Could pulmonary arterial hypertension-specific agents be an option for Takayasu's arteritis related pulmonary hypertension?

Sirs,

Takayasu's arteritis (TAK) may involve the pulmonary arteries (PA) and pulmonary hypertension (PH) can be found at a rate of 10-15% of TAK patients (1-4). The main mechanism of the increased PA pressure is mechanical obstruction (2, 3). Controlling the inflammation of pulmonary vessels with immunosuppressives remains the mainstay of treatment. However, pulmonary vasodilators may also be useful in TAK patients with PH due to PA involvement (PAI) (1, 3). Herein, we report a case with the diagnosis of TAK-related PH and even the PA occlusion persisted with immunosuppressive treatment, a significant decrease in PA pressures was observed with the pulmonary arterial hypertension (PAH)-specific therapy.

A 31-year-old female patient who had TAK with PAI has been in remission for the last 6 years and the latest 3 years with no treatment, presented with fatigue, weight loss and haemoptysis. Her C-reactive protein level (CRP) was 63 mg/L (range 0-5) and erythrocyte sedimentation rate 36 mm/h (0-20). In the pulmonary CT angiography, the pulmonary trunk was enlarged (3.5 cm in diameter), the right lower lobe PA branch could not be visualised, bronchial arteries were prominent and wall irregularities were present in the left lower lobe branch of the PA which were consistent TAK flare. Cyclophosphamide (500 mg/month for 3 months) and high-dose methylprednisolone (1000 mg/day for 3 days) treatment was started as a re-induction. Transthoracic echocardiography was performed due to exertional dyspnoea and revealed an increase in systolic PA pressure (45 mm/Hg). Left ventricular functions and left atrial diameter were normal. The patient was then referred to our tertiary medical centre in December 2019 for the evaluation of possible PH. At admission, her World Health Organisation Functional Capacity (WHO FC) was II-III and 6-minute walking distance (6MWD) was 552 meters. Regarding physical examination, blood pressure was detected as 110/70 mm/Hg in bilateral arms. Peripheral pulses were palpable. No bruit was detected. In laboratory, haemogram, biochemistry and acute phase reactants (APR) were normal. Brain natriuretic peptide (BNP) was normal (<10 pg/mL). Haemodynamic parameters in the right heart catheterisation (RHC) were compatible with precapillary PH (Table I). The patient was considered as group 4 PH due to PAI. Treatment was started with infliximab 5 mg/kg for every 8 weeks with low dose prednisolone (5 mg/day) and sildenafil 20 mg t.i.d. During follow-up, APRs and serum BNP levels remained stable. Occlusive findings persisted in control CT angiography after 14 months (Fig. 1). However, a decreasing trend to normal in mean pulmonary arterial pressure (mPAP) and pulmonary vascular resistance was detected in consecutive RHCs over 2 years (Table I). On her last visit on March 2023, her functional capacity (WHO FC I) was improved and 6MWD was 523 meters. PH due to PAI is a serious complication of TAK and is associated with worse prognosis (5). However, there is no consensus on treatment (6). In a recent study, use of pulmonary vasodilators resulted in significant improvements in haemodynamic and laboratory parameters in TAK-associated PH (3). Several concomitant pathogenetic mechanisms of PH must be considered to explain the therapeutic effect of PAH-specific agents in our patient, despite persistent mechanical obstruction. Vascular damage and remodelling in small vessels due to impaired distribution blood flow in pulmonary circulation similar to chronic thromboembolic pulmonary hypertension patients may contribute to the development of pre-capillary PH (7). The left heart disease and pulmonary parenchymal disease was ruled-out

Table I. Right heart catheterisation results.

Variables	Date of procedure: December 2019 Baseline	February 2021 1 year on treatment	February 2022 2 years on treatment
Mean right atrium pressure, mm/Hg	10	10	6
Right ventricle pressure, mm/Hg			
Systolic	60	55	35
Diastolic	10	10	6
Pulmonary artery pressure, mm/Hg			
Systolic	60	50	30
Diastolic	20	16	14
Mean	40	27	23
Pulmonary capillary wedge pressure	10	12	10
Cardiac output, (Fick method), L/min	3.56	3.93	4.5
Cardiac index, L/min/M2	2.18	2.25	2.7
Pulmonary vascular resistance,WU	8.42	3.8	2.88
Systemic vascular resistance, WU	24.7	18.3	17.77

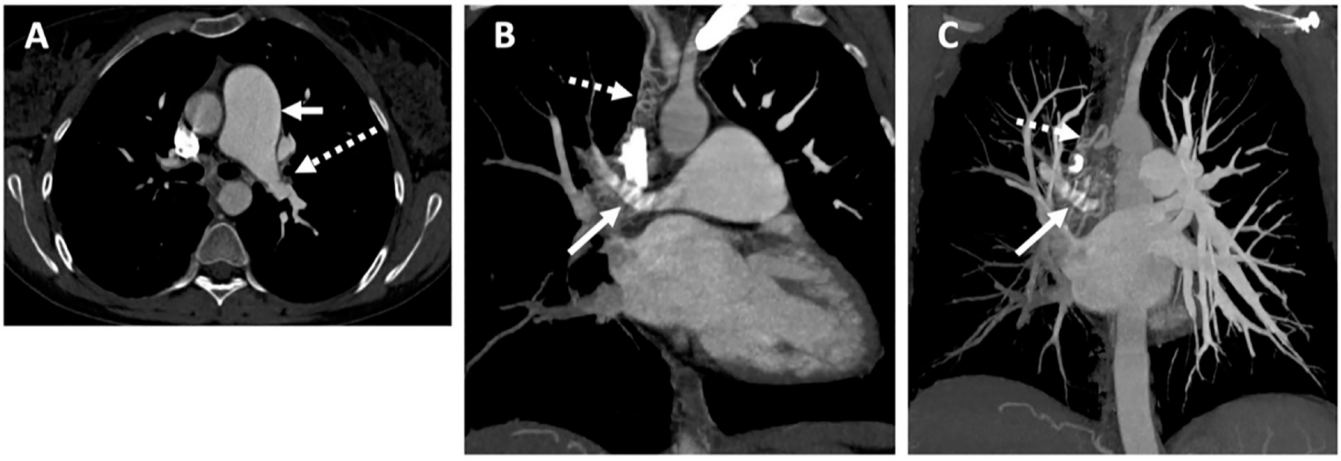

Fig. 1. Axial CT angiography images 1 year after the treatment (**A**) shows enlarged main pulmonary artery (arrow). Also, luminal narrowing and wall irregularity of left interlobar pulmonary artery is observed (dashed arrow). Coronal oblique (**B**) and coronal (**C**) maximum intensity projection (MIP) images show narrowed right upper lobe pulmonary artery (arrow) and multiple collaterals in mediastinum (dashed arrow). The right interlobar, right middle and lower lobe pulmonary arteries are occluded. On coronal MIP image (**C**), diminished pulmonary arterial vasculature is observed in the right lung compared to the left.

in our patient by imaging/haemodynamic evaluations. However, multiple lesions in the right PA could have contributed redistribution of blood flow in lung areas and resulted in hypoxic vasoconstriction, endothelial dysfunction and neurohormonal activation which are other possible factors of PH development in TAK (8-10). Additionally, vasculitis of small PAs in whom immunosuppressive treatment would be effective should always be considered in these patients. To conclude, in selected cases of TAK with PH due to PAI, PAH-specific agents can be a treatment option.

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