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CASE REPORT

First Lung Transplantation on a Latvian patient with Idiopathic Pulmonary Arterial Hypertension

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Summary
This is the case of the first bilateral/double-lung transplantation (DLT) on a Latvian patient which was performed due to right heart failure caused by idiopathic pulmonary arterial hypertension (IPAH). After DLT the patient developed acute kidney failure which was successfully solved with an intermittent hemofiltration. The patient now receives specialized immunosuppressive therapy.
Key words: double-lung transplantation, idiopathic pulmonary arterial hypertension, immunosuppressive therapy

AIM OF THE DEMONSTRATION

The aim of this paper is to report about the first successful DLT on a Latvian patient as well about management of postoperative complications and care.

CASE REPORT

A 32-year old female with diagnosis of IPAH and Swyer syndrome (XY gonadal dysgenesis) had DLT performed on the 15th of April 2014 in Vienna General Hospital (Allgemeines Krankenhaus der Stadt Wien- AKH), Austria.

Since 2011 history of IPAH is known and during this period the patient several times was admitted in Latvian Center of Cardiology in Pauls Stradins Clinical University Hospital.

The diagnosis was confirmed in January 2011when right heart catheterization showed that patient's mean pulmonary artery pressure (mPAP) was 64 mm Hg (normal value is no more than 25 mm Hg), whereas patient's pulmonary vascular resistance (PVR) was 10,7 Wood units (normal value is no more than 2 Wood units);

The disease progressed rapidly despite maximal symptomatic and pathogenetic therapy (on year 2013):
Sildenafil 20 mg 1-1-1;
Ambrisentan 5 mg 1-0-0;
Iloprost inhalations 5 mcg/dose, 6-8 x/day;
Oxygen inhalation4 l/min, 24 h/day;
Warfarin 6,25 mg 0-0-1;
Spironolactone 25 mg 1-0-0;
Digoxin 0,125 mg 1-0-0 6days a week;
Tianeptine 12,5 mg 1-0-0;
Pantoprazole 20 mg 1-0-0;
Ivabradin 2,5 mg 1-0-1.

It is worth noting that all three classes of drugs available at that time, which were approved in pathogenetic therapy of IPAH, were used to treat the patient: a PDE-5 inhibitor, an endothelin receptor antagonist and a prostanoid.

The progression and severity of disease was supported by following clinical evidence:

Development of right heart failure manifested as an extreme dyspnea, ascites, fatigue - patient went from NYHA functional class II to IV in two years, patient's 6-minute walk test (6MWT) result in January 2011 was 380 m, whereas in December 2013 it was only 26 m. On January 2014 due to the decompensated right heart failure 6MWT was already contraindicated. Right heart dysfunction/enlargement was also seen in echocardiographic imaging (Fig. 1);

Elevation of BNP (brain natriuretic peptide) level, a heart failure marker, which rose from 102,8 pg/mL in January 2011 to 2044,7 pg/mL in October 2012, 4128,5 pg/mL in May 2013 and to more than 5000 pg/mL on February 2014.

Considering aforementioned facts, in late 2013 patient was referred to AKH. After all the necessary steps in getting enrolled in their transplant program, the patient was put on the active waiting list of Eurotransplant on February 24th 2014.

First DLT on a Latvian patient under extracorporeal membrane oxygenation (ECMO) support was performed on the 15th of April 2014. The donor was Cytomegalovirus (CMV) negative, whereas recipient – CMV positive. Alemtuzumab (Campath) was used in induction therapy. As the patient had substantial ascites, eight liters of fluid were drained from abdominal cavity during the surgery. The postoperative course was prolonged because of lengthened weaning. Veno-arterial ECMO support was received for 3 days postoperatively. The patient was extubated on April 19th 2014. After the surgery, patient developed postoperative psychosis, which resolved in approximately six days.

Due to an insufficient cough reflex with mucus retention, on April 22nd the patient had to be endotracheally intubated by performing tracheostomy. The intubation was ceased after five days. Furthermore, due to a tachycardia and atrial fibrillation, a therapy with amiodarone and beta-blocker (bisoprolol) was started. In the time period between April 17th and April 27th an intermittent hemofiltration was necessary due to an acute kidney failure.

The patient was transferred to the general ward on May 1st 2014. Further stay was without any severe complications.

CT scan on May 12th 2014 showed a regular postoperative

picture without any signs of infection. Lung function test on May 15th showed about the same lung function parameter values as before DLT (Table 1).
Bronchoscopy was done on the 16th of May. It showed adequate healing of anastomosis, absence of secretion. The patient was discharged on May 21st in good general condition weighting 48.8 kg (at the time of admission patient weighted 60 kg).
Therapy at discharge:
Tacrolimus 5-0-4 mg;
Aprednisolon 25-0-0 mg;
Valganciclovir 450 mg 1-0-0 until 90th post-op day;
Sulfamethoxazole/trimethoprim 800/160 mg 1-0-0 Monday, Tuesday, Wednesday;
Amphotericin B inhalations 10 mg/dose 1-1-1;
Pantoprazole 40 mg 1-0-0;
Amiodarone 200 mg 1-0-0;
Bisoprolol 2,5 mg 1-0-1;
Quetiapine 0-0-50 mg;
Furosemide 40 mg 1-0-0;
Magnesium Verla 2-2-2.
3 months post-op check-up in AKH (July 16th) showed stable recovery signs: chest X-ray was without alteration, spirometry was stable. Bronchoscopy showed that anastomosis were holding, therefore amphotericin B inhalations were stopped. Due to the formed kidney failure and the known elevated risk for ovarian malignancy associated with Swyer syndrome, immunosuppression was switched to low dose tacrolimus (9 mg daily) and everolimus (3 mg daily) combination. Patient currently receives:
Tacrolimus 5-0-4 mg;
Everolimus 0,75 mg 2-0-2;
Aprednisolon 20-0-0 mg;
Sulfamethoxazole/trimethoprim 800/160 mg 1/2-0-0 Monday, Tuesday, Wednesday;
Pantoprazole 40 mg 1-0-0;
Bisoprolol 2,5 mg 1-0-1;
Calcium/Vitamin D3600 mg/400 IU 1-0-1.
Regular gynecological check-up and prophylactic oophorectomy six months post-DLT were recommended. 6-month check-up in AKH is planned on 15th October 2014.
As of August 2014, patient's functional status is very satisfying- 6MWT result was more than 600 m. Echocardiographic imaging shows improvement in functionof right heart,which has shrunken considerably (Fig. 2).

DISCUSSION

Nowadays, lung transplantation is a generally accepted therapy for patients with a wide range of severe lung disorders who are failing maximal medical therapy, or for whom no effective medical therapy exists. There is strong evidence supporting quality of life and survival benefit for lung transplant recipients (4,8). Depending on the case, single-lung, double-lung or heart-lung transplantation is performed. Of these, the double-lung transplantation (DLT) is the most widely used method. According to Eurotransplant data, 688 lung transplant surgeries were performed in Europe in 2013, 613 (89,1%) of which were DLTs. The number of performed lung transplant surgeries is steadily growing year by year (6,8).
Vienna General Hospital (AKH) is one is one of the leading lung transplant reference centers in the world. Since their first lung transplantation in 1989, the center has accumulated vast experience in this area and in 2013 there were 119 lung transplantation surgeries performed in AKH. One of their areas of expertise is surgical treatment of patients with pulmonary hypertension (lung transplantation surgery, balloon angioplasty, pulmonary endarterectomy etc.). Expert opinion is that all surgery for pulmonary hypertension should be performed in centers with experience in these techniques (3).
As mentioned before, the primary aim of lung transplantation is to increase life expectancy. Number of studies show that lung transplantation reaches this goal, especially in the case of progressing cystic fibrosis (CF), idiopathic pulmonary fibrosis (IPF) and IPAH (1,2,5,7).
Analyzing current epidemiologic data in Latvia, the authors believe that each year approximately 10 people need lung transplantation. There should be a discussion in Latvian medical community, whether to create a lung transplant center in Latvia or to cooperate with Estonia and Lithuania to create one center for all three of the Baltic States. Meanwhile it would be necessary to create a national registry of those patients who are in need of lung transplant and if possible refer them to transplantation centers abroad.
Young, economically active individuals, as well as patients suffering from CF, IPF and IPAH should be prioritised in the waiting list.
Physicians of various specialties (pulmonologists, radiologists, thoracic surgeons, transplantologists, rheumatologists, cardiologists and others) in Pauls Stradins Clinical University Hospital have created the pulmonary circulation and right ventricular function working group, who has declared lung transplantation development in Latvia as one of its primary objectives.

Conflict of interest: None

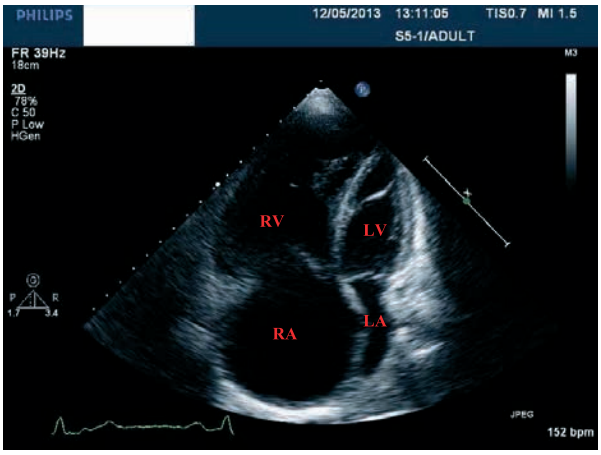

Fig. 1. Echocardiographic image showing patient's apical four chamber view. Recording made on May 12th 2013. Extreme right heart dilatation is seen.
Definition of abbreviations: LA= left atrium; LV= left ventricle; RA= right atrium; RV= right ventricle.

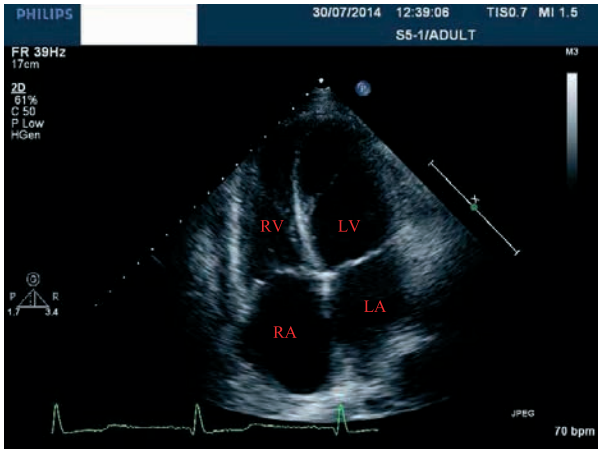

Fig. 2. Echocardiographic image showing patient's apical four chamber view. Recording made on July 30th 2014. Normal cardiac chamber size is seen.
Definition of abbreviations: LA= left atrium; LV= left ventricle; RA= right atrium; RV= right ventricle.

Table 1. Lung function before and after DLT. Ratio of patient's actual results compared to predicted normal values, expressed as a percentage is shown in the brackets.

Date	16.01.2014	15.04.2014 (DLT)	15.05.2014	16.07.2014	14.08.2014
Parameter					
FVC, L (% pred.)	2,69 (58,6%)		2,67 (58,3%)	3,24 (70,0%)	3,38 (83,7%)
FEV1, L (% pred.)	2,43 (61,7%)		2,54 (64,8%)	3,1 (79,0%)	3,06 (87,1%)
MEF50, L/s (% pred.)	4,31 (92,8%)		4,43 (95,7%)	4,9 (106,0%)	4,14 (89,0%)
TLC, L (% pred.)	4,20 (67,5%)		4,20 (67,5%)	-	-

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