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Pulmonary embolism in young woman with massive deep vein thrombosis as a result of oral contraceptives

Zatorowość płucna u młodej kobiety z zakrzepicą żył głębokich po doustnych lekach antykoncepcyjnych

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Abstract

Twenty years old woman was admitted to a local hospital with pain, redness, swelling of the left extremity, general malaise, and fatigue. Performed duplex ultrasound revealed massive thrombus originating in anterior tibial, posterior tibial, and fibular veins, continuing through popliteal and femoral till the external iliac vein. Two months earlier, the patient was ordered oral contraceptive therapy. The treatment regime which was scheduled included low-molecular-weight heparin. Because there was no clinical improvement 12 days later, there was performed computed tomography pulmonary angiography. This diagnostic examination showed that deep vein thrombosis was complicated by pulmonary embolism — there were thrombi in subsegmental pulmonary arteries of the bottom lobes of both lungs. The pulmonary embolism was low-risk because there was no observed hypotony and any signs of myocardial injury — cardiac troponins and B-type natriuretic peptide levels remained within the normal range values. Because there was no improvement few days later, the patient was referred to a higher reference university hospital with Cardiac Intensive Care Unit. In this stage, subcutaneous low-molecular-weight heparin was replaced by an intravenous infusion of unfractionated heparin. After a few days of treatment, symptoms started to deteriorate.

Key words: deep vein thrombosis, pulmonary embolism, oral contraceptives, thrombophilia, post-thrombotic syndrome

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Introduction

A deep vein thrombosis is a blood clot that forms within the deep veins usually of the leg [1]. This disease may have a complicated course. It may be associated with malignancies, immobility, and thrombophilia. Also can be unprovoked — idiopathic. It is a part of the venous thromboembolism disorders which represent the third most common cause of death from cardiovascular diseases after heart attack and stroke [1]. In this article we

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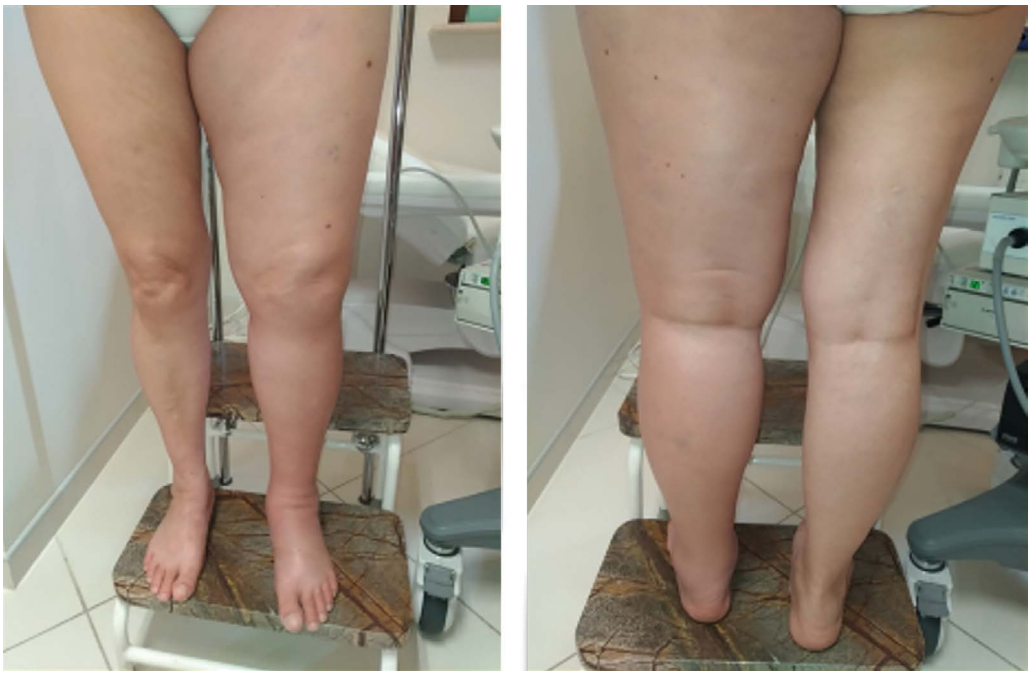

Figure 1. Massive deep vein thrombosis of left extremity

would like to focus on a case of 20 years old woman who developed a thrombus in left femoral vein/left external iliac vein complicated by pulmonary embolism after oral contraceptive therapy.

Case report

Originally patient — 20 years old woman was admitted to a local hospital with dull pain, redness, swelling of left extremity (Figure 1), general malaise, and fatigue. Performed duplex ultrasound revealed massive thrombus originating in anterior tibial, posterior tibial, and fibular veins, continuing through popliteal and femoral till the external iliac vein (Figure 2). Low-molecular-weight heparin in therapeutic dose was administered. Because there was no clinical improvement 12 days later, there was performed computed tomography pulmonary angiography. This diagnostic examination showed that deep vein thrombosis was complicated by pulmonary embolism (Figure 3) — there were thrombi in subsegmental pulmonary arteries of the bottom lobes of both lungs. The pulmonary embolism was low-risk because there were not observed hypotony and any other signs of myocardial injury — cardiac troponins and B-type natriuretic peptide levels remained in the normal range. Because there was no improvement few days later, the patient was referred to a higher reference university hospital with Cardiac Intensive Care Unit. In this stage, subcutaneous low-molecular-weight heparin was replaced by an intravenous infusion of unfractionated heparin. After

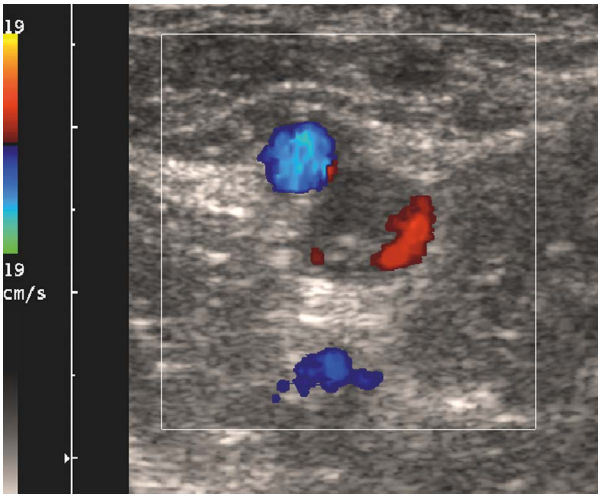

Figure 2. Deep vein thrombosis of left extremity: thrombus in trifurcation area, popliteal, femoral, iliac external, and common iliac veins. It expands to the left renal vein level

a few days of treatment, symptoms started to deteriorate. In the fifth day of treatment, the unfractionated heparin was replaced by a new oral anticoagulant rivaroxaban in dose 15 mg twice daily. In the echocardiographic examination, there were no signs of right ventricle enlargement, volume overload, and pulmonary hypertension. On the last day of the hospital stay patient was without dyspnea, had good tolerance of exercise, however, the oedema of the left

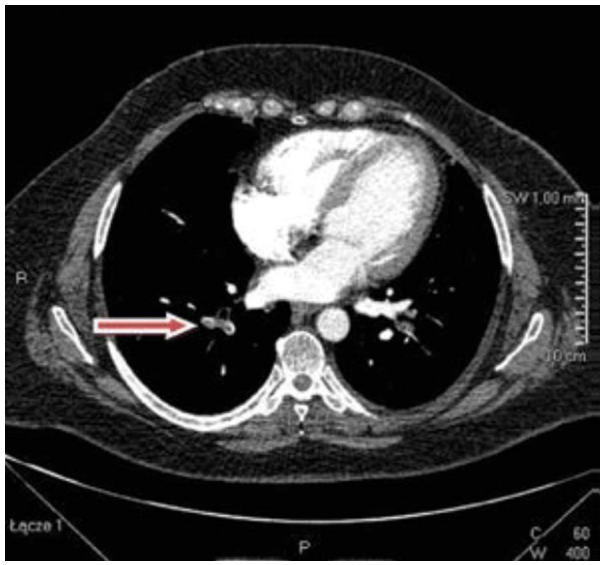

Figure 3. Filling defect in pulmonary segmental arteries

extremity remained. The patient was prescribed rivaroxaban 15 mg twice daily till the end of the third week after pulmonary embolism was diagnosed followed by 20 mg once daily. There was as well recommended compression hosiery therapy in the second class compression (23–32 mm Hg).

Discussion

What is worth mentioning, two months prior symptoms occurred (redness, swelling of left extremity, dull pain, fatigue) patient was administered oral contraceptive therapy.

There are specific contraindications to this type of pharmacotherapy such as cerebrovascular disease or coronary artery disease, a history of deep vein thrombosis, pulmonary embolism or congestive heart failure, untreated hypertension, diabetes with vascular complications, estrogen-dependent neoplasia, breast cancer, undiagnosed abnormal vaginal bleeding, known or suspected pregnancy, active liver disease, and age older than 35 years old and cigarette smoking. Although in this patient there was not observed exactly any of these risk factors, there was a significant other factor, which was a family history of the venous thromboembolic disorder. There were noted cases of deep vein thrombosis or pulmonary embolism in father, grandmother, uncle, aunt, and sister – all the family members were paternal relatives. Furthermore, the aunt was diagnosed with the genetic mutation PAI-1. In case of this patient, such treatment should not be administered due to family history on the father's site of venous thromboembolic disorder.

PAI-1 is a serine protease inhibitor that functions as the principal inhibitor of tissue plasminogen activator and urokinase, the activators of plasminogen and hence the physiological degradation of blood clots.

Plasminogen activator inhibitor-1 also known as endothelial plasminogen activator inhibitor or serpin E1 is a protein that in humans is encoded by the *SERPINE1* gene. Elevated PAI-1 is a risk factor for thrombosis and atherosclerosis.

The patient was referred to Medical Genetics Outpatient Clinic – further investigation revealed the variant 4G of mutation in the PAI-1 gene. Such kind of mutation is not an only risk factor for venous thromboembolic disease, but also may have disruptive effect on fetal-placental circulation. Despite there was such unfavorable combination of risk factors, and the antenatal period was complicated by severe preeclampsia, thepatient delivered healthy baby 10 months after thromboembolic event. However, recent analyses suggest that PAI-1 4G/5G mutation is not a risk factor for female infertility, which is confirmed by presented patient's history [2]. Nowadays, patient receives low-molecular-weight heparin injections each day and is considered to converse the therapy to oral anticoagulants. Although there is general successful outcome, symptoms such as enlarged circumference of the left calf and redness of skin which patient observes while the temperature of surrounding air is warm still remain sixteen months after the first manifestation of venous thromboembolic disease. There is also a risk of development of the post-thrombotic syndrome of the left extremity in this young woman.

Conclusions

What is important, patients must be thoroughly interviewed prior to administration of oral contraceptive therapy. In this case, venous thromboembolism could have been avoided if a proper interview was taken.

Conflict of interest

None of the authors declares conflicts of interest.

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