmonary artery growth, although the reasons for this remain unclear [10]. An optimal management algorithm for treating PPAS associated with Alagille syndrome has not yet been established for the following reasons. First, reports of PPAS with congenital heart defects are relatively rare [11]. Second, few institutions have the ability to perform surgical reconstruction of PPAS. However, one study performed in an institution with substantial experience in surgical reconstruction of PPAS indicated that surgical reconstruction may be superior to the conventional approach using catheter-based interventions [1]. Third, there are different types of PPAS. Some stenoses are discrete and located at the ostia, some are discrete mid-vessel stenoses, and others are long and tubular. Hence, balloon angioplasty and stent implantation are not always applicable to all types of PPAS and do not always effectively relieve the obstruction. In the present case, in which the stenosis was long and tubular, we performed central pulmonary artery enlargement to increase the pulmonary blood flow and thus encourage pulmonary artery growth because of our insufficient experience in surgical reconstruction of PPAS in addition to the long and tubular type of PPAS. Although we focused on the first branches of the right and left pulmonary arteries and the Nakata index as indicators of the growth of the peripheral pulmonary arteries, we confirmed that our strategy led not only to growth of the diameter of the right and left pulmonary arteries and their first branches, and an increase in Nakata index but also to improvement of the right-to-left ventricular systolic pressure ratio (Table 1).

The natural history of PPAS is controversial. PPAS associated with Williams syndrome might undergo a process of spontaneous regression, resulting in improvement of right ventricular hypertension over time [12]. However, there is currently no evidence that the PPAS associated with Alagille syndrome undergoes this same process of spontaneous regression. Therefore, we did not expect the PPAS in the present patient to improve naturally, and treatment was thus required. In the present case, enlargement of the central pulmonary artery without surgical intervention involving the lobar pulmonary artery branches was sufficient to decrease the right-to-left ventricular systolic pressure ratio and foster the development of pulmonary vascular beds.

Considering the uncertain efficacy and risks of complications of balloon dilation as well as many practitioners' insufficient surgical experience with peripheral vessel reconstruction, central pulmonary artery enlargement may be optimal for treating PPAS. Although this is only the first reported case of central pulmonary artery enlargement in a patient with Alagille syndrome, TOF, and PPAS, our findings indicate that even without sufficient surgical experience to treat PPAS, central pulmonary artery enlargement enables the peripheral pulmonary arteries, including the lobar and segmental arteries, to adequately grow with a low risk of complications. This strategy may be a viable treatment option for PPAS.

Conclusion

The reconstruction of the central pulmonary arteries achieves sufficient enlargement of even the peripheral pulmonary arteries.

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