UDC 616.131-008.331.1-07

N.A. Kosheleva*[1,2], K.A. Gamayunova[1]

[1] — State Educational Institution of High Professional Education Saratov State Medical University n.a. V.I. Razumovsky, Saratov, Russia

[2] — State Healthcare Facility Saratov Regional Clinical Hospital of Ministry of Health and Social Development of Saratov Region, Saratov, Russia

CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSIA AT THE YOUNG PATIENT. CLINICAL OBSERVATION

Abstract

The objective of the study: To report a case of onset and course of chronic thromboembolic pulmonary hypertension (CTEPH) at the patient of young age. **Materials and methods**. The patient P., 26 years, was admitted with complaints of dyspnea during mild exercise exertion and at rest, edemas of the lower extremities. Patient had recurrent PE, subclavian and brachial venous thrombosis on the right side in her medical history. **Results**. Echo and ECG signs of pulmonary hypertension were obtained. Repeated MSCT pulmonary angiography showed a dissolution of thrombotic masses in a lumen of a pulmonary artery. No data for thrombophilia or systemic vasculitis were obtained. **Conclusion.** The present clinical observation demonstrates the formation and course of CTEPH in a young patient with recurrent pulmonary embolism. The young age, idiopathic and recurrent character of pulmonary embolism were the predisposing risk factors for CTEPH development.

Key words: *pulmonary embolism, chronic thromboembolic pulmonary hypertension*

For citation: Kosheleva N.A., Gamayunova K.A. CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSIA AT THE YOUNG PATIENT. CLINICAL OBSERVATION. The Russian Archives of Internal Medicine. 2018; 8(2): 146-149. [In Russian]. DOI: 10.20514/2226-6704-2018-8-2-146-149

DOI: 10.20514/2226-6704-2018-8-2-146-149

VTE — venous thromboembolism, DS — duplex study, mPAP — mean pulmonary arterial pressure, MSCT — multislice computed tomography, PE — pulmonary embolism, CTEPH — chronic thromboembolic pulmonary hypertension, Echo — echocardiography

Introduction

The definition of venous thrombosis and thromboembolism comprises deep venous thrombosis and pulmonary embolism. Pulmonary embolism is the third most common cardiovascular disease with prevalence in the range of 100–200 cases per 100,000 population per year. It is characterized by a high mortality rate. [1]. The most significant predisposing risk factors for females are traumas, obesity, prolonged immobility, use of oral contraceptives, antiphospholipid syndrome, infections, and thrombophilia. Pulmonary embolism can also occur in the absence of any known risk factor [2].

The delayed complication of acute pulmonary embolism (PE) is chronic thromboembolic pulmonary hypertension (CTEPH). Some patients with prior PE do not experience complete recanalization of the pulmonary vascular bed. In these patients embolic masses are dissolved only partially, and they are replaced by connective tissue. These embolic masses change the lumen of the pulmonary vessels, which leads to CTEPH formation [3].

* Contacts. e-mail: kosheleva2009@yandex.ru

CTEPH is a rare disease, the prevalence of which is about 5–10 cases per 1 million people per year. The mean age of Russian patients at diagnosis is 45.8 ± 13.7 years according to the National Registry [4]. The prevalence rate is considered equal in male and female populations. When untreated, CTEPH prognosis is unfavorable and depends on the degree of pulmonary hypertension. According to foreign studies, the ten-year survival rate of patients with inoperable CTEPH at a mean pulmonary artery pressure (mPAP) in the range of 31–40 mm Hg is 50 %; at mPAP from 41 to 50 mm Hg it is 20 %; and at mPAP of more than 50 mm Hg it is 5 % [5]. Since the disorder is rare in female young patients, we would like to provide our clinical observation of such case.

Case Report

Female patient P., aged 26, was admitted to the Department of Cardiology of the Regional Clinical Hospital in December 2016. Her chief complaints were mixed dyspnea during mild exercise exertion and at rest, hypotension of 80/60 mm Hg, fatigue, and leg swelling up to knees. The history of present illness: in October 2015, the patient firstly noticed coldness, cyanosis and swelling of her right upper limb. A duplex study of upper extremity veins confirmed subclavian and brachial venous thrombosis on the right side. Treatment with heparin and detralex was prescribed by the vascular surgeon, which had a positive effect in reducing the upper limb swelling. Since thrombosis was revealed screening for its reasons was not carried out. In August 2016, the patient noted hypotension to 80/60 mm Hg, an episode of syncope, mixed dyspnea when walking 3 floors upstairs. Exercise tolerance was further decreasing. In November 2016, a second episode of syncope, hemoptysis, aggravation of the mixed dyspnea on exertion and its onset at rest, and leg swelling up to knees were all noted. According to the past medical history, there were no injuries, prolonged immobility, use of oral contraceptives, infectious diseases. According to the patient's words, she does not smoke or take drugs, including intravenous forms. A chest X-ray showed no cervical rib.

At admission, the patient's condition was severe, due to cardiac and respiratory failure. Mixed dyspnea at rest and aggravated on minimal exertion was noted. Leg swelling was up to knees. The patient was active. BMI was 23 kg/m^2, HR — 102 bpm, RR — 28 per minute, BP — 100/70 mm Hg; oxygen saturation — 88 %. The skin was pale, and acrocyanosis was noted. The heart sounds were muffled, and the rhythm was regular. Accent of S2 over the pulmonary artery and Graham Steele murmur were found. Breathing in the lungs was vesicular, and rales were not heard. The abdomen was soft and nontender. The liver was enlarged, palpable 2 cm below the costal margin. The urine output was decreased. The ECG revealed a sinus tachycardia at 110/min, right axis deviation, "SI, QIII, TIII" pattern, inverted T-wave in V1–V6, and right atrial hypertrophy. Echocardiography (Echo) showed high pulmonary hypertension and signs of right heart overload (Table 1).

MSCT pulmonary angiography scanning showed thrombosis of the lower branch of the right pulmonary artery, and pulmonary infarction (S10) (Figure 1).

A duplex study (DS) showed post-thrombotic changes of the right subclavian vein. D-dimers were negative, no specific findings in the coagulogram. Taking into account negative anti-dsDNA antibodies, antineutrophil cytoplasmic antibodies,

Table 1. *Echo indices in dynamics*

Indices	December, 2016	February, 2017
Right atrium, cm	4.54	5.07
Right ventricle, cm	4.12	4.64
RV anterior wall, cm	0.6	0.78
Pulmonary artery systolic pressure, mm Hg	90	80
Tricuspid regurgitation	3 degree	3-4 degree
Ejection fraction, %	63	63

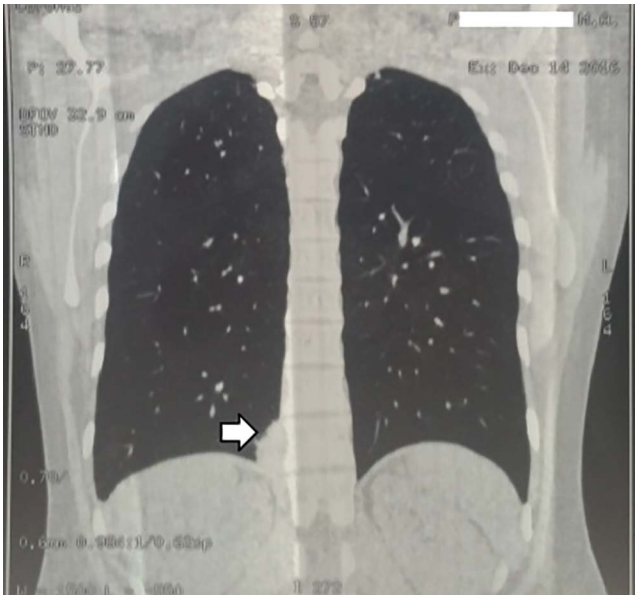

Figure 1. *MSCT: the focus of increased lung density in S10 of the right lung, triangular in shape, widely adjacent to diaphragmatic pleura.*

antinuclear antibodies, lupus anticoagulant, and anticardiolipin antibodies, data for antiphospholipid syndrome or systemic vasculitis have not been revealed. During the examination no data for cancer were received. To exclude primary thrombophilia, the genes were examined (*F5* gene coding the coagulation factor V (Factor V Leiden), *F2* gene coding the coagulation factor II or prothrombin, and MTHFR gene coding methylenetetrahydrofolate reductase, a key enzyme in the conversion of homocysteine amino acid), but no clinically significant mutations were determined.

The principal diagnosis was: Pulmonary embolism (August 2016), recurrent PE (November 2016). Thrombosis of the lower branch of the right pulmonary artery. Pulmonary infarction (S10 of the right lung). Subacute cor pulmonale. 3rd degree of functional tricuspid regurgitation. 3rd degree of pulmonary hypertension. Thrombosis of subclavian and brachial veins on the right in October 2015. Post-thrombotic syndrome of the right upper limb. Complications: respiratory failure of the 2nd degree. Chronic heart failure, NYHA 4. Hemoptysis in November 2016.

The following treatment was provided at the Department of Cardiology: oxygen therapy, enoxaparin 1 mg/kg b.i.d., amlodipine 2.5 mg/day, bisoprolol 2.5 mg/day, torasemide 10 mg/day, and verospiron 50 mg/day. On day 7 rivaroxaban was initiated instead of enoxaparin: 15 mg b.i.d for 3 weeks, then 20 mg/day was prescribed for long-term administration. The patient complied with the recommendations.

In February 2017, the patient was admitted for follow-up. Her state of health has slightly improved: dyspnea when walking 3 floors upstairs decreased (no dyspnea at rest), and no swelling was observed. The lab results, ECG and lower extremities DS data did not show any significant changes. According to Echo, mPAP did not change significantly, and the right heart dilatation increased (Table 1). Repeated MSCT pulmonary angiography showed no thrombotic masses in the pulmonary trunk and pulmonary arteries. Two areas of increased lung density in S9 and S10 of the right lung were revealed, triangular in shape, widely adjacent to diaphragmatic and costal pleura.

The patient was consulted by a cardiac surgeon of the FSBI A. N. Bakulev National Medical Research Center of Cardiovascular Surgery via telemedicine technology. Due to the presence of thrombosis and episodes of PE in the past medical history, the chronic pulmonary heart disease progression, no significant change of mPAP on the background of the adequate three-month anticoagulant therapy, chronic thromboembolic pulmonary hypertension (CTEPH) was proposed. It was recommended to continue the ongoing therapy, including anticoagulants, and sildenafil (20 mg t.i.d.) was added. The follow-up to decide the issue of surgical treatment was recommended in case of no improvement in the patient's state. No significant improvement (according to clinical and instrumental data on the background of adequate therapy) was revealed during the case follow-up with the participation of cardiac surgeons from FSBI A. N. Bakulev National Medical Research Center of Cardiovascular Surgery. In February 2018, the patient was admitted to the Pulmonary Hypertension Department of the Federal Center, and on March 2, 2018, she underwent successful pulmonary thromboendarterectomy.

Discussion

This clinical case shows the formation and further course of CTEPH in a young female patient after recurrent PE. Why do some patients who suffer

from PE develop CTEPH, while others do not? Dissolution of thrombi occurs with the help of local thrombolysis with a full restoration of the pulmonary vascular bed patency. However, in some cases, for unexplained reasons, resorption does not occur and the emboli are converted into organized clots inside the pulmonary artery. Perhaps this process is aggravated by the hemostasis or fibrinolysis disturbance, as well as by recurrent embolism. Currently, scientists continue to investigate congenital and acquired coagulation anomalies in patients with venous thromboembolism (VTE) and CTEPH [6]. Among the coagulation system pathology findings in patients with venous thromboembolism and those who later develop CTEPH, the following are the most often detected: lupus anticoagulant (10 %), antiphospholipid antibodies (20 %), increased factor VII activity (39 %), and fibrinogen genes mutations [7]. In addition to the impairment of coagulation, the following potential risk factors may be involved in the formation of CTEPH: recurrent embolism, large perfusion defect, young age of patients, and idiopathic character of pulmonary embolism [8].

The treatment of choice for the CTEPH management is tromboendarterectomy. It tends to decrease dyspnea, to improve the functional class of CHF, and to prolong the life expectancy of patients. If surgical treatment is not possible and in case of residual pulmonary hypertension, the use of PAH-specific therapy is allowed. Modern PAH-specific medicines possess not only a vasodilating ability, but a number of additional properties, including cytoprotective, antiproliferative, antiaggregational, etc. They affect the targets of the disease pathogenesis: the endothelin system excessive activation (endothelin receptor antagonists), the deficiency of endogenous prostacyclin (prostacyclin analogues — prostanoids) and of nitric oxide (phosphodiesterase type 5 inhibitors, guanylate cyclase stimulants) [9].

Conclusion

The present clinical observation demonstrates the formation and course of chronic thromboembolic pulmonary hypertension in a young patient with recurrent pulmonary embolism. The predisposing risk factors for CTEPH development were young age and the idiopathic and recurrent nature of pulmonary embolism. The decision to conduct a thromboendarterectomy and/or to prescribe PAH-specific therapy is taken jointly with a surgeon at a specialized center.

Conflict of interests

The authors declare no conflict of interests.

References:

1. ESC/ERS recommendations on the diagnostics and treatment patients with an acute embolism of system of a pulmonary artery 2014. Russian Cardiology Journal. 2015; 8(124): 67-110 [in Russian].
2. The Russian clinical references on diagnostics, treatment and prevention of venous tromboembolic episodes. The Phlebology. 2010; 2(4): 1-37 [in Russian].
3. Chazova I. E., Martynyuk T.V. Clinical references on diagnostics and treatment of a chronic thromboembolic pulmonary hypertensia(s). Eurasian Cardiology Journal. 2015; 3: 8-27 [in Russian].
4. Chazova I. E., Martynyuk T.V. Clinical references on diagnostics and treatment of a chronic thromboembolic pulmonary hypertensia(s). Cardiologic Herald. 2016; 4: 3-23 [in Russian].
5. Wijesuriya S. Chronic Pulmonary Emboli and Radiologic Mimics on CT Pulmonary Angiogrphy: A Diagnostic Challenge. Chest. 2016; 143(5): 1460-71.
6. Klimenko A.A., Shostak N.A., Demidova N.A. Chronic post-embolic pulmonary hypertensia: new aspects of formation and advance of a disease. Clinician. 2011; 5(1): 14–17 [in Russian].
7. Kyrle P. A. Venous thrombosis: who should be screened for thrombophilia in 2014? Pol Arch Med Wewn. 2014; 124(1–2): 65–9.
8. Robbins I.M., Pugh M.E., Hemnes A.R. Update on chronic thromboembolic pulmonary hypertension. Trends Cardiovasc. Med. 2016; 1050–1738(16): 30054-8.
9. Allain J.S. Gueret P., Le Gallou T. et al. Hereditary thrombophilia testing and its therapeutic impact on venous thromboembolism disease: Results from a retrospective single centre study of 162 patients. Rev. Med. Interne. 2016; 3(10): 661–6.

Article received on 12.02.2018.
Accepted for publication on 12.03.2018.