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CASE REPORT
Inherited cardiac conditions/cardiomyopathies

Alcohol septal ablation for hypertrophic obstructive cardiomyopathy and bilateral lung transplantation for idiopathic pulmonary fibrosis: a case report

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Background We present an uncommon case of a patient with hypertrophic obstructive cardiomyopathy and idiopathic pulmonary fibrosis. The case demonstrates the importance of pre-transplant cardiology workup and the need of interdisciplinary approach in diagnosing the cause of dyspnoea.

Case summary The 52-year-old male patient was diagnosed with idiopathic pulmonary fibrosis in 2019 and gradually became oxygen dependent due to progression of dyspnoea. Bilateral lung transplantation was recommended in 2021. During pre-transplant cardiology workup, the patient was diagnosed with hypertrophic cardiomyopathy with left ventricular outflow tract (LVOT) obstruction. Considering the high surgical risk of the patient, alcohol septal ablation was performed with subsequent decrease of LVOT gradient. Bilateral lung transplantation was successfully performed afterwards. The patient's symptoms improved to NYHA class II at one year follow-up.

Discussion We present a rare case of combined cause of dyspnoea—coexistence of hypertrophic obstructive cardiomyopathy and idiopathic pulmonary fibrosis in one patient. Due to high surgical risk, the patient underwent alcohol septal ablation with successful elimination of LVOT gradient and subsequently bilateral lung transplantation.

Keywords Case report • Hypertrophic obstructive cardiomyopathy • Alcohol septal ablation • Idiopathic pulmonary fibrosis • Lung transplantation

ESC curriculum 2.2 Echocardiography • 6.5 Cardiomyopathy • 3.4 Coronary angiography

Learning points

- Interdisciplinary approach is essential in diagnosing the cause of dyspnoea. Echocardiography, cardiopulmonary exercise testing, pulmonary function tests, and right heart catheterization are helpful in differential diagnosis.
- Considering the co-morbidities of both pre- and post-transplant patients, usually associated with high surgical risk, alcohol septal ablation is a suitable option for septal reduction therapy in these patients.

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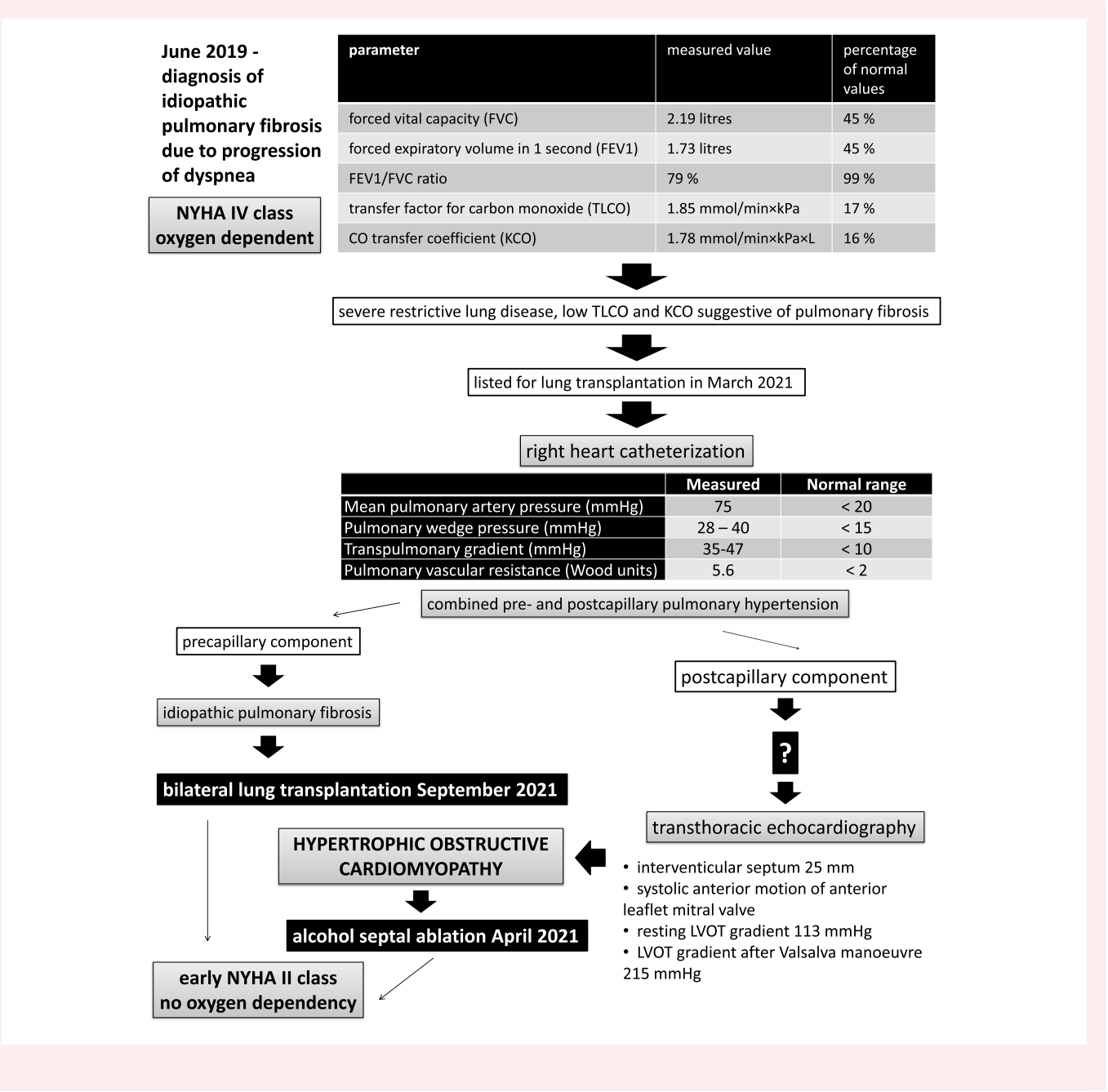
Introduction

The first lung transplantation was performed in 1963 by American surgeon James D. Hardy on a prisoner who was sentenced to death. The patient lived 18 days after the surgery and died of renal failure and pneumonia.[1] Since then, enormous progress has been made in transplantation medicine and survival of transplanted patients has significantly increased.[2] However, post-transplant cardiovascular mortality is still twice as high than in the general population, and coronary artery disease (CAD) is an independent predictor of cardiovascular morbidity and mortality after lung transplantation.[3,4] Therefore, a complex cardiology workup is an essential part of the pre-transplant examination. It is comprised of electrocardiogram, laboratory tests (troponin, NT-proBNP, CK-MB), transthoracic echocardiography (TTE), selective coronary angiography (in patients over 45 years), and right heart catheterization (RHC). In patients with CAD, percutaneous or surgical revascularization is recommended before transplantation. A combined heart–lung transplantation might be considered in end-stage heart disease.[5]

Summary figure

We present a unique case report of an idiopathic pulmonary fibrosis (IPF) patient with hypertrophic obstructive cardiomyopathy (obstructive HCM) that demonstrates the importance of pre-transplant cardiology workup and multidisciplinary approach in the differential diagnosis of dyspnoea.



Case presentation

A 52-year-old male, non-smoker, with a history of arterial hypertension, was diagnosed with IPF as he suffered from the progression of dyspnoea to NYHA class III in June 2019. Despite of antifibrotic therapy (nintedanib 150 mg twice a day until July 2020, pirfenidone 801 mg three times a day since then), pulmonary function decreased, home oxygen therapy was recommended, and the patient was listed for lung transplantation in March 2021. The initial spirometry results at our centre indicated severe restrictive lung disease without obstruction—forced vital capacity (FVC) was 2.19 L (45% of predicted value), forced expiratory volume in 1 s (FEV1) was 1.73 L (45% of predicted value), and the FEV1/FVC ratio was normal (79%, normal value > 75%). Measurement of transfer factor for carbon monoxide (TLCO) showed very severe reduction (1.85 mmol/min × kPa, 17% of predicted value), CO transfer coefficient (KCO) calculated as ratio of TLCO and accessible alveolar volume (VA) was also severely reduced (1.78 mmol/min × kPa × L, 16% of predicted values). These findings were highly suggestive of interstitial lung disease or pulmonary fibrosis (*Figure 1*).

At baseline cardiology assessment, the patient showed no clinical signs of fluid overload (absence of lower extremity oedema and jugular vein distention). Velcro crackles, often associated with IPF, were audible during inspiration. There was a systolic murmur audible at the left sternal border in third and fourth intercostal space. The murmur did not radiate to the left axilla or carotid arteries. Right heart catheterization and selective coronary angiography were performed as a part of pre-transplant examination. Coronary angiography was normal. On the contrary, RHC confirmed severe pulmonary hypertension (PH) and increased pulmonary vascular resistance of 5.6 Wood units (normal value < 2 WU). Mean pulmonary artery pressure was 75 mmHg (normal value < 20 mmHg), pulmonary wedge pressure was between 28 and 40 mmHg (normal value < 10 mmHg), and transpulmonary gradient was 35–47 mmHg (normal value < 10 mmHg). However, PH was classified as combined pre- and post-capillary (*Table 1*) that is not typical for IPF. Therefore, the results suggested another (probably left heart) condition as a cause of the post-capillary component. Screening TTE revealed left ventricular (LV) hypertrophy with maximum LV wall thickness in the interventricular septum of 25 mm (*Figure 2*) (normal range 6–11 mm). There was grade III (severe) systolic anterior motion (SAM) (*Figure 3*) of an elongated anterior mitral valve leaflet (33 mm, normal range 22–23 mm), with only mild mitral regurgitation. The maximum pressure gradient (PG) in the left ventricular outflow tract (LVOT) was 113 mmHg at rest and 215 mmHg (*Figure 4*, Supplementary Material) during the Valsalva manoeuvre (normal value < 30 mmHg). Left ventricular ejection fraction was 70% (normal range 55–70%). Signs of severe PH were present—right ventricle was dilated and hypokinetic (34 mm in parasternal long axis view, normal value < 31 mm), tricuspid regurgitation pressure gradient was 63 mmHg (normal value < 30 mmHg), and inferior vena cava was dilated and did not collapse >50% during inspiration (normal diameter < 21 mm). A diagnosis of obstructive HCM was made. At the time of diagnosis, the patient had been started on a low dose of beta-blockers (1.25 mg of bisoprolol), after the diagnosis, the dose was increased to maximum tolerated dose (2.5 mg of bisoprolol). Although there was no family history of HCM, molecular genetic testing revealed a pathogenic mutation in *MYBPC3* gene. Later, the patient's daughter was screened for HCM. Her TTE showed no signs of HCM, and the genetic testing was negative.

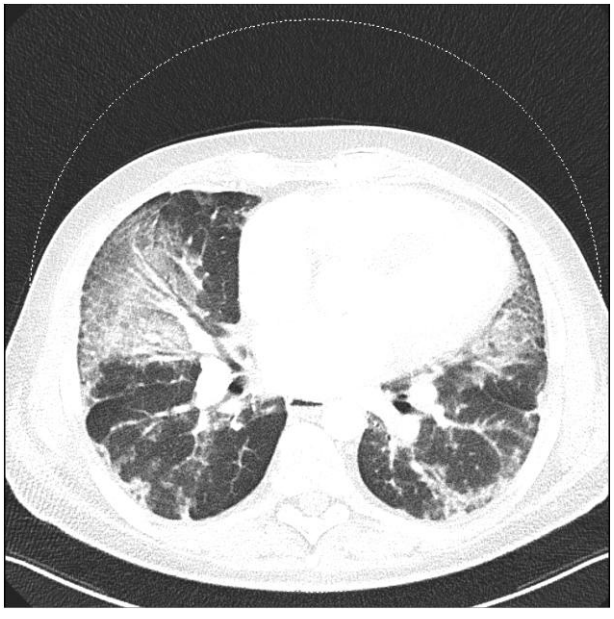


Figure 1 The 'crazy-paving' pattern in idiopathic pulmonary fibrosis on computed tomography scan before lung transplantation.

Based on severe symptoms and planned major thoracic surgery, septal reduction therapy (SRT)–alcohol septal ablation (ASA) was recommended and performed in April 2021 by selective injection of 1.5 and 1.0 mL of 96% ethanol into the first and second septal branch of left anterior descending artery, followed by immediate decrease of LVOT gradient to 10 mmHg within the invasive measurements. A follow-up TTE examination in one month confirmed a low residual LVOT PG of 20 mmHg, the patient described improvement of exertional dyspnoea, but remained dependent on home oxygen therapy due to his severe pulmonary condition.

In September 2021, the bilateral lung transplantation was performed with the support of extracorporeal membrane oxygenation. The patient was extubated on the second post-operative day. The post-operative course was complicated by bacterial pneumonia (*Klebsiella pneumoniae*). After antibiotic treatment (piperacillin 4 g and tazobactam 0.5 g three times a day for 21 days) and pulmonary rehabilitation, the pulmonary graft functions improved and the patient was discharged from the hospital on standard immunosuppressive therapy (prednisone 30 mg daily, tacrolimus 4 mg twice a day, mycophenolate mofetil 1000 mg twice a day).

A follow-up TTE (*Figure 5*, Supplementary Material) in July 2022 showed LVOT gradient of 6 mmHg, no SAM, and normal estimated systolic pulmonary artery pressure (30 mmHg, normal value < 35 mmHg). The patient reported near complete regression of dyspnoea, to NYHA class II functional status. For further risk stratification, 24 h ECG monitoring was performed. No non-sustained ventricular tachycardia was detected. Due to capacity reasons, cardiac MRI was performed after the invasive procedure (Supplementary Material). However, no late gadolinium enhancement was found (except for the scar tissue after

Table 1 Right heart catheterization measurements

	Measured	Normal range
Mean pulmonary artery pressure (mmHg)	75	<20
Pulmonary wedge pressure (mmHg)	28–40	<15
Transpulmonary gradient (mmHg)	35–47	<10
Pulmonary vascular resistance (Wood units)	5.6	<2

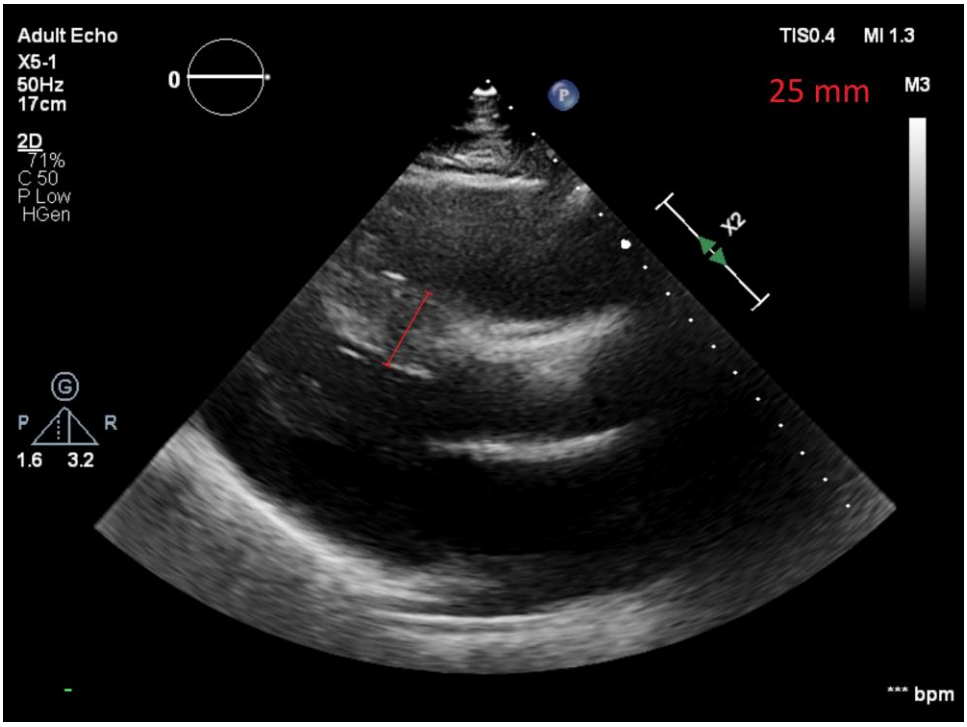


Figure 2 Transthoracic echocardiography—parasternal long axis view. Maximum interventricular septum thickness.

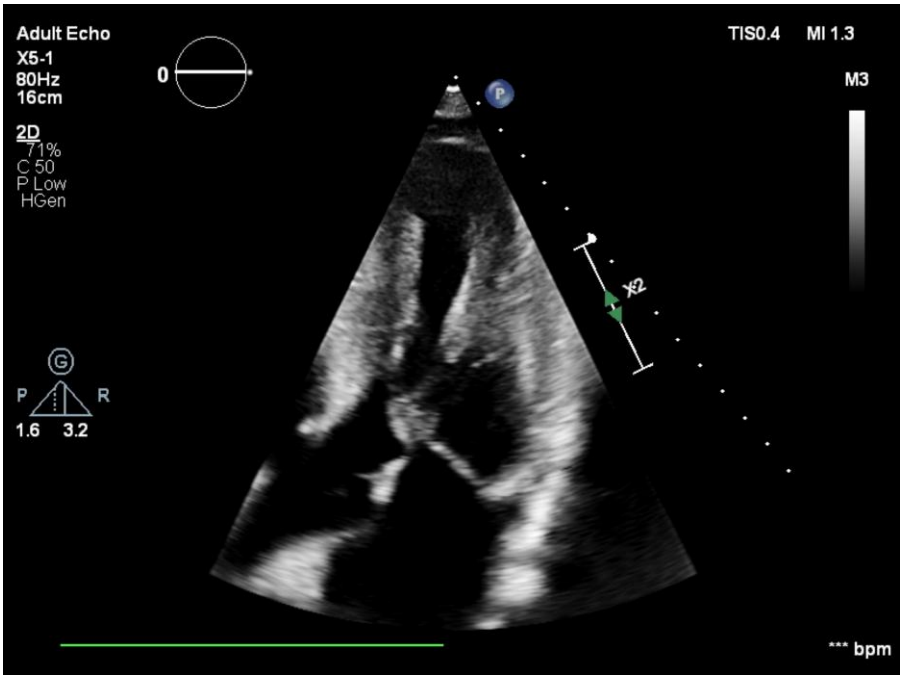


Figure 3 Transthoracic echocardiography—apical five-chamber view. Hypertrophic left ventricle, systolic anterior motion (SAM) of the anterior leaflet of the mitral valve during systole.

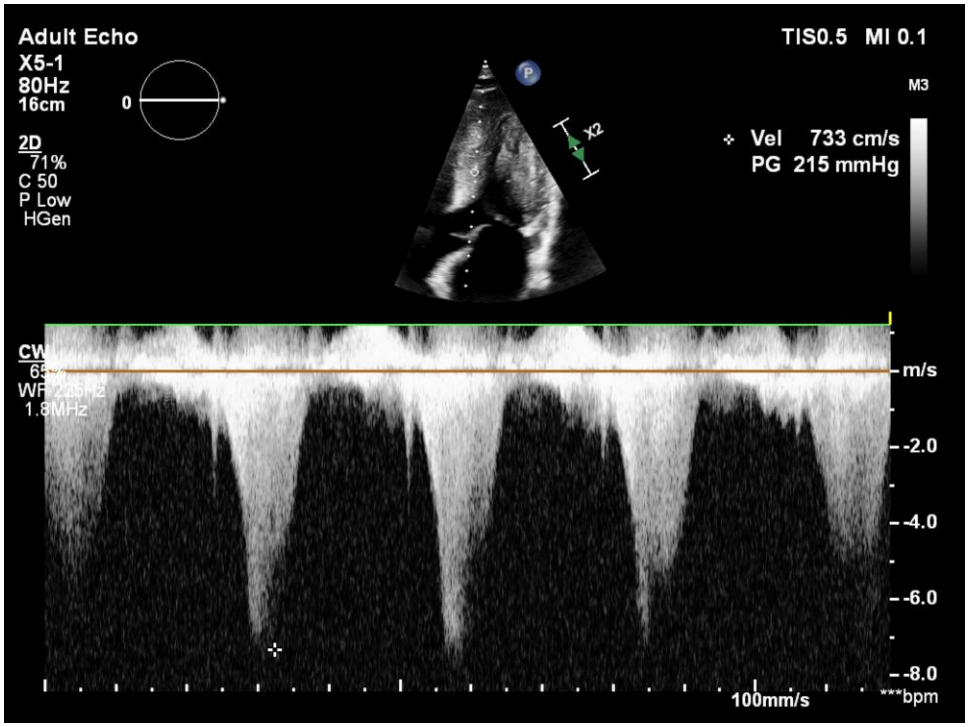


Figure 4 Transthoracic echocardiography—pre-procedural maximum left ventricular outflow tract gradient.

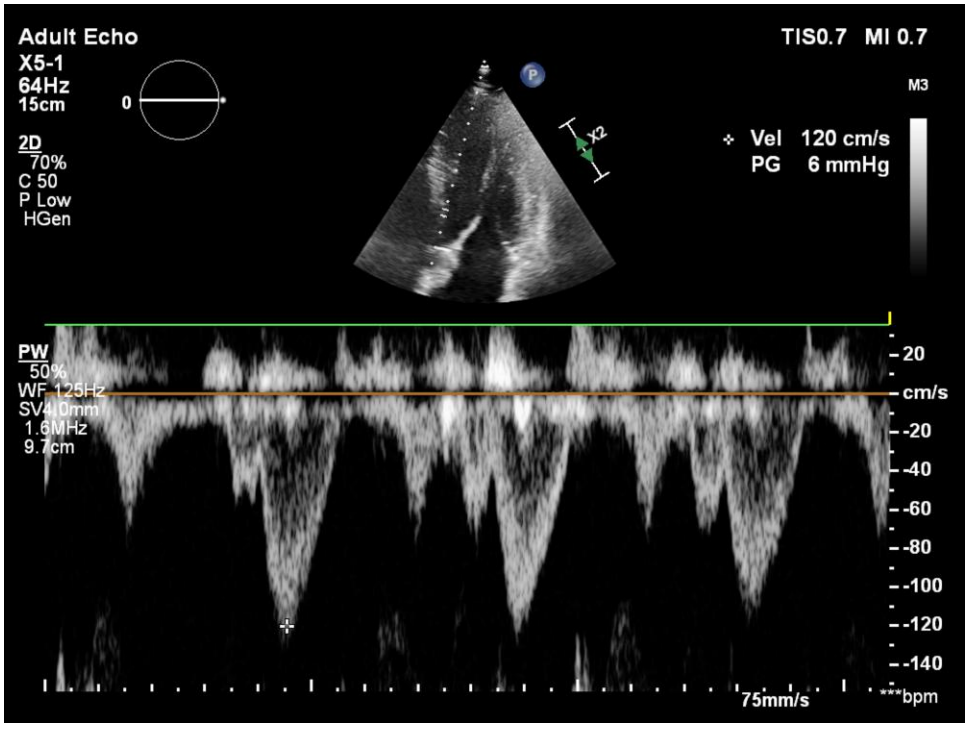


Figure 5 Transthoracic echocardiography—post-procedural maximum left ventricular outflow tract gradient.

alcohol septal ablation). The patient's sudden cardiac death risk was 1.99%. Therefore, ICD (implantable cardioverter-defibrillator) implantation was not recommended.

Discussion

Our case is unique because of coexistence of two separate uncommon diseases. It demonstrates the need of complex pre-transplant examination and simultaneously the need of interdisciplinary approach in diagnosing the cause of dyspnoea.

Dyspnoea is a predominant symptom of many pulmonary and cardiovascular diseases. To differentiate between the two causes, imaging and functional tests need to be done. To confirm a respiratory cause, we perform pulmonary function tests, body plethysmography, and lung diffusion testing. Chest X-ray and chest CT scan are used to evaluate morphology of both lungs and heart. Electrocardiogram, TTE, and/or coronary angiography are necessary in diagnosing cardiovascular disease. Elevated serum levels of troponin and NT-proBNP are suggestive of cardiac cause of dyspnoea. Right heart catheterization helps to distinguish the type of PH—post-capillary PH is typical for left heart disease, on the other hand, pre-capillary PH is typical for pulmonary disease.

In our patient, restrictive pattern in spirometry significantly decreased TLCO and destruction of lung parenchyma in chest CT scan led to the diagnosis of IPF that was probably the primary cause of dyspnoea. Significant post-capillary hypertension, severe LVOT obstruction, and elevation of NT-proBNP confirmed a cardiovascular component of dyspnoea.

Our patient was recommended for lung transplantation, but it was contraindicated because of the significant LVOT obstruction. Three options were considered. The first option was combined procedure of lung transplantation and septal myectomy. In expert centres, the mortality of septal myectomy is very low (under 1%) with favourable outcomes.[6] However, the results might not be as impressive in lower-volume centres and in patients that are at high surgical risk.[7] The second option for SRT was performing ASA. Mortality of ASA is equal to or lower than that of septal myectomy, and the long-term results and survival are similar.[8,9] In our centre, the number of performed ASA procedures is higher than the number of septal myectomy surgeries. It is also much less invasive using a transfemoral approach instead of sternotomy. Therefore, we ultimately decided to choose ASA for our patient. In case ASA was not successful and septal myectomy would not be technically feasible, the third option—combined heart–lung transplantation—could be considered. Nevertheless, combined heart–lung transplantation is designated for patients with end-stage heart disease, and our patient did not fulfil the criteria.

Considering the co-morbidities of both pre- and post-transplant patients, usually associated with high surgical risk, ASA is a suitable option for SRT in these patients. Although ASA is a less invasive procedure, it might result in some complications. Rare, but severe complications include death, ventricular tachycardia or ventricular fibrillation caused by iatrogenic myocardial infarction, ventricular septal defect, and extensive myocardial infarction in case ethanol leaks into left anterior descending artery. A more common complication, around 10% to 12%, is the need for a pacemaker implantation due to complete heart block.[10,11]

In the near future, a new drug class, myosin inhibitors, might be another option for obstructive HCM. In the VALOR-HCM study, patients with obstructive HCM, eligible for SRT, were treated with mavacamten for 16 weeks. At the end of the study, the LVOT obstruction was significantly decreased and only 18% of patients treated by mavacamten stayed eligible for SRT.[12] It is possible that pharmacological treatment might lower the need for invasive SRT. Of note, myosin inhibitors were not available to our patient and are not yet approved in Europe by EMA at the time of writing this case report.

Conclusion

We presented a unique case of coexistence of obstructive HCM and IPF in one patient causing dyspnoea with oxygen dependency. The patient who was at high surgical risk underwent ASA with successful elimination of LVOT gradient and subsequently bilateral lung transplantation. The case demonstrates the need for a multidisciplinary approach in the diagnosis and treatment of dyspnoea and the importance of cardiology pre-transplant workup.

Lead author biography

Dr Veronika Puchnerova is a resident and a post-graduate student at the Department of Cardiology, University Motol Hospital in Prague, Czech Republic since 2020. The subjects of her interest are echocardiography and hypertrophic cardiomyopathy.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

Consent: The authors confirm that written consent for submission and publication has been obtained from the patient in line with the COPE guidelines.

Conflict of interest: None declared.

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Data availability

The data underlying this article are available in the article and in its online *supplementary material*.

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