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Case Report

Usefulness of acute pulmonary vasoreactivity test of sildenafil in treatment of portopulmonary hypertension. A case report

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Summary A 50-year-old man diagnosed with liver cirrhosis type C was referred to our hospital because of right heart failure with pulmonary hypertension. Echocardiography revealed enlargement of the right atrium and ventricle with severe tricuspid regurgitation. The peak flow velocity of tricuspid regurgitation by continuous wave Doppler echocardiography was 452 cm/s. Right heart catheterization demonstrated severe pulmonary hypertension [pulmonary arterial pressure (PAP) systolic/diastolic/mean = 73/20/41 mmHg and pulmonary vascular resistance (PVR) = 509 dyn s cm^{-5}] with portal hypertension. We diagnosed the patient as having portopulmonary hypertension (PoPH). Although we treated the patient with a prostacyclin analog, tricuspid regurgitation velocity was increased to 480 cm/s four years after the start of the therapy. To select drugs for the treatment of PoPH, we performed an acute vasoreactivity test of sildenafil during right heart catheterization. Since single administration of sildenafil (20 mg) decreased PAP (93/30/55—77/27/44 mmHg) and PVR (908—833 dyn s cm^{-5}), we added sildenafil (20 mg, t.i.d.) to the prostacyclin analog. Tricuspid regurgitation velocity decreased to 403 cm/s one year after the addition of sildenafil. An acute vasoreactivity test of sildenafil during right heart catheterization was useful for the decision of the drug to be used in the treatment of PoPH.

Introduction

Portopulmonary hypertension (PoPH) is a rare and refractory disease. Although new drugs have become available for specific treatment of pulmonary arterial hypertension, treatment of PoPH has not been established. An acute

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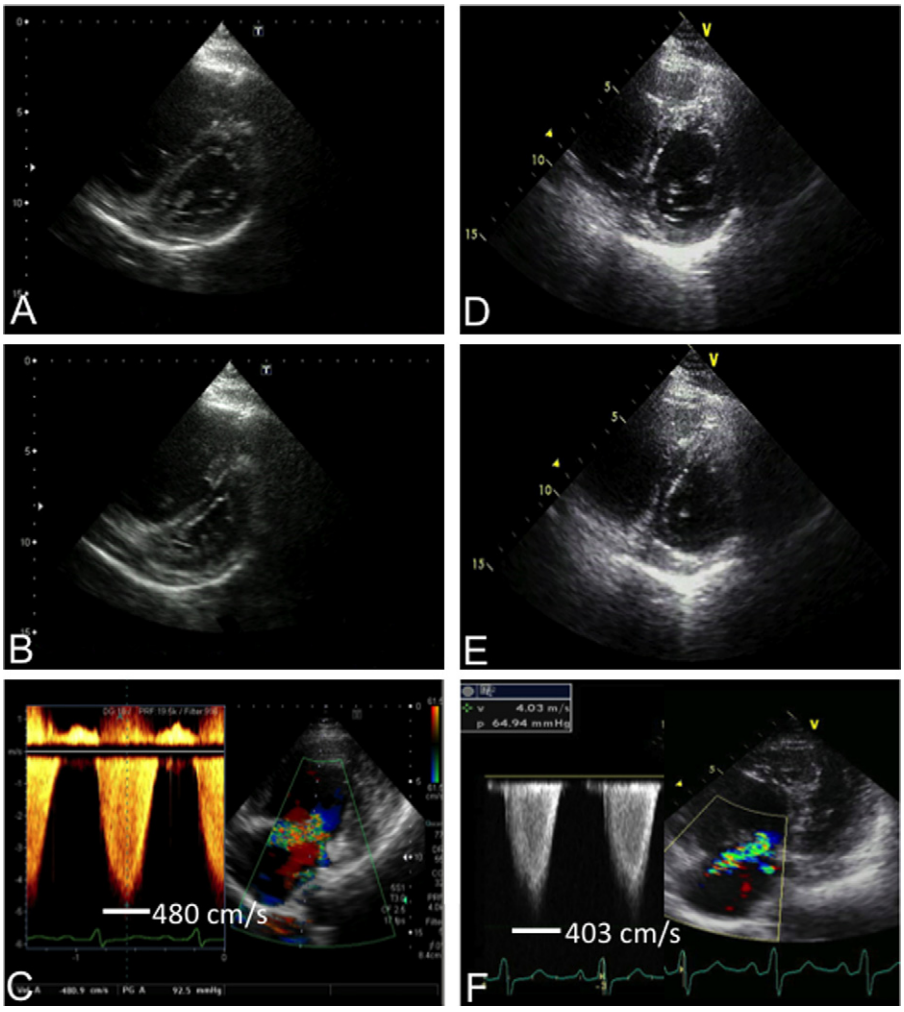

Figure 1 Transthoracic echocardiography. Left panels: four years after the start of treatment with a prostacyclin analog and before sildenafil treatment. Right panels: one year after the addition of sildenafil. Parasternal short-axis view recorded in diastole (A and D) and end-systole (B and E). Tricuspid regurgitation velocity (C and F). Four years after the start of prostacyclin analog treatment before sildenafil treatment, left ventricle was D-shaped during systole and end-diastole due to the enlargement of the right ventricle. Tricuspid regurgitation velocity was 480 cm/s. One year after the addition of sildenafil, D-shape of left ventricle was improved and tricuspid regurgitation velocity decreased to 403 cm/s.

pulmonary vasoreactivity test has been used for decision of the treatment in idiopathic pulmonary arterial hypertension [1]. However, the usefulness of the test in PoPH has not been reported. We present a case in which an acute vasoreactivity test of sildenafil, a phosphodiesterase-5 inhibitor, was useful in the treatment of PoPH.

Case report

A 50-year-old man was diagnosed with liver cirrhosis type C in 2003. Pulmonary hypertension (PH) was not detected at that time. He was referred to our hospital in 2004 because of right heart failure with PH. Echocardiography showed enlargement of the right atrium and ventricle with ventricular septum flattening during systole. The peak flow velocity of tricuspid regurgitation by continuous wave Doppler echocardiography was 452 cm/s. Right heart catheterization demonstrated severe PH [pulmonary artery pressure (PAP) systolic/diastolic/mean = 73/20/41 mmHg, pulmonary vascular resistance (PVR) = 509 dyn s cm^{-5}] with the elevation of portal pressure [portal pressure of 12 mmHg (normal < 11 mmHg)]. Results of pulmonary arteriography and oxymetry were normal. A pulmonary perfusion scintigram did not suggest the presence of thromboembolism. A blood examination showed elevations of total bilirubin (2.1 mg/dl), aspartate aminotransferase (63 IU/L), brain natriuretic peptide (BNP) (219 pg/mL), and reduction of platelet count ($4.0 \times 10^4/\mu L$). Anti-DNA antibody and anti-RNP antibody levels were slightly elevated. However, collagen disease was excluded as the cause of PH because of the absence of other collagen-related findings. According to these findings, we diagnosed the patient as having PoPH. We started to treat the patient with a prostacyclin analog. Since right heart failure had occurred in 2007, we added an inotropic agent, pimobendan. However, D-shaped left ventricle progressed (Video 1) and tricuspid regurgitation velocity increased to 480 cm/s in 2008 (Fig. 1A—C). To select

Table 1 Response to single administration of sildenafil at right heart catheterization.

	HR	BP (s/d/m)	PAP (s/d/m)	CI	PVR
Baseline	90	112/65/82	93/30/50	2.4	908
After 1 h	92	110/62/78	87/27/47	—	—
After 2 h	87	116/66/83	82/27/45	—	—
After 3 h	87	115/63/81	77/27/44	2.3	833

HR, heart rate (1/min); BP, noninvasive blood pressure (mmHg); s/d/m, systolic/diastolic/mean; PAP, pulmonary artery pressure (mmHg); CI, cardiac index (l/min/m^2); PVR, pulmonary vascular resistance (dyn s cm^{-5}).

drugs for the treatment of PoPH, we performed an acute vasoreactivity test of sildenafil during right heart catheterization. Since single administration of sildenafil (20 mg) decreased PAP and PVR without reduction of blood pressure (BP) and cardiac index (CI) after 3 h (Table 1), we added sildenafil (20 mg t.i.d.) to the prostacyclin analog. One year after the addition of sildenafil, he had no signs of deterioration of clinical symptoms in right heart failure and PH such as dyspnea, general fatigue, and leg edema. The level of BNP was 10.5 pg/mL. Echocardiography showed that D-shaped left ventricle was improved (Video 2) and tricuspid regurgitation velocity decreased to 403 cm/s one year after the addition of sildenafil (Fig. 1D—F).

Discussion

PoPH is defined as the elevation of mean PAP (≧25 mmHg) and PVR (≧240 dyn s cm^{-5}), normal pulmonary capillary wedge pressure (≦15 mmHg), and presence of portal hypertension [2]. Portal hypertension, rather than the presence of underlying liver disease, is important for the development of PoPH [2,3]. Medial hypertrophy and plexiform lesion in the pulmonary artery are hallmarks of PoPH as well as idiopathic pulmonary arterial hypertension [4]. Long-term prognosis has been shown to be related to the presence and severity of liver cirrhosis and to cardiac function [5]. Results of several studies on PoPH-specific therapies including intravenous administration of epoprostenol, bosentan, and sildenafil in patients with PoPH have been published [5—7]. Although there is no consensus on the treatment of PoPH [8], sildenafil is thought to have an advantage for the oral treatment of PoPH because there is a low risk of hepatotoxicity and the treatment is noninvasive.

An acute pulmonary vasoreactivity test of sildenafil in PoPH has not been reported, although it has been reported in idiopathic pulmonary arterial hypertension [9]. In the present case, we evaluated the hemodynamic response to the single administration of sildenafil during right heart catheterization. Since single administration of sildenafil decreased PAP and PVR without reduction of BP and CI, we decided to treat the patient with sildenafil. The treatment with sildenafil improved PoPH one year after the start of therapy. Although PoPH is often resistant to therapy, an acute vasoreactivity test of sildenafil is useful for determining the choice of drugs in the treatment of PoPH.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jccase.2011.04.001.

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