SARCOIDOSIS VASCULITIS AND DIFFUSE LUNG DISEASES 2020; 37 (2); 239-242 DOI: 10.36141/svdld.v37i2.8987

Pulmonary hypertension secondary to takayasu's arteritis: management using a combined medical and interventional approach

Matthew Nitzberg[1], *Raj Parikh*[2], *Praveen Govender*[2], *Harrison W. Farber*[3]

[1]Pulmonary Critical Care Medicine, Newton-Wellesley Hospital, Newton, MA; [2]The Pulmonary Center, Boston University School of Medicine, Boston, MA; [3] Division of Pulmonary, Critical Care and Sleep Medicine, Tufts Medical Center, Boston, MA

Key words: Takayasu's Arteritis (TA), Pulmonary Hypertension, Pulmonary Arterial Hypertension, Epoprostenol, Endovascular Stent

To the editor:

Takayasu's Arteritis (TA) is a chronic, large-vessel vasculitis that typically occurs in women between the ages of 10 and 40.[1] Glucocorticoids, steroid-sparing immunosuppressive agents, and biologics are commonly used for the medical management of TA; however, large-vessel stenoses may require stenting or bypass procedures.[2] The pulmonary artery (PA) network is affected in up to 50% of TA cases, which may result in severe pulmonary hypertension (PH) due to PA stenoses.[3] Successful cases of PA stenting have been reported; however, none has reported the use of a combination of medical and interventional therapies nor documented the long term effects of PA stenting on cardiopulmonary hemodynamics measured by right-heart catheterization (RHC).[4]

We present a 48-year-old female who presented with 3 years of progressive shortness of breath and exertional chest pain. Her past medical history was significant for Takayasu's arteritis diagnosed at the age of 27 by angiogram revealing left subclavian artery stenosis. She had previously been treated with prednisone 40mg and transitioned to methotrexate for 10 years, resulting in clinical remission. At that point, all medications were discontinued; she was lost to follow-up until occurrence of respiratory symptoms.

At the time of presentation, she had World Health Organization (WHO) Functional Class (FC) IIIb symptoms and an exam significant for asymmetric blood pressures between her upper extremities, resting pulse oximetry of 94% which decreased to 88% with ambulation, and a loud S2 with grade III holosystolic murmur at the right sternal border. There was no clubbing, peripheral edema, jugular venous distention, or crackles on lung examination. Echocardiogram revealed moderate right ventricular dilation, severe right atrial dilation, 3+ tricuspid regurgitation, and an estimated PA systolic pressure of 167 mmHg; ejection fraction estimated at 70%. RHC confirmed severe PH (PA systolic: 150 mmHg, PA diastolic: 41 mmHg, mean PA pressure: 65 mmHg, pulmonary vascular resistance: 1219 dynes•s/cm5; pulmonary capillary wedge pressure: 17 mmHg; cardiac index: 1.85 L/min). Computer tomography pulmonary angiogram revealed diffuse narrowing of the right PA, focal stenosis of the left PA with distal aneurysmal dilatation, and no pulmonary emboli (Figure 1). Erythrocyte sedimentation rate was normal. The patient was initiated on

Received: 26 October 2019
Accepted after revision: 20 May 2020
Correspondence: Raj Parikh
The Pulmonary Center
Boston University School of Medicine,
72 East Concord Street, R-304
Boston, MA 02118
Raj.parikh@bmc.org

continuous epoprostenol through a tunneled central catheter; it was gradually uptitrated to 34 ng/kg/min over a 10-month period with clinical improvement. Repeat RHC at 10 months revealed improvement in hemodynamics (Table 1); however, at 34 months, she presented with worsening peripheral edema, and hemodynamic findings of RV dysfunction (Table 1). Pulmonary arteriogram demonstrated an 8 cm 80% stenosis of the right main PA with an elevated trans-stenotic pressure gradient (peak 90 mmHg, mean 42 mmHg); there were no hemodynamically significant stenosis of the left PA. The patient was reluctant to undergo an interventional procedure and thus, medical management was intensified. Epoprostenol was uptitrated to 52 ng/kg/min.

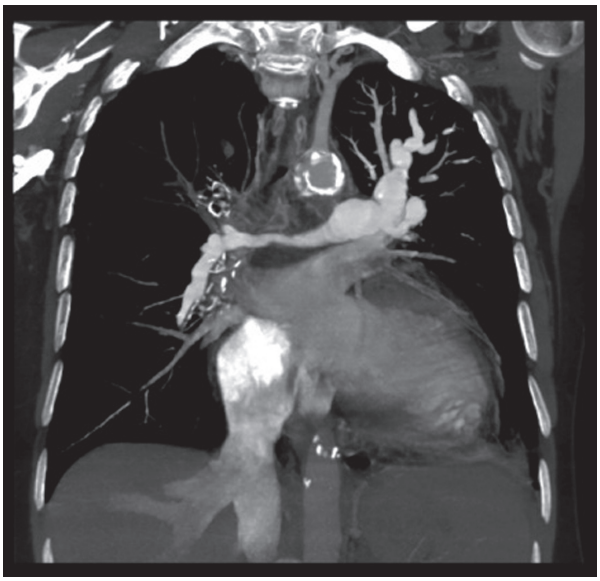

Fig. 1.

Despite 4 years of medical therapy, right heart failure progressed and the patient developed ascites, required frequent hospitalizations, and deteriorated to FC IV. At this point, the patient agreed to stenting and two overlapping balloon expandable stents were deployed in the right main PA. The peak trans-stenotic gradient deceased from 82 mmHg to 35 mmHg after deployment of the stents. Post-procedure course was complicated by pulmonary edema of the right lung due to the rapid increase in perfusion to the chronically hypo-perfused tissue; however, this responded effectively to furosemide and a short course of inhaled nitric oxide. The patient also received 500mg of intravenous methylprednisolone one day prior to and for three days after the procedure, followed by a 2-week prednisone taper to mitigate a procedure-related arteritis flare. Epoprostenol was continued at 52 ng/kg/min. One week after stent placement, renal function and liver function tests normalized, oxygen requirements decreased, and she improved to FC III. Four years after stent placement, she remained on Epoprostenol and had improved to FC II, no longer requiring supplemental oxygen. RHC demonstrated markedly improved hemodynamics and cardiac function. The PA stent was patent and free-flowing (Figure 2).

This is an interesting case of TA induced PA stenosis and severe PH treated with a combination of Epoprostenol and PA stenting. With Epoprostenol,

Table 1. Major diagnostic and therapeutic interventions

Event	RHC 1 and Epo initiation	RHC 2	RHC 3	PA stent placement	RHC 4
Time since epo initiation (months)	0	10	34	49	114
Epo Dose (ng/kg/min)	0	34	52	52	36
CVP (mmHg)	12	8	15	n/a	9
PAP (mmHg)	150/41	135/18	120/24	n/a	94/17
Mean PAP (mmHg)	65	59	58	n/a	46
PCWP (mmHg)	17	14	20	n/a	13
CI (L/min)	1.85	2.3	1.80	n/a	2.91
PVR dyn•sec/cm5	1219	983	1012	n/a	530

Epo – epoprostenol; RHC – Right Hearth Catheterization; PA – Pulmonary Artery; CVP – central venous pressure; PAP – pulmonary artery pressure; PCWP – pulmonary capillary wedge pressure; CI – cardiac index; PVR – pulmonary vascular resistance

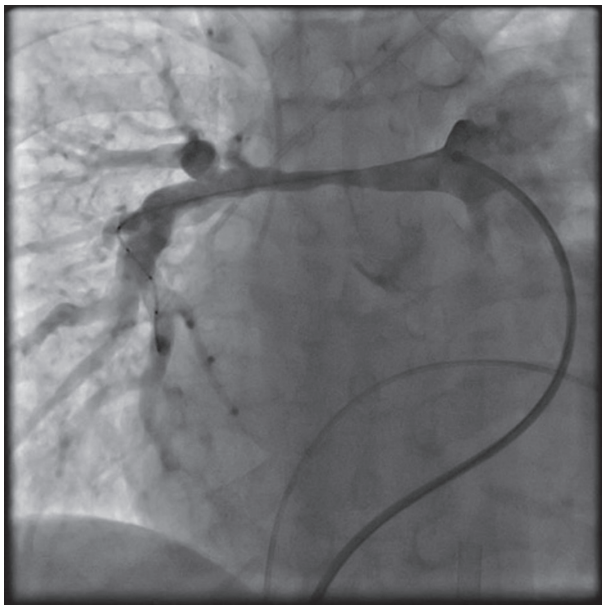

Fig. 2.

the patient survived 4 years to stent placement. For patients who have a contraindication to PA stenting, or who do not wish to undergo the procedure, pulmonary vasodilator therapy may be an option albeit there have been no studies evaluating efficacy and safety of vasodilator therapy in this entity. Given the rarity of TA-associated PH, it is unlikely a placebo-controlled study would be feasible. This case is the first to report long-term hemodynamic follow-up after stenting for PA stenosis from TA. The RHC information, in this case, provides objective support for use of PA stenting in TA-associated PH by demonstrating marked and sustained hemodynamic improvement over a 5-year period. The one prior case series of PA stenosis from TA showed good clinical outcomes with stenting.[4] In this series, 3 of 4 patients underwent stenting of the stenosis and had sustained clinical response and maintained lower pulmonary pressures by image-based surrogate measurements. The one patient who underwent only balloon angioplasty developed recurrence of symptoms at 18 months. All of the patients in this series remained on prednisone at the end of their follow-up periods and the authors suggest corticosteroid maintenance to prevent re-stenosis. Our patient only used corticosteroids for a brief peri-procedural period and had no evidence of re-stenosis on angiogram 4 years after stenting.

PA stenting is an effective treatment in the management of selected patients with TA-induced PA stenosis. In TA-associated PH, pulmonary vasodilators, such as Epoprostenol, may be effective since this entity is a form of connective tissue disease related PH. Further studies are needed to support these conclusions.

References

1. Weyand, C. M. & Goronzy, J. J. Medium- and large-vessel vasculitis. N. Engl. J. Med. 349, 160–169 (2003).
2. Keser, G., Direskeneli, H. & Aksu, K. Management of Takayasu arteritis: a systematic review. Rheumatology ket320 (2013). doi:10.1093/rheumatology/ket320
3. Moore, J. W., Reardon, M. J., Cooley, D. A. & Vargo, T. A. Severe Takayasu's arteritis of the pulmonary arteries: Report of a case with successful surgical treatment. J. Am. Coll. Cardiol. 5, 369–373 (1985).
4. Qin, L., Hong-Liang, Z., Zhi-Hong, L., Chang-Ming, X. & Xin-Hai, N. Percutaneous transluminal angioplasty and stenting for pulmonary stenosis due to Takayasu's arteritis: clinical outcome and four-year follow-up. Clin. Cardiol. 32, 639–643 (2009).