Coll. Antropol. **33** (2009) 1: 331–333
Case report

Pulmonary Hypertension in Patient with Elevated Homocystein Level and Blast Injuries

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A B S T R A C T

38-year-old man had chronic deep venous thrombosis (DVT) as a result of multiple injuries caused by an explosion of grenade 12 years ago, with recurrent pulmonary thromboembolisms and pulmonary hypertension which was unrecognized for a decade. Patient was admitted with a progressive dyspnea and exercise intolerance (NYHA II). The diagnosis was established according to clinical symptoms, transthoracic echocardiography, phlebography, lung scintigraphy and pulmonary angiography. Oral anticoagulant therapy was introduced and cava filter indicated to implant. During phlebography a floating thrombus was found in the inferior cava vein underneath renal vein. Implantation was delayed and patient received systemic fibrinolytic therapy with streptokinase (7 500 000 UI within 4 days), followed by heparin infusion and warfarin. Post-fibrinolytic phlebography showed clear lumen of inferior vena cava. Fibrinolysis had also affected pulmonary hypertension-systolic pressure in the right ventricle measured by Doppler echocardiography decreased from 90 to 65 mmHg. Permanent intravenous cava filter was implanted.

Key words: *pulmonary hypertension, homocystein level, blast injuries*

Introduction

Most patients with chronic thromboembolic pulmonary hypertension present late in the course of the disease, remaining asymptomatic for months or years. The pathophysiological events in the progression of pulmonary hypertension during this period have not been well defined[1].

We report an successful use of high dose fibrinolytic therapy with streptokinase infusion (Streptase, Hoechest Marion Roussel) in resolving a newly-formed thrombus in vena cava and reducing right ventricle pressure. The role of fibrinolytic therapy with streptokinase in treating pulmonary embolism was studied in different clinical trials and published[2,3,4].

According to our knowledge, in medical literature there is no data about effects of streptokinase on pulmonary hypertension caused by chronic thromboembolism.

We also present the result of molecular DNA diagnostic method (real time PCR). It confirmed that patient is homozygous for methylen – tetrahydrolate – reductase mutation of high thromboembolic incidence, what is one of risk factors for his clinical state.

Case Report

A 38-year-old man was injured in the right shin bone by rifle-grenade explosion twelve years ago. Taking into account his sedentary life style and office work, he did not have any specific symptoms which could direct attention to his condition for years. The overload of the right heart was noticed on ECG by general practicioner ten years later. It was interpreted as pulmonary hypertension and suspected atrial septal defect (ASD). Echocardiography showed elevated pressure in the right ventricle (90 mm Hg), but ASD was not found. The first admission to our Department was 8 months ago with symptoms of progressive dyspnea and exercise intolerance worsening within last six months (NYHA class II). On physical examination pulmonic component of the sec-

Received for publication May 16, 2006

ond heart sound (P2) was loud, demonstrating fixed splitting. Systolic ejection murmur was heard over aortic and pulmonic area without propagation. On his right shin bone there were multiple old injuries and varicose veins. The measured circumference of right shin bone was 4 cm greater than the left one. On transtoracic echocardiography, enlargement of right ventricle showed pulmonary hypertension and Doppler scaning of lower extremities showed normal venous perfusion. Suspecting deep venous thrombosis (DVT), despite negative Doppler results, other diagnostic methods were done to confirm it. Venography of the lower extremities showed multiple thrombi in the right distal extremity veins, obstructing the perfusion in tibial anterior veins, fibular veins, right popliteal and femoral vein together with right external iliac and common iliac vein. The collateral circulation was developed. Chest computed tomographic scaning (CT) showed asymemetric wall thickening along the lateral aspect of pulmonary artery truncus narrowing its distal branches. Radioisotopic ventilation-perfusion scanning presented mismatched, segmental defects, left apical, posterior and anterior lobus. Transfemoral right--heart catheterization measured pulmonary artery pressure of 55/9 mm Hg and tested reversibility of hypertension with intravenously prostacyclin was negative. Pulmonary angiography showed intraluminal filling defect of main left pulmonary artery for apical lobus (Figure 1). Molecular diagnostic method (real time PCR) for DNA analyses identified MTHFR 677 TT genotype and showed that patient is homozygous for mutation as one of risk factors for his clinical state. Homocystein level was 25,61 μmol/L (normal range 5–15 μmol/L) Vitamin B12 and folic acid supplementation was introduce in therapy.

Warfarin therapy was introduced and controlled by PT and INR. We took into consideration implantation of a cava filter to prevent further thromboembolisms. After two months of anticoagulant therapy, cavography was performed due to positioning of cava filter. Surprisingly, a new floating thrombus was found 3 cm caudally from the distal renal vein (Figure 2). We receded from cava filter placement and introduced intravenous fibrinolytic therapy with 7 500 000 UI of streptokinase through 4 days, continued with unfractionated heparin for a week. Then, we performed ultrasonography and phlebography which showed clear lumen of inferior vena cava. On transthoracic echocardiography, right ventricle pressure was reduced from 90 mmHg to 65 mmHg. Homocystein level after supplementation vitamin B12 and folic acid therapy was in the normal range, 14,2 μmol/L. Patient clinical state improved in functional class to NYHA I. Finally, permanent cava filter was implanted (Figure 3). The patient was dismissed and continued to receive life-

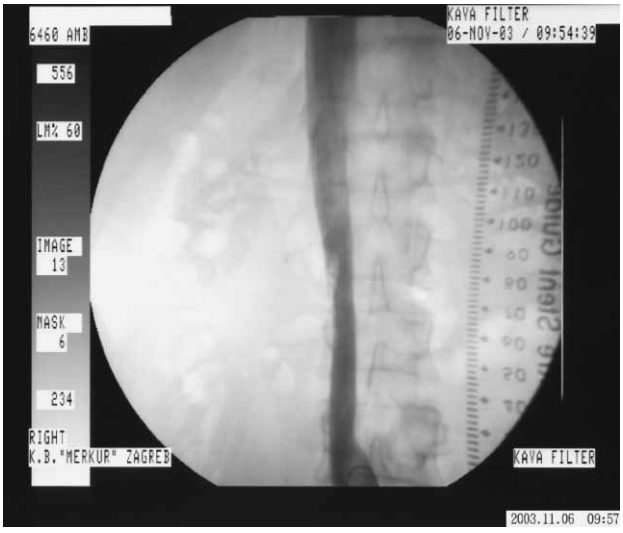

Fig. 2. Cavography – floating thrombus in inferior vena cava.

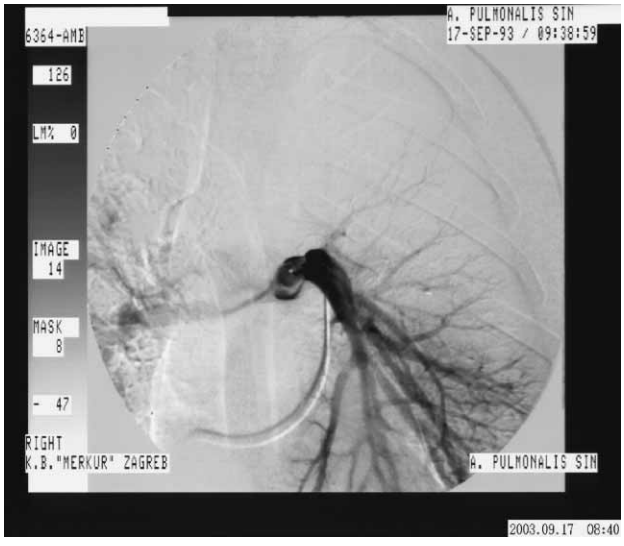

Fig. 1. Pulmonary angiography – intrluminal filling defect of main left pulmonary artery.

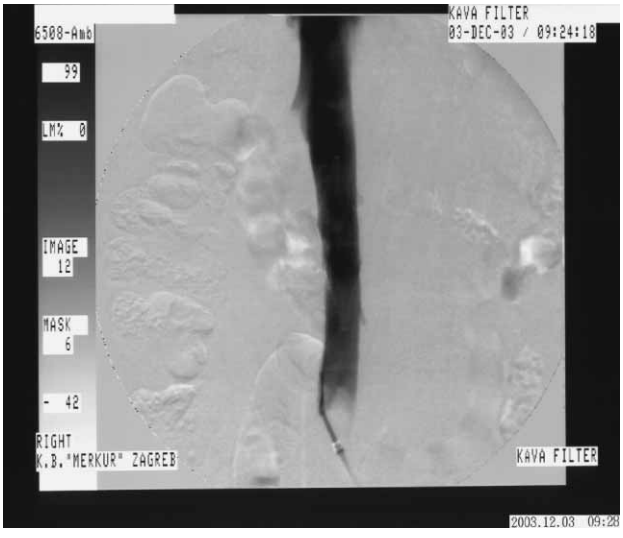

Fig. 3. Inferior vena cava phlebography after fibrinolytic therapy with cava filter.

long anticoagulant therapy and vitamin B12 and folic acid supplementation therapy.

Discussion

In this paper, we report a case of a patient with pulmonary hypertension as a result of chronic thromboembolism in whome fibrinolytic therapy was considered to resolve inferior vena cava thrombus, before permanent vena cava filter implantation. Additionally, after the therapy right ventricle pressure was 65 mmHg vs. 90 mmHg before fibrinolysis and patient condition improved. In the literature, there are data on successful using of fibrinolytic treatment of pulmonary thromboembolism[5,6]. According to our results, the pressure in the right ventricle showed significant decrease after fibrinolytic therapy (Δ 25 mmHg), comparing to a study by Jerjes-Sanchez et al.[2] where pulmonary artery pressure post-thrombolysis was 23 mmHg and pre-thrombolysis was 38 mm Hg (Δ 15 mmHg).

Real time PCR as method of DNA analyses identified MTHFR 677 TT genotype (enzym MTHFR is responsible for regeneration of metionin from homocystein). Enzymatic mutation (677 TT) increases concentration of serum homocystein and has significance in evolution of atheroslerosis, cardiovascular disease, dementia, hyperhomocysteinemia[7]. Important concept is that patient is homozygous for mutation of clinical risk for thromboembolic incidecences.

We concluded that fibrinolytic therapy was, in our case, primary therapeutic option for inferior vena cava thrombosis, but additionally, it improved patient's clinical condition and severity of pulmonary hypertension estimated by echocardiography.

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PLUĆNA HIPERTENZIJA U BOLESNIKA S POVIŠENIM HOMOCISTEINOM I OZLJEDAMA NAKON EKSPLOZIJE GRANATE

SAŽETAK

Bolesnik, star 38 godina sa kroničnom dubokom venskom trombozom kao posljedicom povišene razine homocisteina i brojnih ozljeda potkoljenic kao posljedica eksplozije granate prije 12 godina, te ponovljajućim plućnim embolijama i plućnom hipertenzijom koji nisu bili prepoznati čitavo desetljeće. Bolesnik je primljen putem hitne službe zbog progresivne zaduhe i intolerancije napora. Dijagnoza je postavljena temeljem ehokardiografije, flebografije, scintigrafije pluća i plućne angiografije. Tijekom flebografije nađen je flotirajući tromb u donjoj šupljoj veni te je bolesnik dobio fibrinolitičku treapiju streptokinazom (7 500 000 IU kroz 4 dana), te potom kontinuirani heparin i warfarin. Post – fibrinolitička flebografija pokazala je uredan lumen donje šuplje vene. Fibrinoliza je također utjecala na smanjenje tlaka u plućnoj arteriji sa 90 na 65 mmHg. Konačno, ugrađen je trajni filter u donju šuplju venu.