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Pulmonary arterial hypertension in a patient with unilateral pulmonary artery absence (RCD code: II-2A.1)

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Abstract

Pulmonary artery absence is a rare congenital defect, occurring in 1 out of 100 000 individuals. In its isolated unilateral form only one in three cases concerns the left artery. The first symptoms usually appear in young age. Pulmonary hypertension associates this defect in 44% of patients.

We present a 41-year-old female who was referred to our institution in January 2014 for further examination with preliminary diagnosis of central pulmonary embolism based on computed tomography angiograms. There were also echocardiographic signs of pulmonary hypertension. The lady was severely dyspnoeic and her complaints included palpitations and dry cough. She had been previously treated for chronic bronchitis and sinusitis, allergic rash and anemia. In 2013 she also suffered left-sided pneumonia. Until December 2013 she had been a smoker. She gave birth thrice, all the pregnancies went uncomplicated.

We established a final diagnosis of isolated unilateral left pulmonary artery absence without lung hypoplasia and precapillary pulmonary hypertension based on right heart catheterization. Therapy with sildenafil 20 mg tid was initiated and it was escalated shortly after to sildenafil plus iloprost due to the lack of clinical and hemodynamic improvement. Finally, being on dual therapy for 14 months now, the patient responded to treatment with symptomatic improvement from WHO class IV to class II. Furthermore there is a moderate regression of pulmonary vascular resistance and some improvement in cardiac index as documented in a follow-up right heart catheterization. The patient is listed for bilateral lung transplantation. JRCD 2015; 2 (4): 119–122

Key words: combination therapy, pulmonary arterial hypertension, congenital defect, pulmonary artery absence, computed tomography, atresia, right heart catheterization, iloprost, sildenafil, tricuspid regurgitation

Case presentation

In January 2014 a 41-year-old caucasian woman with severe exertional dyspnea was referred to our department from another hospital. She was suspected to have a probable pulmonary hypertension, possibly caused by the presence of the left pulmonary artery embolisation. The patient complained of fatigue, lowered exercise tolerance and dry cough which had been escalating during the previous year. She suffered from dyspnea and palpitations during slight exertion. There was no history of hemoptysis. She used to smoke cigarettes until December 2013 and had been diagnosed with chronic bronchitis and sinusitis. The patient's medical history included also normocytic anemia, allergic rash and caries. She had had three uncomplicated pregnancies and had given birth thrice. In December 2013 the patient had been treated in a regional hospital for left-sided bronchopneumonia. During that hospitalisation she went through chest X-ray, where left hilar shadow was absent. A transthoracic echocardiographic examination (TTE) showed a moderate tricuspid regurgitation (TR) and a probable pulmonary hypertension (PH). In two chest computed tomography (CT) angiograms the differential diagnosis of pulmonary embolism or unilateral absence of the left pulmonary artery (UAPA) with left lung hypoplasia was established.

On admission to our department the woman's symptoms remained unchanged, the signs consisted of slightly weakened breath sounds over the left lung, a Levine 3/6 systolic heart murmur and carious teeth. In electrocardiogram there was a sinus rhythm of

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Table 1. Laboratory results – January 2014

NT-proBNP (0–125 pg/ml)	1605
Troponin T hs (0–14 ng/l)	4.48
Hemoglobin (12–16 g/dl)	12.4
Hematocrit (37–49%)	38.6
Creatinine (0.5–0.9 mg/dl)	0.58
eGFR (ml/min/1.73m^2)	>60
Uric acid (2.5–5.7 mg/dl)	5.4
AST (5–32 U/l)	17
ALT (5–31 U/l)	14

NT-proBNP – N-terminal of the prohormone brain natriuretic peptide, eGFR – glomerular filtration rate,AST – aspartate transaminase, ALT – Alanine transaminase

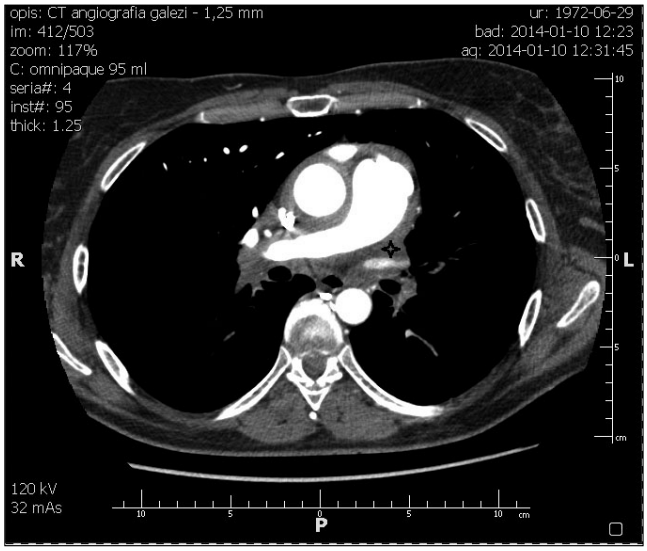

Figure 1. High resolution computed tomography angiogram – absence of the left pulmonary artery (star)

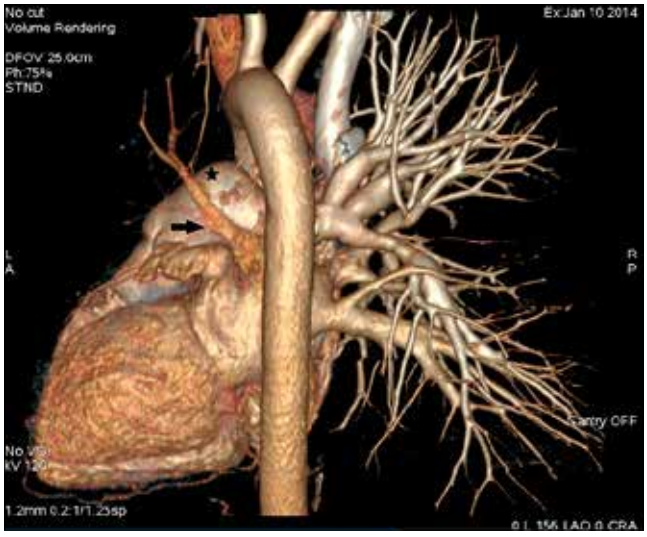

Figure 2. High resolution computed tomography reconstruction – absence of the left pulmonary artery (star), reduced diameter of left-sided pulmonary veins (arrow)

80 bpm, dextrogram and signs of right ventricle hypertrophy and strain. The laboratory tests were normal except of NT-proBNP value of 1605 pg/ml (Table 1). We repeated TTE where the image of a moderate TR (vena contracta of 0.5 cm, regurgitation area 8.0 cm^2) and a probable PH (pulmonary arterial systolic pressure [PASP] 118 mm Hg, right ventricle enlarged, compressing the left ventricle) was confirmed. In spirometry neither obturation nor restriction were observed. Diffusing capacity for carbon monoxide (DLCO) was 5,19 mmol/min/kPa (57% of normal).

The CT angiogram showed the pulmonary trunk of 30 mm, normal right pulmonary artery and its branches and aplasia of the left pulmonary artery with compensatory well developed bronchial arteries (Figure 1). Left-sided pulmonary veins had reduced diameter (Figure 2). In the left lung there were some moderately severe inflammatory and fibrotic changes, also probably post-infarction parenchymal consolidation, and in both lobes thin-walled cysts, the largest 18 mm. There was no lung hypoplasia.

In the right heart catheterisation (RHC) we confirmed a non-reactive precapillary pulmonary hypertension with mean pulmonary artery pressure (mPAP) of 40 mm Hg at rest and 36 mmHg after acute vasoreactivity test, pulmonary wedge pressure (PWP) of 9 mm Hg, pulmonary vascular resistance (PVR) of 7.17 Wood units – Table 2). Coronary angiography showed no significant changes in major epicardial vessels. The final diagnosis was precapillary arterial PH, WHO/NYHA functional class III and UAPA.

Review of literature

UAPA was first described by Fraentzel in 1868 [1]. It is a rare congenital vascular defect found in 1 out of 100,000 individuals, often in conjunction with other abnormalities, e.g. tetralogy of Fallot or cardiac septal defects [2]. Its two times less frequent isolated form most often concerns the right side [3]. The pathogenesis is likely to be different on each side, however the process always takes place during embryological development of the sixth aortic arch which proximal portions becomes pulmonary arteries. The right distal portion normally disappears at about fourth week and the left one changes into the arterial duct [4]. The distal pulmonary branches come from other vessels and thus remain intact in case of UAPA. They stay supplied by bronchial, intercostal, internal mammary, subdiaphragmatic, subclavian, or even coronary arteries [5].

The symptoms of UAPA may develop after many years. They tend to start with exercise limitation (40%) and frequent respiratory infections (37%). Hemoptysis appears in 20% of the patients and up to 30% of them remain asymptomatic [2,3]. Dyspnea, typically unmasked by pregnancy or high altitude, is usually a symptom of PH which occurs in about 44% of affected individuals [3]. Its etiology may consist of the imbalance between the decreased pulmonary vascular bed and the increased blood flow [6]. Nevertheless, it may as

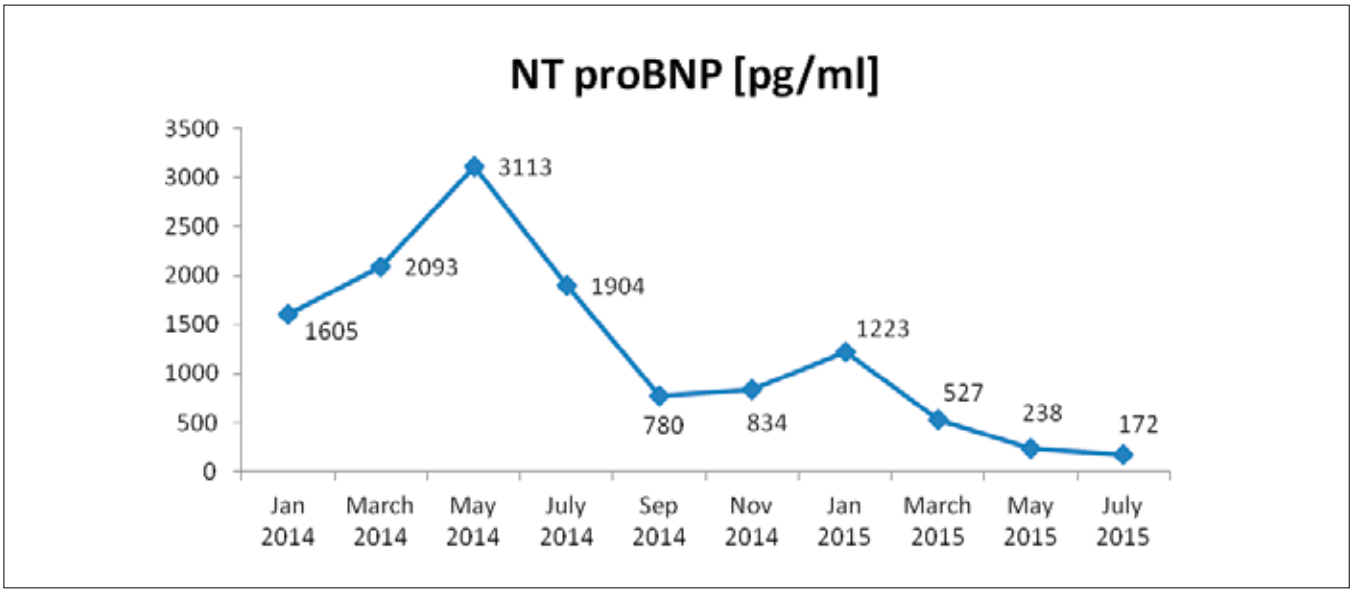

Figure 3. NT-proBNP levels from January 2014 to July 2015

well be idiopathic. The overall mortality of 7% is mainly the effect of the development of PH and of bleeding [3]. Hemoptysis happens due to excessive collateral circulation of fragile vessels. It rarely leads to massive hemorrhage and death, usually is self-limiting. The frequent infections may lead to the development of bronchiectasis [7].

All the above-mentioned symptoms are quite unspecific thus leading to a significant time delay between their onset and the diagnosis. In some cases it takes more than 30 years [8]. In chest radiograms there can be seen an asymmetry of lung fields, ipsilateral absence of the hilar shadow and diaphragm elevation, and contralateral lung may seem plethoric because of the excessive blood flow whereas mediastinum shifts to the affected side [2,3,9]. Transthoracic echocardiography is used to exclude other cardiovascular abnormalities and to discover signs of PH – which can be helpful in monitoring of the asymptomatic patients [10]. Magnetic resonance imaging and high-resolution CT are even better in diagnosing coinciding congenital heart defects. CT shows the peripheral pulmonary vasculature with collaterals and also bronchiectasis in cases of recurrent pulmonary infections [2,7,9]. Most importantly, it can be seen that the absent pulmonary artery terminates within 1 cm of its expected origin from the main pulmonary artery [2]. Ventilation perfusion scanning isn't necessary to establish the diagnosis, it can confirm limited perfusion of the affected lung though [2]. Finally, the golden standard of heart catheterization typically serves as a measure of preoperative evaluation [3].

The ways to treat UAPA complications are the attempts of interventional revascularization, the vasodilator therapy of PH and the management of pulmonary hemorrhage. The revascularization of peripheral branches to the pulmonary hilum can be successful when identifiable artery can be found. There are cases in pediatric population with up to 7 years of follow-up after such procedures [11–13]. In most patients with symptomatic PH drug treatment typical for primary pulmonary arterial hypertention (PAH) gives good results [3, 14]. In case of repeated hemoptysis the embolization of visualized in angiography collateral vessels is safe and effective [15]. If it doesn't help the procedures of lobectomy and pulmonectomy may be performed although any surgery brings the risk of complications by systemic collaterals [7].

Patient management and follow-up

After diagnosis in January 2014 our patient started to receive the first line treatment for PAH, i.e. sildenafil 20 mg t.i.d. Concomitant medications were: torasemide 5 mg, theophylline 300 mg, bilastine 20 mg, supplementation of potassium chloride, ferrous sulphate and folic acid. There was no oral anticoagulation initiated because of the heightened risk of bleeding from bronchial arteries, which would be very dangerous and might require transcutaneous embolisation.

During the first hospitalisation the six minute walking distance (6MWT) was 336 m and the test was interrupted by dyspnea and cough. The Borg index was 10/10, no desaturation nor hypotonia occurred. Cardiopulmonary exercise testing (CPET) at the beginning of therapy showed extremely limited exercise tolerance – 2.63 MET at 02'45" with maximal oxygen uptake (VO_2max) 9.2 ml/min/kg. In May 2014 the 6MWT slightly improved to 420 m, Borg 8. Regardless, after four months the patient remained in WHO FC III. After control RHC, due to the lack of clinical improvement and even further hemodynamic deterioration (cardiac index decreased from 2.31 to 1.54 l/min/m^2), we intensified the treatment by adding inhaled iloprost. At that time the process of qualification to bilateral lung transplantation began.

In July 2014 the patient was able to perform 3.65 MET during CPET, with VO_2max still low – 11.2 ml/min/kg. In September these values were 3.44 MET and 12 ml/min/kg. The distance of 6MWT increased to over 500 m in January 2015. In another RHC in July 2015 all the parameters were significantly better (Table 2), as were NT-proBNP levels (Figure 3). After over a year of second line double antiproliferative therapy our patient remains in WHO FC II, lung transplantation active listing has been suspended.

Table 2. Right heart catheterization – improvement of hemodynamic parameters in July 2015

	REST (01/2014)	AFTER ILOPROST INHALATION (01/2014)	REST (05/2014)	REST (07/2015)
RA (mmHg)	5	4	5	3
PA (mmHg)	40	36	44	38
RV (mmHg)	98/01	83/03	98/01	84/00
PCWP (mmHg)	9	9	8	6
CO (l/min)	4.32	3.85	2.88	5.17
CI (l/min/m^2)	2.31	2.06	1.54	2.71
PVR (WE)	7.17	7.01	12.5	6.19
SVR (WE)	19.66	21.55	29.5	16.24

RA – right artery, PA – pulmonary artery, RV – right ventricle, PCWP – pulmonary capillary wedge pressure, CO – cardiac output, CI – cardiac index, PVR – pulmonary vascular resistance, WE – Wood unit, SVR – systemic vascular resistance

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