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ORIGINAL ARTICLE

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Pulmonary vein stenosis with collateralization via esophageal varices: Long-term follow-up after successful treatment with drug-eluting stent

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Abstract

Objective: We describe the long-term follow-up of a child with recurrent hemoptysis due to severe pulmonary vein stenosis decompressing via collaterals to esophageal varices.

Design: Case report

Setting: Tertiary children's hospital

Patient: Single child through ages 2- to 11-year old

Interventions: The child underwent cutting balloon angioplasty, bare metal stenting, and implantation of a PTFE-covered stent, all of which failed rapidly. Only after placement of a paclitaxel drug eluting stent did he have prolonged relief from hemoptysis and long-term patency of the treated vein. The stents were serially dilated to keep up with somatic growth of the child, eventually culminating in the need to induce intentional stent fracture.

Conclusions: We highlight novel transcatheter techniques to treat this vexing condition, discuss mechanisms of disease treatment and progression, and present the only patient with this rare combination of lesions to have achieved both longstanding pulmonary vein patency and resolution of esophageal varices.

KEYWORDS
drug eluting stent, esophageal varives, pulmonary hypertension, pulmonary vein stenosis

1 | INTRODUCTION

Pulmonary vein stenosis (PVS) is an uncommon disorder that can present in isolation or with other forms of congenital heart disease.[1–3] PVS can occur spontaneously or postoperatively, such as after repair of anomalous pulmonary venous connection (TAPVC), and can result in morbidity from pulmonary edema, hemoptysis, and pulmonary hypertension.[1–4] In severe PVS or complete pulmonary vein (PV) atresia, the affected lobe drains via collateral veins to an adjacent, less affected, lobe, or to the systemic venous circulation.[5] Only rarely has collateralization been documented to occur via esophageal varices.[6,7] Results of PVS treatment via operative or transcatheter techniques have been poor.[2,8,9] Implantation of bare metal stents (BMS) has been used as therapy for this disease since the early 1990s, however, restenosis with BMS appears to be virtually universal.[5,10] We present a rare case of PVS with collateralization via esophageal varices that was successfully treated with drug eluting stent (DES) after failure of other catheter-based techniques, and we describe the sustained long-term success of the therapy.

2 | PRESENTATION AND INITIAL INTERVENTION

An infant born prematurely at 23 weeks gestation developed chronic lung disease requiring prolonged mechanical ventilation, resulting subglottic stenosis, and subsequent tracheostomy. He presented several times between the ages of 22 and 29 months with major hemoptysis, and inability to wean his home ventilator settings. Computed

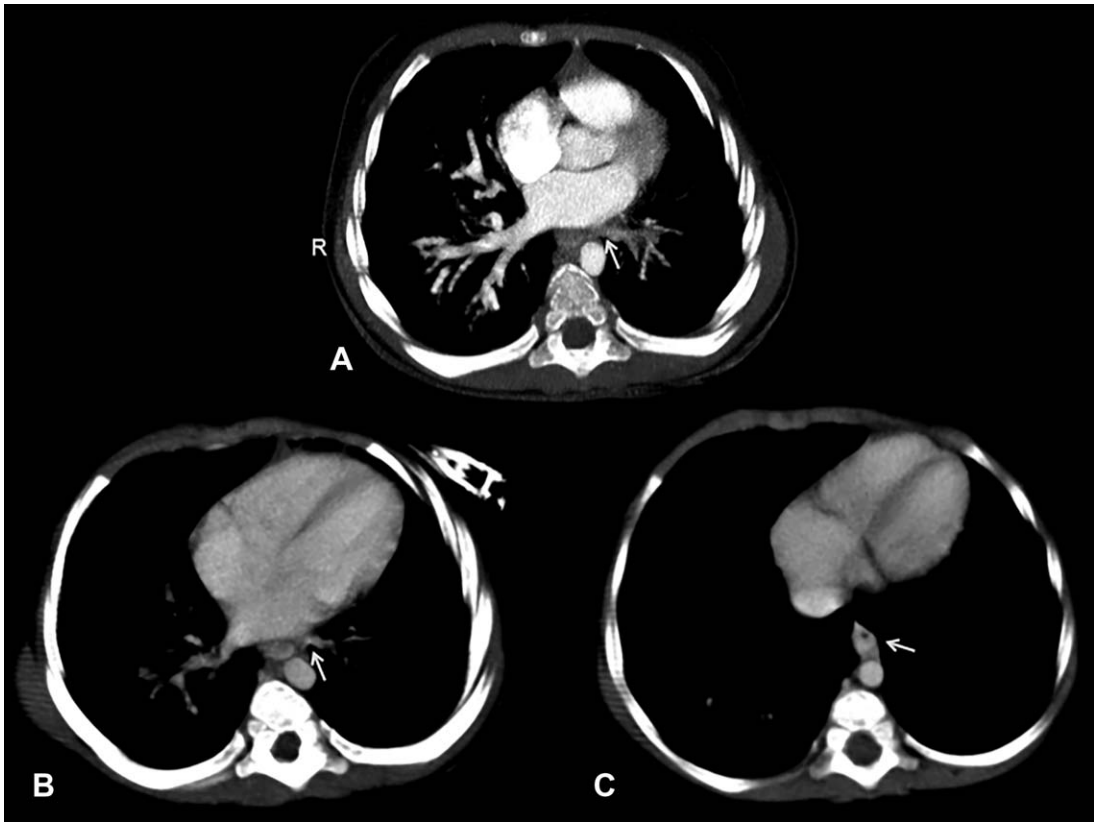

FIGURE 1 Chest CT on initial presentation. (A) Lack of enhancement of the left lower pulmonary vein (arrow) on the first-pass contrast enhanced study, as compared to the right-sided pulmonary veins. (B) Delayed phase image showing minimal filling of the left lower pulmonary vein, suggestive of significant stenosis (arrow). (C) Enhancement of submucosal esophageal varices (arrow) on the delayed phase, due to collateral flow from the pulmonary veins to the esophageal venous plexus

tomography (CT) of the chest with contrast injection was performed to look for a source of pulmonary bleeding, resulting in the diagnosis of left upper and left lower pulmonary vein atresia (Figure 1). The left lung and left pulmonary artery (PA) were hypoplastic, with diffuse ground-glass opacities and interlobular septal thickening.

He was felt to be a poor candidate for surgical pulmonary vein (PV) repair, and catheter-based intervention was offered despite the known high failure rate, with the understanding that left pneumonectomy would be the last resort. At catheterization (Table 1), PA pressures were mildly elevated (mean 17 mm Hg), with discrepant mean PA wedge pressures: 5 mm Hg in all right lung lobes, and 17 mm Hg in the left lower lobe. PA saturations were also discrepant (64% in the right and 96% in the left), indicative of retrograde flow of oxygenated blood in the left PA. PA wedge angiography was normal in the right lung, but revealed long-segment PV atresia in the left upper lobe with diminutive distal veins and collateralization to the left lower PV (LLPV) as well as pinhole patency of the LLPV with collateralization to esophageal varices that ultimately drained into the azygos and innominate veins (Figure 2A,B). Transseptal puncture revealed a mean left atrial pressure of 3 mm Hg (i.e., 14 mm Hg gradient from left lower PA wedge to left atrium. The LLPV was crossed with a 0.018" V18 Control wire (Boston Scientific, Natick, Massachusetts). Angioplasty using conventional and cutting balloons followed by placement of a 6 mm diameter × 12 mm long Palmaz Genesis premounted (medium) BMS (Cordis, Cardinal Health, Milpitas, California) was performed, with care taken to avoid jailing of distal PV branches (Table 1). An excellent angiographic and hemodynamic result was achieved, with nonvisualization of esophageal varices angiographically (Figure 2C).

3 | SUBSEQUENT INTERVENTION

He was seen in follow-up 2½ months later, and was free of hemoptysis, and the echocardiogram showed a widely patent LLPV with low-velocity phasic flow with a calculated mean gradient of < 1 mm Hg. Knowing that PVS recurrence is common after stenting, we recommended catheterization within 1 month. Unfortunately, this was not done, and he presented 5 months after BMS placement with hemoptysis, and echocardiography could not disclose flow in the LLPV. At catheterization, left lower PA wedge angiography showed recurrence of large esophageal varices and complete occlusion of the previously placed LLPV BMS (Figure 3A). Esophagoscopy was performed, revealing large esophageal varices that were strikingly brighter red than those typically seen in the setting of portal hypertension, consistent with pulmonary venous rather than portal venous flow within them (Figure 3B). The occluded stent was successfully crossed, and angiography revealed abundant ingrowth of neointimal tissue within the BMS. Repeat stenting was performed, this time with a 6 mm × 16 mm iCAST polytetrafluoroethylene (PTFE)-covered stent (Atrium Medical Corporation,

TABLE 1 Description of serial catheterizations in patient with pulmonary vein stenosis

Age	Weight	Angiographic finding	LA to LLPV gradient	LLPV intervention performed	Gradient result	Angiographic result
29 mos.	10.8 kg	Pinhole patency of the LLPV into the LA, with collateralization via large esophageal varices draining to azygous and left innominate veins	14 mm Hg	Angioplasty with 4 mm balloon and 5 mm cutting balloon, placement of 6 mm diameter × 12 mm long Palmaz Genesis premounted (medium) stent	3 mm Hg	Resumption of blood flow through LLPV orifice
35 mos.	11.9 kg	Complete occlusion of LLPV BMS due to abundant neointimal tissue	19 mm Hg	Placement of 6 mm × 16 mm Atrium iCAST PTFE covered stent	2 mm Hg	Improved LLPV blood flow with greatly diminished flow in the esophageal varices
3 y, 1 mo.	11.6 kg	Stent patent, nonvisualization of esophageal varices	—	None	—	—
3 y, 5 mos.	12.2 kg	Severe in-stent stenosis, with thread-like jet of flow	9 mm Hg	Placement of 4 mm × 20 mm Taxus Liberte DES within previous stents, postdilated to 6 mm	3 mm Hg	Improved LLPV flow
5 y, 5 mos.	16 kg	No in-stent stenosis in DES, significant growth of distal LLPV branches	—	None	—	—
6 y, 8 mos.	18.1 kg	Discrete in-stent stenosis	4 mm Hg	Redilation with ultra-high-pressure 8 mm × 2 cm Dorado balloon to > 30 atm	2 mm Hg	Intentional DES, interval fracture, widely patent LLPV
10 y 8 mos.	29.9 kg	Recurrent discrete in-stent stenosis, growth of distal LLPV branches	9 mm Hg	Redilation using 8 mm × 2 cm balloon and 7 mm IN.PACT Admiral paclitaxel-coated balloon	2 mm Hg	Increase in LLPV stent caliber

Abbreviations: BMS, bare metal stent; DES, drug-eluting stent; LA, left atrium; LLPV, left lower pulmonary vein; PTFE, polytetrafluoroethylene.

Hudson, New Hampshire) with the hope that this would help prevent tissue ingrowth between the stent struts. This longer covered stent was placed deeper into the LLPV, partially covering the collateral leading to the esophageal varices (complete coverage of this collateral was avoided because of the uncertain risk for future stent occlusion and the potential beneficial role of the varices in decompressing the left PVs). After intervention, PA wedge angiography revealed diminished esophageal variceal flow (Figure 3C).

The patient underwent a repeat surveillance catheterization 10 weeks later, confirming short-term stent patency, as well as involution of the esophageal varices both by angiography and esophagoscopy. Four months later, he developed hemoptysis again. Echocardiography revealed near-complete LLPV occlusion, and quantitative nuclear lung perfusion scan showed no flow to the left lung. At catheterization angiography showed a thread-like jet of contrast through the stented LLPV with a large amount of recurrent neointimal tissue obstructing the stent lumen (Figure 4A), with nonvisualization of esophageal varices on angiography and esophagoscopy (Figure 5). As a last resort, we decided to place a 4 mm × 20 mm Taxus Liberte (Boston Scientific) paclitaxel-eluting DES, and postdilated it to 6 mm to anchor it within the previously placed stents, with the hope that this could inhibit intractable neointimal proliferation. This resulted in angiographic resolution of LLPV stenosis (Figure 4B). On the following day, lung perfusion scan showed 15% flow to the left lung.

The patient did well after DES placement. Repeat lung perfusion scan 3 months later revealed increased flow to the left lung (22%). He was seen serially in the outpatient setting, with no further hemoptysis and echocardiograms demonstrating a patent left lower pulmonary vein. He was taken back to the catheterization laboratory 24 months after DES placement, and there was no evidence of neointimal proliferation, with significant interval growth of the intrapulmonary venous branches in the left lower lobe (Figure 6).

At 6 years of age, lung perfusion scan showed 10% flow to the left lung, prompting repeat catheterization. The LLPV was redilated using an ultra-high-pressure 8 mm × 2 cm Dorado balloon (Bard, Tempe, Arizona), taken to a pressure of >30 atm, resulting in fluoroscopically evident intentional longitudinal stent fracture (presumably of the innermost DES, given that the previously placed BMS and PTFE-covered stent were expected to reach a diameter of 8 mm without fracture), resulting in a widely patent LLPV, with no evidence of vessel wall injury. Strikingly, the distal LLPV had grown tremendously in the intervening 3 years since DES stent placement; indeed even the untreated left upper PV showed dramatic growth, benefiting from unobstructed venous drainage of the left lower lobe because of a large intrapulmonary venous collateral (Figure 7). At 10 years of age, he again underwent angioplasty up to 8 mm, including the use of a 7 mm IN.PACT Admiral paclitaxel-coated balloon (Medtronic, Minneapolis, Minnesota). Nuclear lung perfusion scan showed 16% flow to the left lung afterward.

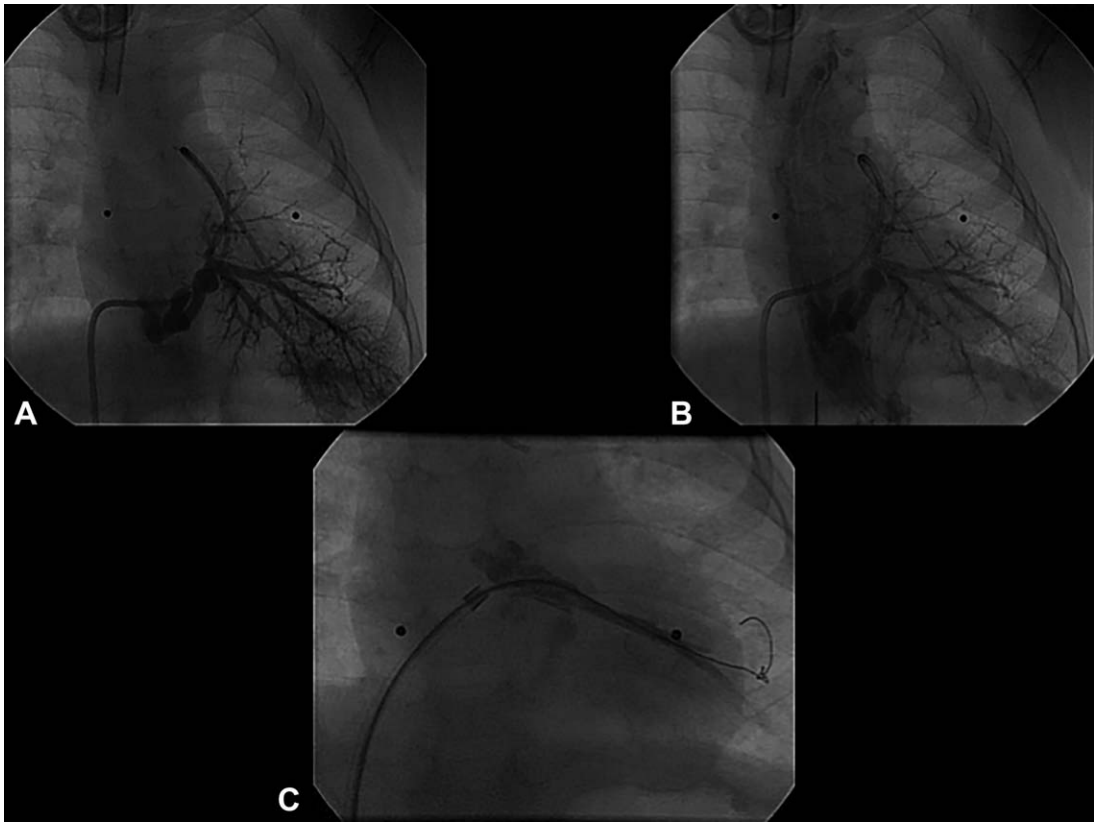

FIGURE 2 Initial catheterization with pulmonary vein near-atresia and esophageal varies. (A) Contrast injection into the left lower pulmonary artery wedge position demonstrating a severe stenosis of the left lower pulmonary vein ostium into the left atrium. (B) A later frame of the previous angiogram showing a large collateral vessel arising inferiorly and leading to esophageal varices. (C) Poststent placement, angiography reveals good patency achieved through the stent and into the left atrium. This image also reveals much decreased collateral blood flow through the collateral vessel into the esophageal varices. Of note, the orifice of the collateral vessel was not jailed by this stent

4 | LONG-TERM RESULTS

At the time of this publication, the patient is 11 years old, and has never had a recurrence of hemoptysis during the 8 years since DES placement. He is growing well, but remains with tracheostomy due to severe subglottic stenosis. He continues to receive antiplatelet therapy with daily aspirin, which was started after initial BMS placement. We plan to follow this patient with an echocardiogram every 6 months, and anticipate another catheterization for stent redilation in the next 3–5 years.

5 | DISCUSSION

This case possesses a number of unique characteristics. First, it represents only the third described case of PV stenosis or atresia collateralized via esophageal varices despite absent connection to the portal veins. Our case involved successful catheter-based treatment, while the two previously reported cases did not undergo attempt at anatomic correction, and were treated instead with pneumonectomy.[6,7]

An important point emphasized by this case is the discrepancy between the initial diagnosis provided by CT scan versus catheterization with conventional angiography: despite a CT scan suggesting LLPV atresia, angiography found that there was indeed pinhole patency of the LLPV, permitting catheter-based intervention. That pinhole patency of PVs can be missed by CT angiography has been previously described,[11] and highlights a number of advantages of conventional angiography over CT, such as higher spatial and temporal resolution, and the ability of pulmonary artery wedge angiography to force contrast through a pinhole PV ostium that might not be visible by CT.

This case also underlines the potential important role of DES in the treatment of PVS, a disease with a poorly understood prognosis, requiring frequent surveillance with echocardiography and repeat catheterization. Prior to DES placement, rapid restenosis of bare-metal and PTFE-covered stents occurred in our patient. Prior reports confirm that cutting balloons, bare-metal, and PTFE-covered stents, when used to treat PVS, are commonly plagued by recurrent stenosis with poor long-term results.[2,10,12] In our case, the DES was uniquely able to provide long-term PV patency and clinical relief from hemoptysis. Several investigators have endorsed that PVS is a relentlessly progressive disease, extending deep into the lung, resulting in diffuse hypoplasia and eventually atresia of the affected PVs.[5,8,12,13] In contrast, in our case after DES placement we noted impressive growth of distal PVs in the

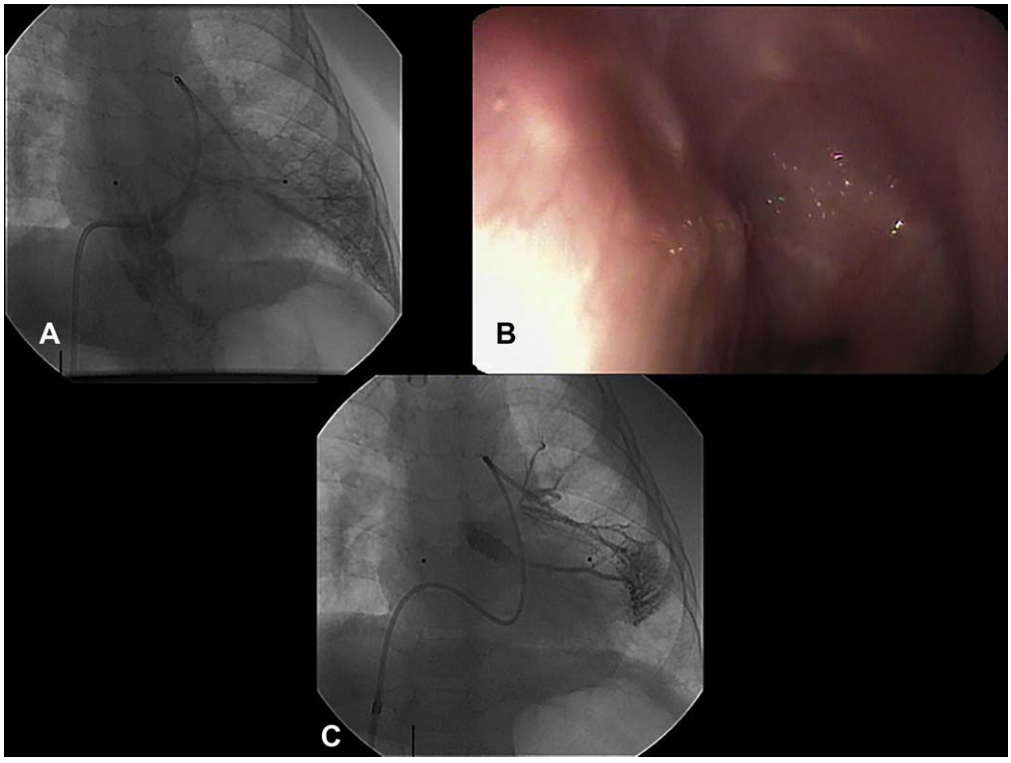

FIGURE 3 (A) Left pulmonary artery wedge angiography shows contrast flowing into the left lower pulmonary vein and then to the distal half of the pulmonary vein stent. Flow then does not proceed through the stent but rather into an ectatic venovenous collateral and from this into a paraesophageal venous plexus. Faint filling of esophageal varices is noted. Contrast is noted to remain in the lung parenchyma. (B) Esophagoscopy shows massive esophageal varices. (C) After PTFE-covered stent placement, left pulmonary artery wedge angiography shows free flow through the stent to the left atrium as well as filling of the left upper pulmonary vein which is atretic

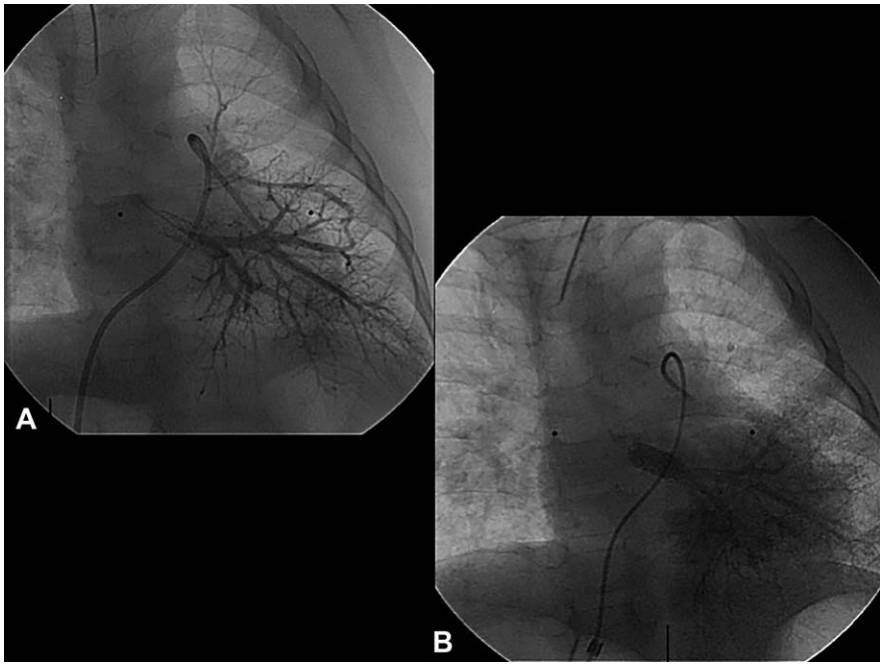

FIGURE 4 (A) Wedge angiogram showing a thread-like jet of contrast through the stented left lower pulmonary vein. Also seen are few collaterals from the left lower lobe to the left upper lobe with transient filling of the left upper pulmonary capillary network. (B) Postdeployment of 4 mm × 20 mm Taxus Liberte drug-eluting stent. Contrast is injected into the left pulmonary artery and seen filling the left pulmonary arterioles and capillary bed with unobstructed return of blood flow through the left lower pulmonary vein through the stents into the left atrium

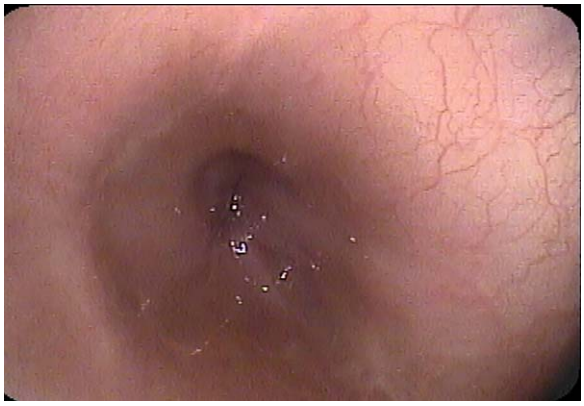

FIGURE 5 Repeat esophagoscopy documented resolution of esophageal varices

entire lung, both in the treated left lower lobe and in the untreated left upper lobe. This finding may suggest that typical failure of surgical or percutaneous therapies for PVS, with consequent distal "upstream" disease progression, may, in some cases, stem from inability to maintain a patent venous ostium due to intractable intimal proliferation, although further data are needed to examine this hypothesis. Our case illustrates instead that with provision of adequate pulmonary venous drainage via a patent ostium there can be striking growth and development of intrapulmonary veins. Prior publications on the use of DES for PVS are few, and the effect on distal vessel growth was not documented, given that only short-term results were provided.[10,14–18]

Current generations of balloon-expandable DES are designed for coronary use, and, thus, have limited potential for redilation, typically

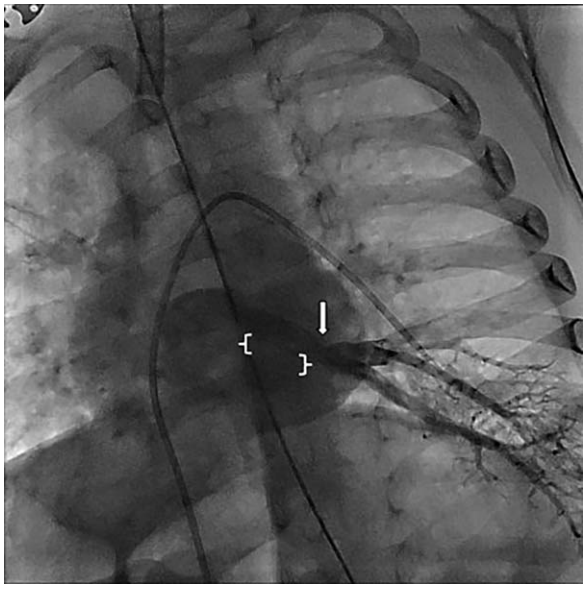

FIGURE 6 Left pulmonary wedge angiogram shows interval patency of the left lower pulmonary vein with no evidence of obstruction within the stent. No intervention was performed during this catheterization. The distal pulmonary vein is seen to exceed the diameter of the stent, which is delineated in brackets, indicative of interval growth in the pulmonary vein distal to the stent (arrow)

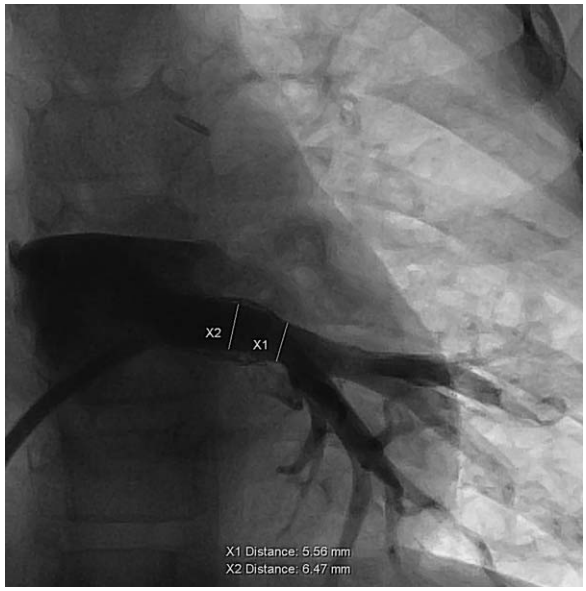

FIGURE 7 After balloon angioplasty, left lower pulmonary vein angiography shows that the left lower pulmonary vein stent has been increased in caliber tremendously, and now slightly exceeds the intraparenchymal pulmonary vein diameter. The distal left lower pulmonary vein has grown significantly in diameter over time

to a maximal diameter of approximately 6 mm. We acknowledge this important limitation, and accordingly used DES as a last resort in our patient, an approach that we feel was justified given the severity of his disease. At the time of DES implantation, the stent was postdilated to 6 mm, and this may have contributed to good long term patency, as it has been shown larger stent diameter at time of stent implantation for PVS has been associated with improved stent patency.[10] When he outgrew the maximal possible DES diameter, we performed intentional DES fracture, resulting in increased diameter of the stented LLPV without evidence of vessel injury. Intentional stent fracture, therefore, overcame the most important limitation that these stents pose for pediatric use in vessels that are destined to grow beyond the maximal stent diameter. The approach of inducing intentional stent fractures for under-sized stents in children has been previously reported in pulmonary arteries,[19,20] although we believe this to be the first clinical report of an intentional stent fracture for PVS. Additional studies will be necessary to confirm the feasibility and safety of intentional stent fracture as a strategy to overcome undersized stents used for treatment of PVS.

6 | CONCLUSIONS

The child presented herein was afforded successful relief of PVS and hemoptysis after severe PVS with collateralization via esophageal varices. Most reports of surgical and percutaneous treatments for PVS have poor outcomes, attributed to an apparently progressive disease process. DES may play an important role in the treatment of PVS by retarding the development of intimal proliferation at the pulmonary venous ostium, thereby allowing growth of intrapulmonary veins. The limited redilation potential of current-generation DES pose an

important challenge to their applicability in growing children, although this limitation may be overcome by performing intentional stent fracture using ultra-high pressure balloons.

AUTHOR CONTRIBUTIONS

Case Review, Manuscript Writing and Editing, Compilation of Figures: Goldberg

Manuscript Advice, Specialty-Driven Editing, Compilation of Esophagoscopy Figures: Jensen

Compilation of Radiologic Figures: Krishnamurthy

Specialty-Driven Editing, Contribution of Sources: Varghese

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