Reversal of right-ventricular dysfunction in pulmonary arterial hypertension following sildenafil therapy

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A 42-year-old-woman with known chronic pulmonary-sarcoidosis on long-term prednisone and home-oxygen therapy was referred to cardiology with symptoms of exertional chest tightness. Physical examination was notable for a palpable right-ventricular (RV) heave and a loud second heart sound (P2). Plasma B-natriuretic peptide (BNP) levels were elevated at 183 pg/mL. Transthoracic-echocardiography was suggestive of severe RV enlargement and systolic dysfunction with an estimated pulmonary systolic pressure of 60 mmHg. Cardiac magnetic resonance imaging confirmed severe RV enlargement (RVEDV = 218 mL) and systolic dysfunction (RVEF = 27%) without significant valvular disease (Panel A, Supplementary material online, Video 1). Peak RV longitudinal free-wall strain was significantly reduced (−7%) indicative of impaired myocardial contractility (Panel B). Cardiac-catheterization demonstrated normal coronary arteries with moderate pulmonary arterial hypertension (pulmonary arterial pressure = 58/32 mmHg, pulmonary capillary wedge pressure = 4 mmHg, pulmonary vascular resistance = 10.2 Wood Units) and no reversibility. She was able to walk 270 m during a 6-min walk test and was initiated on Sildenafil 20 mg t.i.d.

At 1-year follow-up, her functional status had significantly improved and she walked 305 m during a 6-min walk test. Plasma BNP was normal at 4 pg/mL. Repeat imaging showed normalization of RV function (RVEF = 55%) and size (RVEDV = 177 mL) (Panel C, Supplementary material online, Video 2), with recovery of peak RV longitudinal free-wall strain (−22%) (Panel D). Cardiac catheterization demonstrated reduction in pulmonary arterial pressures (47/22 mmHg) with normalization of pulmonary vascular resistance (1.3 Wood Units).

Right ventricular function is a major determinant of outcomes in patients with pulmonary hypertension. However, this case shows that RV function can demonstrate marked recovery in some cases. Although, the primary mechanism of action for sildenafil is inhibition of phosphodiesterase-5 in pulmonary smooth muscle, direct effects on myocardial phosphodiesterase-5 may also play a role. It is important to emphasize that the purpose of acute vasodilator testing is to identify the small subgroup of patients who are more likely to have a sustained beneficial response to oral calcium-channel blockers and can be treated with these less-expensive drugs. Although the majority of patients with pulmonary hypertension do not demonstrate acute vasodilator reversibility, they can demonstrate long-term beneficial responses to therapy including improvements in pulmonary artery pressure, pulmonary vascular resistance, RV-function, 6-min walk times and possibly survival.

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