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HEART FAILURE

ADVANCED

CASE REPORT: CLINICAL CASE

Heart Failure in a Child

Multimodality Approach Leading to an Unusual Cause

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ABSTRACT

Heart failure secondary to isolated pulmonary artery vasculitis is rarely described in children. We describe a 10-year-old child who presented with right heart failure symptoms, severe pulmonary hypertension, and bilateral branch pulmonary artery stenosis secondary to isolated pulmonary artery vasculitis. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2021;3:1869–1876) © 2021 Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 10-year-old girl presented with dyspnea during ordinary physical activity and anasarca for 6 months. She had experienced accompanying low-grade intermittent fever and generalized malaise for a year. There was no history of paroxysmal nocturnal dyspnea, orthopnea, chest pain, cough, hemoptysis, limb claudication, loss of appetite, or weight loss. The birth history and family history were unremarkable. On examination, there was no facial dysmorphism or other syndromic characteristics. The jugular venous pulse was elevated, with prominent C-V waves and tender hepatomegaly (6 cm below the right costal margin in the right midclavicular line). All peripheral pulses were normal on examination. There was a loud pulmonary component of second heart sound and grade 3/6 pansystolic murmur at the left lower parasternal area. The respiratory system examination was normal.

LEARNING OBJECTIVES

- To formulate a differential diagnosis of right heart failure with pulmonary hypertension in a child.
- To recognize the importance of a multimodality approach to the treatment of patients with right heart failure and pulmonary hypertension.
- To discuss the management options for isolated pulmonary artery vasculitis.

MEDICAL HISTORY

There was no history of joint pain, prolonged immobilization, chronic drug intake, cardiovascular disease, tuberculosis, or family history of Takayasu arteritis (TA).

DIFFERENTIAL DIAGNOSIS

The differentials considered were pulmonary arterial hypertension, chronic thromboembolic pulmonary hypertension, and pulmonary hypertension secondary to peripheral pulmonary artery stenosis (PPS).

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ABBREVIATIONS AND ACRONYMS

ESR = erythrocyte sedimentation rate

FDG-PET = fluorodeoxyglucose-positron emission tomography

LPA = left pulmonary artery

MPA = main pulmonary artery

PA = pulmonary artery

PPS = peripheral pulmonary artery stenosis

RA = right atrium

RPA = right pulmonary artery

RV = right ventricle

TA = Takayasu arteritis

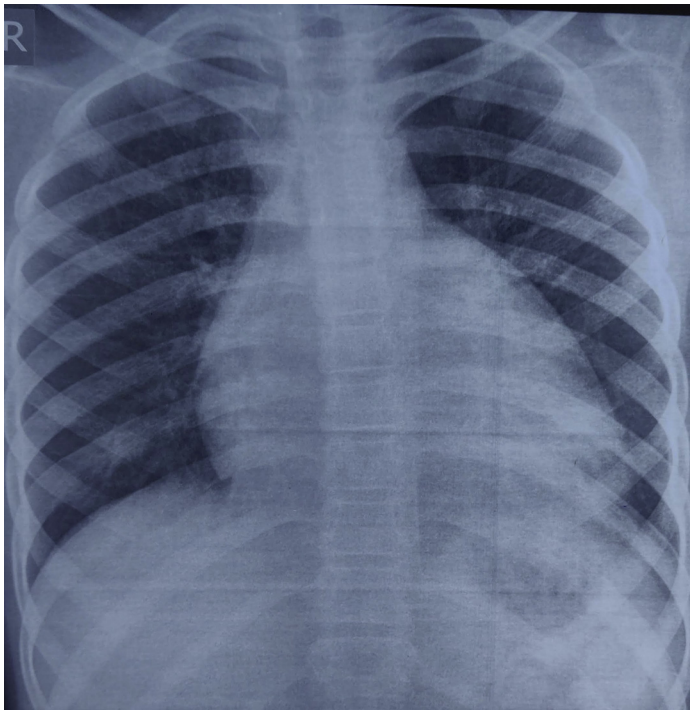
INVESTIGATIONS

The complete blood count and hepatic and renal function tests were normal. The inflammatory markers were elevated: C-reactive protein 3 mg/dL, erythrocyte sedimentation rate (ESR) 20 mm/h. Antinuclear antibodies and antineutrophil cytoplasmic antibodies were negative. The ear, nose, and throat and renal and ophthalmologic evaluations excluded systemic vasculitic involvement. The results of a workup for tuberculosis (Mantoux test, family screening, sputum for acid-fast bacilli, gene expert of induced sputum, ultrasound of the abdomen) were negative. Viral markers (hepatitis B and C, human immunodeficiency virus), hypercoagulable work-up (MTHFR gene mutation, protein C and S, lupus anticoagulant, β-2 glycoprotein, factor V Leiden and prothrombin gene mutation), COVID-19 RT-PCR and SARS-CoV-2 IgG antibodies were also negative. No infection focus was identified clinically, and the result of sepsis workup was negative.

Chest radiograph (**Figure 1**) showed cardiomegaly with prominent right atrium (RA) and main pulmonary artery (MPA) segment with peripheral pruning. Electrocardiogram (**Figure 2**) showed sinus tachycardia, RA enlargement, and right ventricular (RV) strain pattern. Transthoracic echocardiography revealed dilated RA, RV, severe tricuspid regurgitation (TR) (estimated RV systolic pressure 95 mm Hg + RA pressure) with severe RV dysfunction and with no structural abnormalities (**Figure 3,** Video 1). The MPA was dilated, and bilateral branch pulmonary arteries (PA) had severe discrete stenosis. Computed tomographic angiography depicted tight focal stenosis of the right pulmonary artery (RPA) and left pulmonary artery (LPA) in the mid to distal parts with poststenotic dilatation (**Figure 4**). No intraluminal thrombus or webs were seen. The PA branches to the upper lobes were poorly visualized bilaterally. Mild eccentric mural wall thickening of the RPA and LPA was noted in addition to ill-defined soft tissue adjacent to the sites of PA stenosis, which prompted further evaluation to characterize the extraluminal pathologic changes. The aorta and arch vessels were normal (**Figure 4**). MRI demonstrated eccentric wall thickening along the left lateral wall of the MPA, LPA, and RPA with mild enhancement on postcontrast imaging. There was no abnormal mediastinal soft tissue (**Figure 5**). Fluorodeoxyglucose positron emission tomography (**Figure 6**) revealed focal areas of increased metabolic activity in the MPA and LPA. Therefore, imaging modalities were suggestive of isolated bilateral PA vasculitis. Owing to the absence of phenotypic features and family history, a genetic study for syndromes associated with PPS (Williams, Alagille, and Noonan syndrome) was not performed.

We made a presumptive diagnosis of isolated PA vasculitis secondary to TA based on the age, gender, ethnicity, duration of illness, raised inflammatory biomarkers, and radiologic evidence of active vessel wall inflammation.

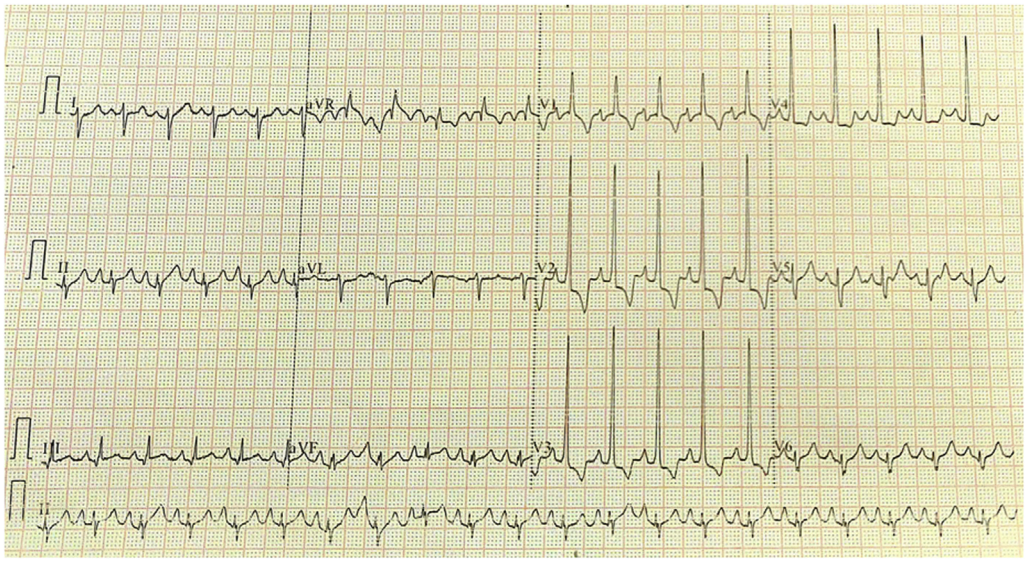
FIGURE 1 Chest Radiograph at Admission



MANAGEMENT

The child was initially given decongestive measures and oral prednisolone 1mg/kg per day. After 3 months of steroids, the inflammatory biomarkers normalized, and the symptoms of right heart failure reduced, but exertional dyspnea persisted. Therefore, the child was planned for endovascular balloon dilatation of bilateral branch PA. RPA angiography showed significant stenosis 4 cm from the MPA bifurcation with a minimum diameter of 2.8 mm and adjacent proximal and distal vessel measuring 8.3 mm and 7.5 mm, respectively (**Figure 7**). LPA angiography showed significant stenosis 2.6 cm from the MPA bifurcation with a minimum diameter of 3 mm, adjacent proximal and distal vessel measuring 8.6 mm and 7 mm, respectively (**Figure 7**). The RPA was accessed with a

FIGURE 2 Electrocardiogram at Admission



5-F MPA2 catheter and dilated with a Tyshak II 8 × 20mm balloon followed by Sterling 7 × 20 mm at 8 atm for 30 s, thrice (Video 2). The LPA was accessed with some difficulty with a 5-F MPA2 catheter and dilated thrice with Sterling 7 × 20 mm at 8 atm pressure for 30 s (Video 3). After the procedure, the RPA and LPA showed improved flow without rupture or intimal flap, and the narrowest diameters increased to 4.3 mm and 4.6 mm, respectively (**Figure 8,** Videos 4 and 5). Echocardiographically, the RV systolic pressure reduced to 53 mm Hg + RA pressure (**Figure 9**), and RV function also improved.

FIGURE 3 Continuous-Wave Doppler Image of Tricuspid Regurgitant Jet

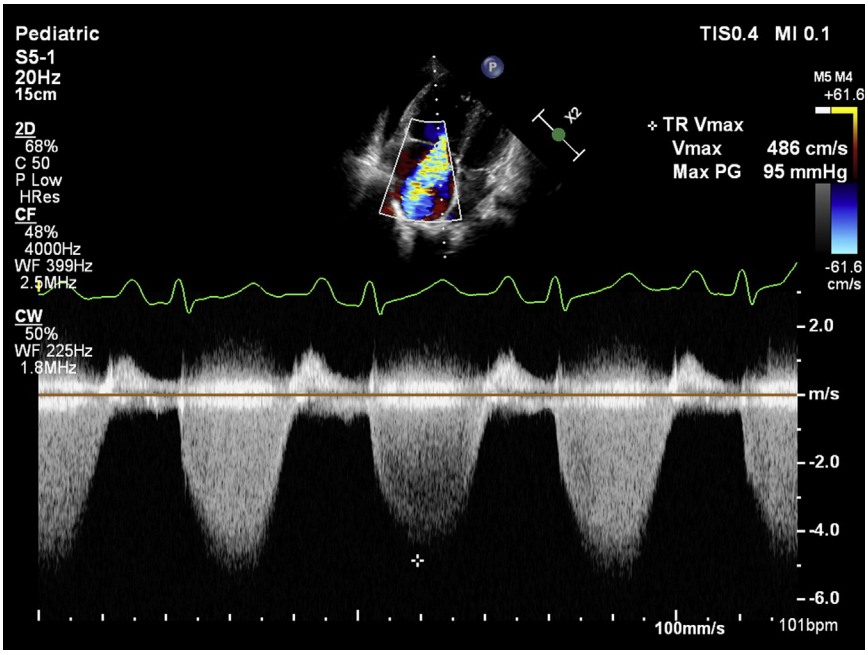
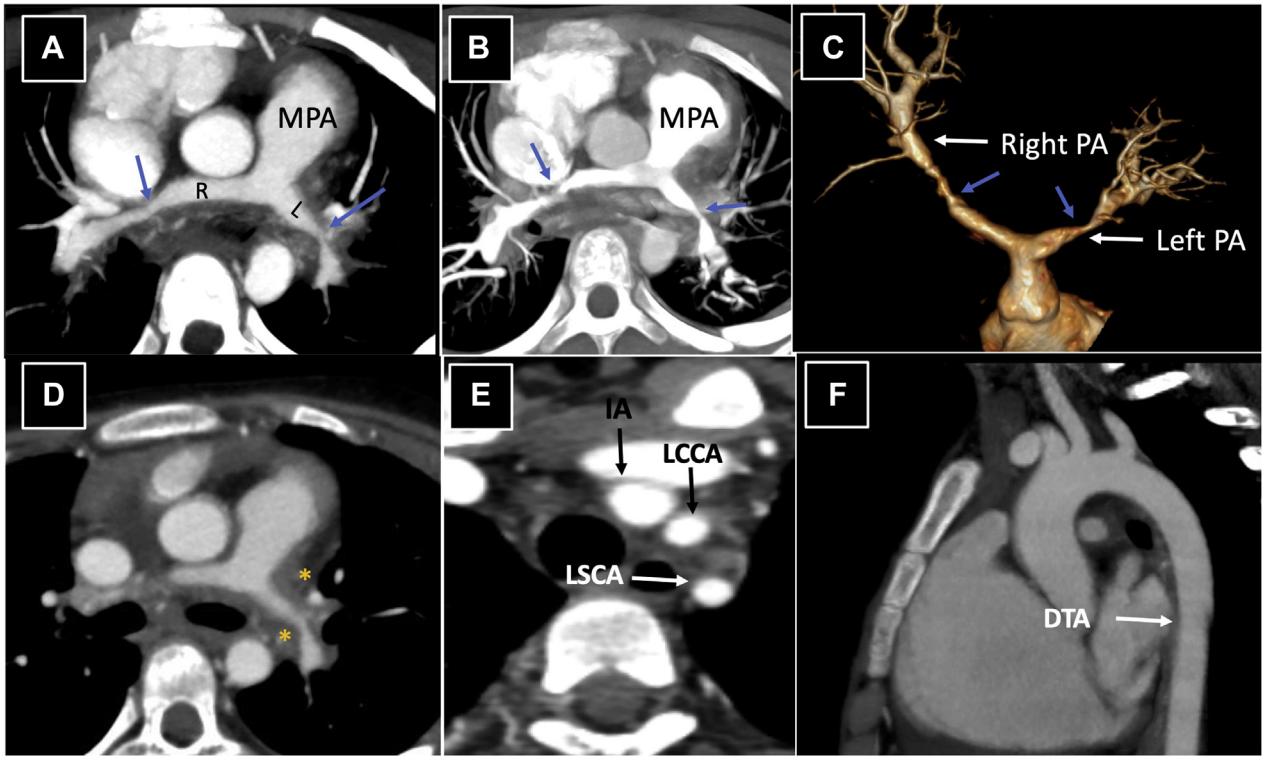


FIGURE 4 Computed Tomographic Angiograms



(A) Axial section depicting mural thickening of pulmonary arteries (PAs) with stenosis in mid to distal part. **(B)** Maximum-intensity and **(C)** volume-rendered images demonstrating PA stenosis. **(D)** Ill-defined soft tissue around PAs. **(E)** Axial and **(F)** sagittal oblique images depicting normal arch vessels and thoracic aorta.
DTA = descending thoracic aorta; IA = innominate artery; L = left pulmonary artery; LCCA = left common carotid artery; LSCA = left subclavian artery; MPA = main pulmonary artery; R = right pulmonary artery.

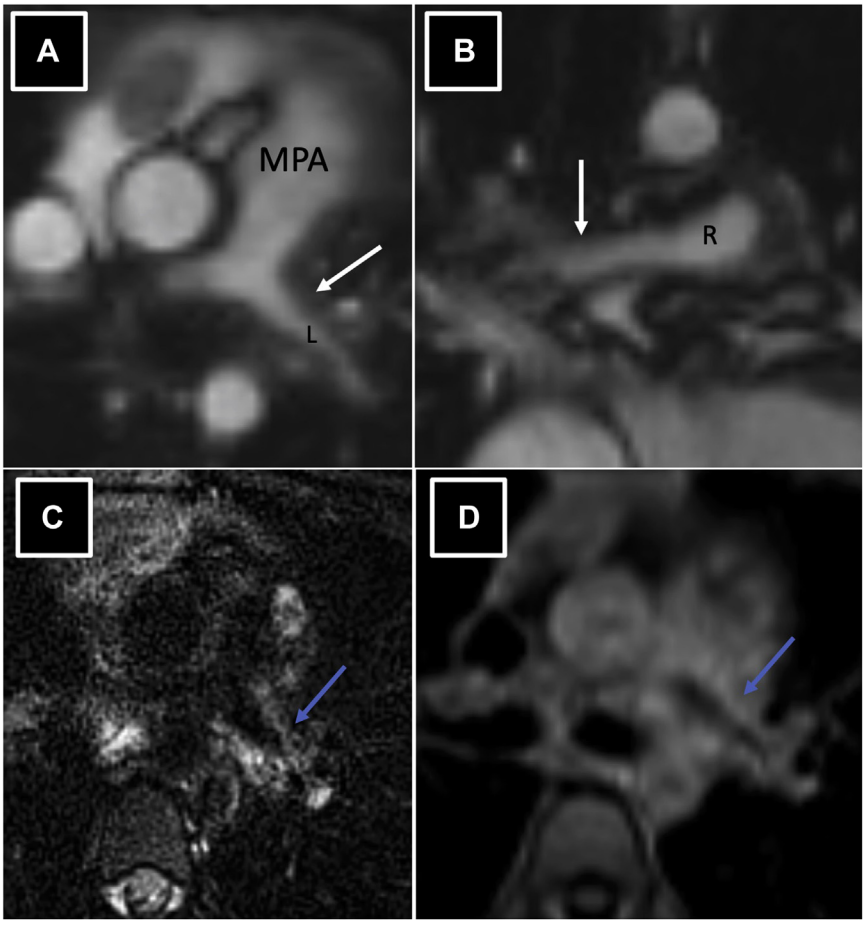
The patient was discharged to take oral prednisolone with a plan to serially monitor RV pressure and function and consider repeat balloon dilatation or stenting in the future, in case of worsening or no further improvement. The maintenance dose of steroid was continued.

DISCUSSION

In children, heart failure with severe pulmonary hypertension is secondary to left-to-right shunt lesions. PPS is an uncommon cause of heart failure in children and is usually congenital. PA vasculitis, an acquired cause of PPS, is extremely rare and is most commonly associated with TA. The incidence of pulmonary vasculitis in TA is estimated to be 14% to 86%, with the majority of patients having subclinical involvement (1). It comes to attention once complications develop, like pulmonary hemorrhage, pulmonary embolism, severe pulmonary hypertension due to PPS, and RV dysfunction. In our case, the child presented with bilateral PPS and RV dysfunction. Isolated PA vasculitis due to TA is extremely rare in children with a single report in the existing literature (2).

Chronic obstruction of PAs may result from congenital PPS, endoluminal obstruction (thromboembolic disease), extraluminal compression, and systemic disorders (eg, TA, Behcet disease). Congenital PPS usually presents in infancy, has variable presentation, and rarely leads to right heart failure. The absence of associated lung parenchymal abnormalities, aortopulmonary collaterals, and evidence of inflammation in our case excluded this diagnosis. Cross-sectional imaging modalities help in differentiating between intraluminal and extraluminal pathologic changes and assessing involvement of other vessels. TA frequently involves upper lobe vessels, causing poor visualization, as seen in our case (3). The lack of PA aneurysms, mass lesions, venous thrombosis, and oral/genital ulcers, ruled out Behcet disease and Hughes-Stovin disease. In light of recent

FIGURE 5 Magnetic Resonance Imaging



(A, B) Bright blood images depicting mural thickening along pulmonary arteries. **(C)** Mural thickening shows hyperintensity on fat saturated T2 image and **(D)** enhancement on postcontrast image. MPA = main pulmonary artery; R = right pulmonary artery.

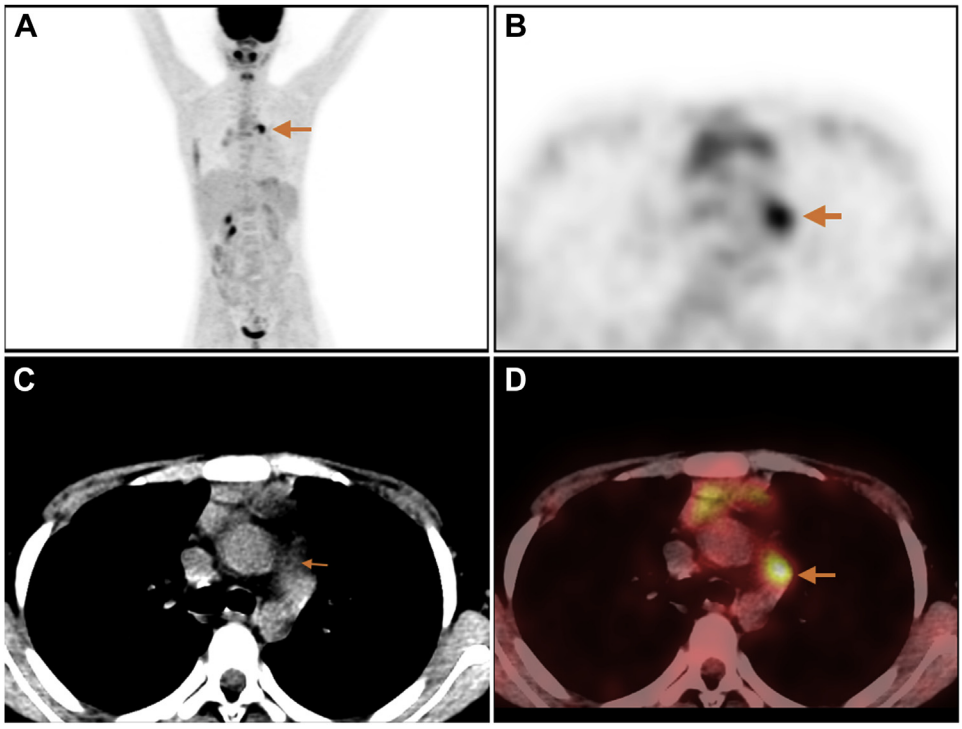
literature on COVID-19-associated thrombotic complications, COVID-19 was also ruled out.

We made a presumptive diagnosis of isolated PA vasculitis secondary to TA. TA is well known to increase cardiovascular morbidity in children under 10 years of age because of its atypical features and delayed diagnosis. Isolated PA vasculitis secondary to TA is difficult to prove. The majority of cases are diagnosed on the basis of biopsy findings or retrospectively when systemic arteries are involved (2-9). Pulmonary vasculitis patients with pulmonary hypertension are at increased risk of early mortality (10). During the acute inflammatory stage, immunosuppression results in symptomatic improvement in most patients, although improvement in stenotic lesions is rare (**Table 1**). Existing data suggest that established pulmonary hypertension and PA stenosis does not reverse completely by medical treatment alone and requires pulmonary revascularization using endovascular or surgical therapy as a complementary strategy in most patients (11).

FOLLOW-UP

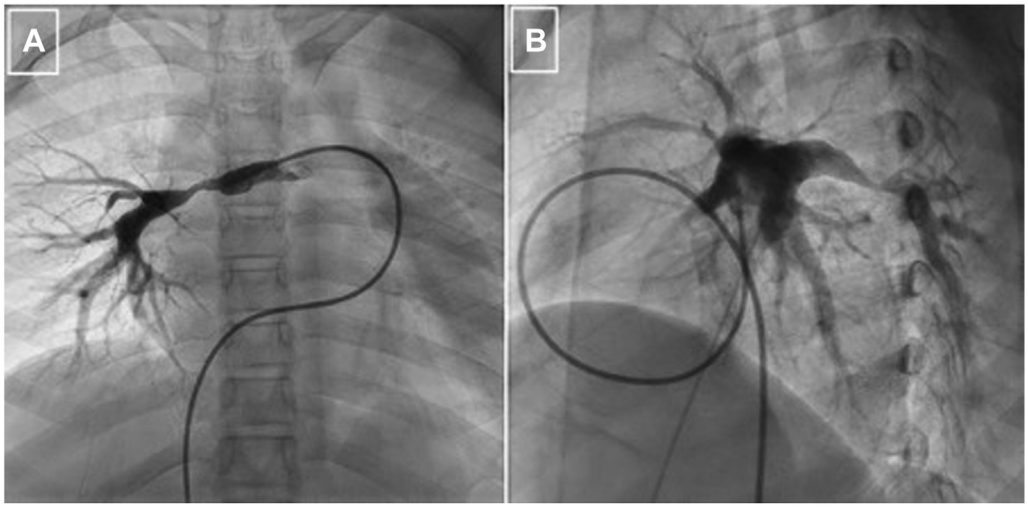
At the 6-month follow-up visit, the patient had significant symptomatic improvement. There was no systemic artery involvement. However, echocardiography showed persistent bilateral PPS, RV dysfunction, and severe tricuspid regurgitation (RV systolic pressure 83 mm Hg + RA pressure). The inflammatory markers were raised (ESR 35 mm/h, CRP 31.5 mg/L); therefore, prednisolone 1 mg/kg per day was started again. We anticipate that she would require additional steroid-sparing

FIGURE 6 FDG-PET Computed Tomographic Imaging



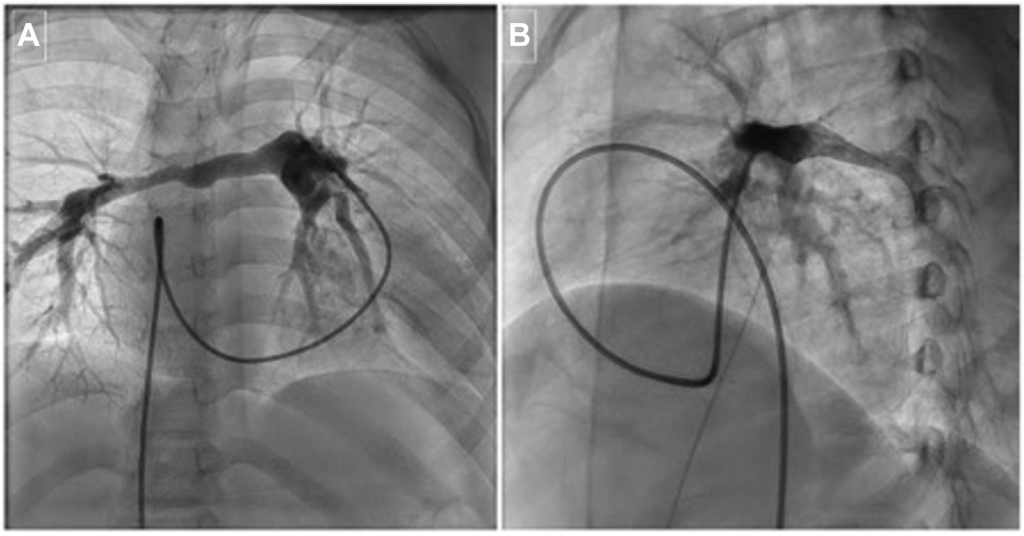
(A, B) Maximum-intensity projection images of fluorodeoxyglucose-positron emission tomography (FDG-PET) computed tomography showing focal area of increased tracer uptake in left thoracic region, corresponding to subtle hypodensity on computed tomography thorax **(C)**. **(D)** Increased FDG uptake on fused PET-CT image.

FIGURE 7 Pre-Balloon Dilatation Angiograms



(A) Right pulmonary artery (RPA) angiogram in frontal plane showing severe mid RPA stenosis. **(B)** Left pulmonary artery (LPA) angiogram in left anterior oblique plane showing severe mid LPA stenosis.

FIGURE 8 **Post-Balloon Dilatation Angiogram**



(A) Right pulmonary artery (RPA) angiogram in the frontal plane showing mid-RPA diameter of 4.3 mm after balloon dilatation. **(B)** Left pulmonary artery (LPA) angiogram in left anterior oblique plane showing mid-LPA diameter of 4.6 mm after balloon dilatation.

FIGURE 9 **Post-Balloon Dilatation Continuous-Wave Doppler Image of Tricuspid Regurgitant Jet**

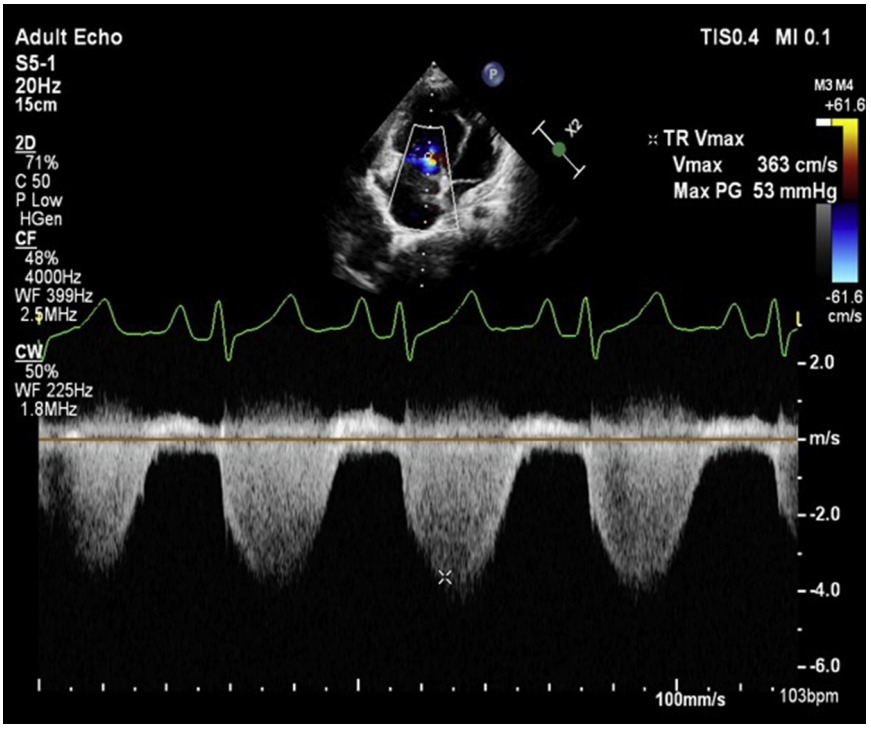


TABLE 1 Review of Studies of Treatment Modalities and Outcomes in Patients with Isolated Pulmonary Artery Vasculitis Due to Takayasu Arteritis

First Author, Year (Ref. #)	Age (y)	Presentation	Involved Vessels	Treatment	Outcome	Follow-Up Duration
Ferretti et al, 1996 (4)	34	Right hemithoracic pain	Stenosis and occlusion of RPA	Corticosteroids and heparin	Improvement in symptoms and RPA caliber	1 y
Chan et al, 2007 (2)	10	Massive hemoptysis	Aneurysms in second branch of left main PA and branch arteries of right upper and middle lobe	Left upper lobe embolization, left upper lobe and left lingular lobectomy; corticosteroids and cyclophosphamide for 4 months followed by methotrexate	Improvement in hemoptysis and vessel wall thickness	9 mo
Fukuda et al, 2008 (5)	73	Right heart failure	Severe stenosis of MPA and LPA	Corticosteroids	Improvement in symptoms but no significant change in stenotic lesions	1 y
Qin et al, 2009 (6)	32 (Median) (n = 4)	Exertional dyspnea and lower limb edema	Severe stenosis of 1 or more branches of RPA and LPA	One patient underwent balloon dilatation and 3 underwent dilatation + stenting; all received oral corticosteroids	Improvement in symptoms and improved lung perfusion in 3 patients; 1 experienced restenosis at 1.5 y	1-4 y
Hagan et al, 2011 (7)	40 and 53 (n = 2)	Exertional dyspnea	Stenosis of RPA and LPA	1. Limited endarterectomy with steroids and cyclophosphamide → cyclophosphamide replaced with azathioprine → 15 months later, started on mycophenolate mofetil and infliximab.	Improvement in symptoms	3 y
				2. Limited endarterectomy with steroids and azathioprine	25% reduction in PA pressure (mPAP 40 > 30) Improvement in 6-minute walk distance	3 mo 1 y
Leibscher et al, 2017 (8)	56	Exertional dyspnea, syncope, and chest pain	Diffuse stenosis of MPA and RPA	Corticosteroids (3 mo) and azathioprine → relapsed in few months → methyl prednisolone (3 d) and methotrexate	Improvement in symptoms but PA stenosis persisted	18 mo
Alizadehasl et al, 2020 (9)	30	Progressive dyspnea and fatigue	Severe stenosis of RPA and LPA	Corticosteroids and azathioprine	Improvement in symptoms and significant reduction of PA pressure (>50%)	3 y

immunosuppressant therapy and repeated balloon dilatation/stenting in case of inadequate response.

CONCLUSIONS

We describe a rare case of a child who presented with heart failure secondary to isolated PA vasculitis. The combination of immunosuppression and endovascular intervention can help in treating this rare and difficult entity.

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KEY WORDS congestive heart failure, peripheral pulmonary artery stenosis, pulmonary artery intervention, pulmonary artery vasculitis, Takayasu arteritis

APPENDIX For supplemental videos, please see the online version of this article.