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PULMONARY THROMBOEMBOLISM AND PERICARDIAL EFFUSION AS CARDIOVASCULAR COMPLICATIONS OF COVID–19 INFECTION

Summary: Systemic activation of coagulation and pulmonary thrombo-inflammation with local vascular damage caused by SARS-CoV-2 infection increases the risk of developing thromboembolic complications: stroke, pulmonary arterial thrombosis (pulmonary thromboembolism) and deep vein thrombosis. Myopericarditis may occurs in COVID-19 patients as part of or after the onset of respiratory symptoms. Minor pericardial effusions up to 1 cm that accompany pericardial involvement are common. In our patient during hospitalization due to bilateral pneumonia caused by SARS-Cov-2 virus during a routine control of D-dimer, elevated values 2.3 fold higher than the reference range were observed, with elevated biomarkers of inflammation. She had symptoms of a respiratory infection and no pronounced clinical symptoms that would indicate pulmonary thromboembolism. MSCT pulmonary angiography was performed and low-risk thromboembolism was confirmed. Anticoagulant therapy was started - therapeutic doses of low molecular weight heparin (enoxaparin), which was extended after discharge from the hospital with DOAC (Rivaroxaban) according to the protocol for the treatment of pulmonary thromboembolism. At the control examination after 3 weeks, pericarditis with moderate pericardial effusion was determined. Anticoagulant therapy (DOAC) was extended with the inclusion of colchicine in the therapy according to the protocol for the treatment of pericarditis with effusion. After 3 months of hospitalization in our patient with mild respiratory symptoms, bronchopneumonia of the right lung developed with slightly elevated biomarkers of inflammation and normal values of D-dimer. With prescribed antibiotic therapy and current therapy (DOAC and colchicine), there was a withdrawal of symptoms and regression of pericardial effusion and a reduction in right ventricular overload. At the follow-up examination 5 months after hospitalization, complete regression of pericardial effusion was confirmed with normal

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biomarkers of inflammation and D-dimer values. It is advisable to exclude anticoagulant therapy (DOAC) with continued low-dose aspirin therapy.

Keywords: COVID-19, SARS-CoV-2, pulmonary thromboembolism, pericarditis, pericardial effusion, D-dimer, anticoagulant therapy.

Introduction

COVID-19 disease caused by the SARS-CoV-2 virus is a disease that manifests itself in a wide range of disorders that primarily affect the respiratory system with different symptoms and severity of the clinical conditions: from asymptomatic cases, through fever and mild respiratory disorders to the development of acute respiratory distress syndrome, shock and multiorgan failure leading to an increased risk of death. In addition to respiratory complications, patients with COVID-19 infection may have several symptoms that include cardiac and neurological complications and conditions as a consequence of hypercoagulability. There is a wide range of cardiovascular and thromboembolic complications within acute COVID-19 cardiovascular syndrome. Cardiac complications include acute coronary syndrome with coronary artery obstruction, acute myocardial damage as part of non-obstructive coronary artery disease, heart failure, cardiogenic shock, nonischemic cardiomyopathy, stress cardiomyopathy, myocardial infarction, arrhythmia, pericarditis, pericardial effusion, and cardiac tamponade (1).

Systemic activation of coagulation and pulmonary thrombo-inflammation with local vascular damage caused by SARS-CoV-2 infection increases the risk of developing thromboembolic complications: stroke, pulmonary arterial thrombosis (pulmonary thromboembolism) and deep vein thrombosis (2).

Observational studies have shown that the incidence of venous thromboembolism (VTE) is 15 to 25%, with an increase in the incidence with the severity of the clinical conditions: 58-69% in intensive care units despite the use of pharmacological thromboprophylaxis (3).

The SARS-CoV-2 virus enters the alveolar epithelium via angiotensin-converting enzyme 2 (ACE2) receptors leading to the extensive release of proinflammatory cytokines (IL-1, IL-6, IL-8, TNF-alpha, etc.) which further leads to activation of epithelial cells, monocytes and neutrophils, which lead to vasoconstriction and initiate a systemic inflammatory response - ”cytokine storm” (4). Endothelial cells can be directly infected via ACE2 receptors leading to endothelial activation and dysfunction that activates the coagulation cascade that generates thrombin and fibrin clots. This condition leads to a significant increase in fibrinogen, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), interleukin-6 (IL-6) and ferritin levels. COVID-19 infection also leads to a comprehensive hypercoagulable state of the organism that leads to macrovascular and microvascular thrombosis (5). Studies have shown that

abnormal coagulation parameters in COVID-19 patients are often associated with poorer prognosis and increased mortality. A significant increase of D-dimer, as a sign of coagulation activation and fibrinolysis, is a good indicator for the identification of a high-risk population for the development of venous thromboembolism (VTE) within COVID-19 infection. D-dimer is a test of high sensitivity, but low specificity for detection of an active thrombotic process. An increase in the neutrophil-lymphocyte ratio (NLR) and a decreased lymphocytes count increases the risk of thrombosis and the development of VTE. Prolonged prothrombin time (PT) and elevated fibrinogen are associated with a more severe clinical picture and higher mortality (6,7). Antiphospholipid antibodies (lupus anticoagulants-LA, anticardiolipin and anti-beta-2 glycoprotein antibodies) have also been found in severe COVID-19 infections, which further increases the risk of thrombosis (8).

Risk factors for the development of venous thromboembolism (VTE) in COVID-19 patients include older age, male gender, obesity, immobilization, smoking, and comorbidities such as diabetes, previous history of VTE, chronic kidney disease, malignant tumour, heart and respiratory failure, sepsis, hypoxia, infection (9).

Like other viruses, the SARS-Cov-2 virus can cause myocarditis by itself or as part of myopericarditis. Cardiac tamponade is rare as a complication of COVID-19 infection. Myopericarditis may occur in COVID-19 patients as part of or after the onset of respiratory symptoms. Minor pericardial effusions up to 1 cm that accompany pericardial involvement are common. Previous cardiovascular comorbidities may increase the risk of COVID-19 myopericarditis. Troponinin as a sensitive marker of myocardial damage is elevated in almost all cases of myopericarditis. Myopericardial damage can be differentiated by transthoracic echocardiography (TTE) or cardiac magnetic resonance imaging (MRI) (10). On the ECG, ST elevation in multiple leads or nonspecific ST changes can be observed. Treatment of myopericarditis includes nonsteroidal anti-inflammatory drugs (NSAIDs), acetyl-salicylic acid, glucocorticoids and colchicine (11,12).

Case report:

A 68-year-old female patient appears at the first cardiologist examination, after COVID-19 infection. Three weeks before the examination, the patient was hospitalized for 8 days with an infectious disease ward due to bilateral pneumonia. Three days before hospitalization, she had fatigue, dry cough, muscle pain, fever for 2 days - the highest measured body temperature was up to 37.6 C, and that was caused her to go to the COVID ambulance. Laboratory analyzes showed increased erythrocyte sedimentation rate (ESR): 28 mm/h and CRP: 36 mg/L (normally less than 5 mg/L) with leukopenia (Le-2.7x10^9), lymphopenia (Ly-0.9x10^9), mild thrombocytopenia (Plt- 131x10^9) and elevated LDH values: 405 U/l (normally less than 241U/L) and

ferritin: 560 ng/mL (normal range 15-160 ng/mL). Lungs X-ray showed bilateral basally inhomogeneous banded shadows that indicated bilateral bronchopneumonia with auscultatory attenuated respiratory sound at the lung bases. She was referred for hospital treatment in the infectious clinic. Tested for SARS-CoV-2 (nasopharyngeal swab) with a positive result. Treatment protocol therapy for COVID-19 infection was conducted along with prophylactic doses of LMWH (enoxaparin). During hospitalization, she was afebrile and had mild dyspnea with a dry cough without chest pain or a fast pulse. She didn't need oxygen support therapy; oxygen saturation was in the normal range (SpO2: 94-96%). The patient denies previous chronic diseases and no indications of risk factors for cardiovascular diseases. On the second day of hospitalization, D- dimer was tested and it was high values: 2320 μg/L (normally less than 500 μg/L) with normal troponin values TnI-0.1 ng/mL (normally less than 0.3 ng/mL). The patient was hemodynamically stable - blood pressure values were from 110-120/70-80 mm Hg with pulse values (70-85/min). MSCT pulmonary angiography was performed showing pulmonary artery flow defects with occlusive thrombus for the lateral and anterior segment of the upper lobe of the right lung. An assessment of the severity of pulmonary thromboembolism was performed. Anamnestic data were without significant risk factors for the development of venous thromboembolism. A therapeutic dose of LMWH (enoxaparin) was prescribed according to the protocol for the treatment of low-risk thromboembolism (13). Blood urea nitrogen values were in the normal range (BUN-6.7mmol/L) and creatinine-85 umol/L. Two days after starting with therapeutic doses of LMWH, our patient was without symptoms and on the seventh day of starting LMWH therapy, she was switched to DOAC (Rivaroxaban 2x15 mg for the next 3 weeks, and then 20 mg once a day) advising further cardiologist check-ups 3 weeks after discharge.

Three weeks after hospitalization on control check-up, the patient was without symptoms - no fatigue, with good effort tolerance and without arrhythmias. Auscultatory on the lungs audible normal respiratory sound, and the lower-left edge of the sternum systolic murmur without propagation. Blood pressure values were in the normal range (BP: 110/70mm Hg). ECG findings: sinus rhythm, HR: 65/min, lower voltage, incomplete RBBB, reduced R from V1-4 with ST depression to 0.5 mm in inferior leads. On the performed transthoracic echocardiographic (TTE) examination: the dimension of the thoracic aorta: root-29 mm, bulbous-32 mm, ascending aorta-29 mm, aortic arch-26 mm, descending aorta-19 mm. The aortic valve is three-leafleted, of normal flow over the valve-1.0 m/s with little aortic regurgitation (AR: 1+). More voluminous mitral valves are observed, without criteria for prolapse, with mitral regurgitation (MR: 1-2+) in the normal left atrium (LA: 35 mm). The left ventricle has normal wall dimensions: septum-9 mm, posterior wall-9 mm and regular endocavitary dimensions of the left ventricle (EDDLV/ESDLV: 45/24 mm), with first-degree diastolic dysfunction, and with good contractility and good ejection fraction (EF):

65%. The right ventricle has a discreet oversize: 28mm, good contractility, without the presence of thrombus masses and with tricuspid regurgitation (TR:2-3+) and right ventricle systolic pressure (RVSP): 40-45 mm Hg. The pericardium is hyperechogenic and thickened behind the posterior and inferior wall and behind the posterior wall is the pericardial effusion up to 8 mm and in front of the right ventricle the pericardial effusion up to 10 mm without signs of right ventricular collapse. On the colour-duplex scan of the arteries and veins of the lower extremities, deep and superficial veins of the lower extremities of normal flow are observed, without signs of thrombosis. Discrete varicose veins of the vessel branches in the distal part of both lower legs, more shown on the left leg; arteries of the lower extremities without significant stenotic lesions, without pathological dilatations, with physiological waves of flow over them. D-dimer values was in the reference range: 84.28 ng/mL (normally less than 500 ng/mL), as well as troponin values TnI-0.02 ng/mL (normally less than 0.3 ng/mL) with slightly elevated CRP values: 9 mg/L and erythrocyte sedimentation rate (ESR): 18 mm/h. It was suggested to continue therapy with DOAC (Rivaroxaban 20 mg daily) with proton pump inhibitors (PPIs) -Omeprazole 40 mg once daily and Colchicine 2 x 0.5 mg were included in therapy. Avoiding physical exertion is advised.

Six weeks after the hospitalization on control check-up, the patient was without symptoms, without fatigue and with good tolerance of moderate physical effort. On control transthoracic echocardiographic examination pericardial effusion was in regression: behind the posterior wall of left ventricle pericardial effusion up to 6 mm, and in front of the right ventricle effusion up to 8 mm, without signs of right ventricular collapse, which is smaller than the previous examination RV-27 mm, with RVSP: 35-40 mmHg. In laboratory tests D-dimer values in the reference range: 87.6 ng/mL (normally less than 500 ng/mL), with slightly elevated CRP values: 6 mg/L, ESR- 25 mm/h and ferritin: 221 ng/mL (normal range 15-160ng/mL). Other biochemical parameters of blood were in the reference range. With current therapy, she was advised to take a small dose of beta-blockers (Bisoprolol 1.25 mg in the morning).

At the control check-up after 10 weeks of hospitalization, the patient was without symptoms. On control transthoracic echocardiographic examination, pericardial effusion was in regression: pericardial effusion behind the posterior wall of left ventricle up to 4 mm, and in front of the right ventricle effusion up to 6 mm, without signs of right ventricular collapse, RV dimension-27 mm with RVSP: 35 mm Hg. In laboratory analyzes, D-dimer values was in the reference range: 190 ng/mL (normally less than 500 ng/mL), with slightly elevated CRP values: 10 mg/L, ESR: 15 mm/h. Other biochemical parameters of blood were in the reference range. She was advised to do a control MSCT pulmonary angiography. Continuation of current therapy was advised.

At the follow-up examination 3 months after hospitalization, she felt well until 10 days ago, when she developed a fever of up to 37.4 C with a weakness for one day, mild dyspnea and vomiting. She performed laboratory analyzes in which the ignition

parameters were elevated: CRP values: 33.7 mg/L and ESR values: 23 mm/h. D-dimer values were in the reference range: 224 ng/mL (normally less than 500 ng/mL). On the performed MSCT of the chest: a wider zone of inhomogeneous, weakly intensive consolidation of the appearance of the ”ground glass” on the right posterior-basal in the lung parenchyma and fibrous changes was observed in the left basal lung parenchyma. Both pleural spaces without fluid content; thoracic aorta and pulmonary arteries of regular dimensions. No pericardial effusion. The finding of MSCT thorax corresponds to bronchopneumonia of the right lung. Tested for SARS-CoV-2 - nasopharyngeal swab was done with a negative result. She was treated with antibiotic therapy. She has not had a fever or weakness since then. There is a dry cough, occasional headache and fatigue, which is more pronounced when walking up the stairs. In the performed control laboratory analyzes, the inflammation parameters were slightly elevated: CRP: 6 mg/L, ESR: 17 mm / h, as well as LDH values: 395 U/l (normally less than 241 U/L). Blood count finding in the reference range: leukocytes: 5.2 x 10^9, haemoglobin-144 g L, platelets count-187x10^9. Creatinine kinase and cardio specific creatinine kinase values were in the normal range (CK: 56 u/ L, CK-MB: 14 u/L), as well as D dimer values: 74 ng/mL (normally less than 500 ng/ mL). On control transthoracic echocardiographic examination pericardial effusion was in regression compared to the previous examination: behind the posterior wall of left ventricle pericardial effusion up to 2 mm and in front of the right ventricle effusion up to 3 mm without signs of the collapse of the right ventricle; RV dimension-26 mm with RVSP: 30-35 mm Hg. It was recommended that he continue to take the prescribed antibiotic therapy for another 3 days. It was advised to continue therapy with Colchicine 2 x 0.5 mg for another month and then to exclude from therapy, and to continue with DOAC (Rivaroxaban), a proton pump inhibitor (Omeprazole) and a low dose of beta-blocker (Bisoprolol) until the next control.

At the control check-up after 5 months from hospitalization, she states that for another 3 weeks from the last check-up, she occasionally had a dry cough and fatigue when walking up the stairs, and for the past month she has had no symptoms. She stopped taking Colchicine a month ago as advised. In the performed control laboratory analyzes, the inflammation parameters were in the reference range: CRP: 4.3 mg/L, ESR: 10 mm/h, as well as D- dimer values: 300 ng/mL (normally less than 500 ng/mL). On control transthoracic echocardiographic examination there was without signs of pericardial effusion. The pericardium is thickened and hyperechogenic behind the posterior and inferior wall of the left ventricle, the right ventricle is of normal dimensions-26 mm, tricuspid regurgitation (TR: 2+); RVSP: 32 mm Hg. Other echocardiographic parameters of the heart were as like on the first examination. It was recommended to continue DOAC (Rivaroxaban 20 mg daily) for another month, followed by acetylsalicylic acid (Aspirin 75 mg daily), a small dose of beta-blocker (Bisoprolol 1.25 mg in the morning) and Omeprazole 40 mg in the morning. A check-up in 2 months was advised.

Discussion

Venous thromboembolism (VTE) is a common complication in the clinical course in patients with COVID-19 infection, regardless of receiving thromboprophylaxis (14). The meta-analyzes of 11 cohort studies indicated that among hospitalized COVID-19 patients, 23.9% developed venous thromboembolism (VTE), regardless of receiving anticoagulant therapy during hospitalization. Pulmonary embolism (PE) was detected in 11.6% and deep vein thrombosis (DVT) in 11.9%. Patients in intensive care units had a higher risk for VTE (30.4%) compared to patients outside intensive care units (13%). Pulmonary embolism (PE) during clinical presentation often overlaps with pneumonia in COVID-19 infection, which makes it difficult to recognize PE symptoms in patients who most often have dyspnoea (15).

Venous thromboembolism (VTE) also occurs in hospitalized patients with a milder form of COVID-19 infection in hospitalized patients. In a retrospective cohort study of 289 patients with a milder clinical condition, VTE was detected in 17% of patients. PE was detected in 14.5% of patients, cerebral venous thrombosis in 1% and DVT in 4.2% of patients (16).

Pulmonary embolism (PE) within COVID-19 infection can develop in the absence of recognisable risks for the development of deep vein thrombosis and most often develops primary in-situ thrombosis (pulmonary arterial thrombosis) rather than embolism, resulting in thrombotic occlusion of small and medium pulmonary arteries and successive pulmonary parenchymal infarcts. COVID-19 patients have widespread thrombosis with microangiopathy. Alveolar capillary micro thrombosis has a 9 fold higher prevalence in COVID-19 patients than in patients with influenza. This type of thromboembolism is characterized by hypercoagulability associated with an intense immuno-inflammatory response, resulting in diffuse occlusive thrombotic microangiopathy with alveolar damage and vascular angiogenesis. Impaired fibrinolysis that coexists with exacerbation of thrombotic processes leads to the persistence of micro thrombosis (17).

High levels of D-dimer in the initial presentation of the disease are predictive of complications associated with coagulation during hospitalization, critical illness development, and mortality. A D-dimer higher than 2500 ng/mL increases the risk for thrombosis by 6.79 fold and bleeding by 3.56 fold. Other biomarkers during initial presentation predictive of intrahospital thrombosis included platelet count greater than $450x10^9$, C-reactive protein (CRP) greater than 100 mg/L, and erythrocyte sedimentation rate (ESR) greater than 40 mm/h. Fibrinogen, ferritin and procalcitonin are increased in patients with thrombotic complications compared to those without thrombosis (18).

The thromboprophylaxis strategy is a key factor to prevent potentially lethal complications. Potential therapeutic options for the prevention of thrombosis in CO-

VID-19 infection include low molecular weight heparin (LMWH), unfractionated heparin (UFH), direct oral anticoagulants (DOAC), antiplatelet drugs, FXII inhibitors, and thrombolytic drugs. Most of these drugs have pleomorphic effects, in addition to antithrombotic and anti-inflammatory or antiviral effects (19).

In documented or highly suspected venous thromboembolism (VTE), anticoagulant therapy is the mainstay of therapy. Low molecular weight heparin (LMWH) is the most commonly used and safest therapeutic protocol. LMWH has an advantage over unfractionated heparin (UFH) due to easier administration (once or twice daily), less possibility of staff contamination, predictable pharmacokinetics with less plasma protein binding and does not require monitoring of aPTT which is unstable during COVID-19 infection. All guidelines for the treatment of COVID-19 infection agree that all patients hospitalized for COVID-19 infection should receive thromboprophylaxis most preferably low molecular weight heparin (LMWH), regardless of the level of D-dimer in the blood. Direct oral anticoagulants (DOAC): apixaban and rivaroxaban, have the advantage of being easier to use at home and do not require testing of blood parameters. In cases of submassive pulmonary embolism (PE), systemic fibrinolysis should be considered, with the use of a direct catheter through the pulmonary artery as an alternative. For patients with PE who are hemodynamically unstable, systemic fibrinolysis, or direct catheter therapy should be the therapy of choice. Interventional procedures such as aspiration thrombectomy can reduce thrombus masses and improve flow in the pulmonary arteries which may lead to clinical improvement in patients with massive or submassive PE (20).

An observational cohort study of 163 patients with COVID-19 infection discharged from the hospital without anticoagulant therapy had a cumulative incidence of thrombosis (arterial and venous thrombotic events) of 2.5% within 30 days of discharge, of which VTE was 0.6% and major bleeding in 0.7% (21).

There is no clear consensus of the use of prophylactic anticoagulant therapy after discharge from the hospital of patients with COVID-19 infection who did not have a thromboembolic event. Patients with D-dimer 6 fold higher than normal values on discharge from hospital, as well as patients at higher risk for thromboembolic events (obesity, immobilization, postpartum period) should receive thromboprophylaxis after discharge from hospital, taking into account individual risk assessment from bleeding (22,23).

Extrapulmonary manifestations of COVID-19 infection are on the rise and are often associated with changes in the lungs. Acute effusive pericarditis is a rare manifestation of COVID-19, especially without associated pulmonary disease or myocardial damage (24).

The pathophysiology of effusive pericarditis in COVID-19 is unknown, but there are hypotheses that it occurs secondarily during the systemic inflammatory response as a consequence of cytotoxic and immune-mediated effects associated with SARS-

CoV2 infection. Inflammatory markers and autoantibody tests are often abnormal during acute infection and often require a clinical examination to define the aetiology of pericarditis. Valid tests for testing SARS-CoV-2 in a pericardial fluid are still under development and a complete biochemical, bacteriological, and cytological analysis of pericardial fluid is recommended to rule out other etiologies of pericardial effusion (25).

There are currently no established guidelines for the treatment of pericarditis during and after COVID-19 infection. In the cases published so far, patients have been treated with colchicine, hydroxychloroquine, corticosteroids and antiviral drugs.

High doses of aspirin and NSAIDs are the basis, ie the first line of therapy for acute pericarditis. Another therapeutic protocol includes colchicine. Corticosteroids in smaller doses are reserved for cases with contraindications or failure of first-line therapy. In some cases, corticosteroids and NSAIDs have worsened the clinical condition of patients with COVID-19 and should be avoided in patients with associated myocardial damage (STEMI and NSTEMI). NSAIDs used in chronic conditions do not have to be discontinued in patients with COVID-19. There is no clear evidence that the use of NSAIDs (ibuprofen) can cause adverse cardiovascular or respiratory effects in COVID-19 patients. It is recommended that patients with myocardial infarction and acute pericarditis start with high doses of aspirin. The use of high doses of aspirin in the treatment of patients with acute pericarditis during COVID-19 infection should be individualized. Colchicine can be added to NSAIDs or Aspirin for the treatment of acute viral pericarditis, and can be used as monotherapy at a dose of 2 x 0.5 mg daily for up to 3 months and is well tolerated. There are no contraindications for the use of colchicine in the treatment of pericarditis in COVID-19 patients (26,27).

In our patient during hospitalization due to bilateral pneumonia caused by SARS-CoV-2 virus during a routine control of D-dimer, elevated values 2.3 fold higher than the reference range were observed, with elevated biomarkers of inflammation. She had symptoms of a respiratory infection and no pronounced clinical symptoms that would indicate pulmonary thromboembolism. Due to the increased prevalence of thromboembolic complications during COVID-19 infection and the increased value of D-dimer in the further diagnostic procedure, MSCT pulmonary angiography was performed and low-risk thromboembolism was confirmed. She had no elevated biomarkers of myocardial damage. According to the protocol for the treatment of pulmonary thromboembolism, anticoagulant therapy was introduced - therapeutic doses of low molecular weight heparin (enoxaparin), which was extended after discharge from the hospital with DOAC (Rivaroxaban) according to the protocol for the treatment of pulmonary thromboembolism (13). At the control examination after 3 weeks, routine transthoracic echocardiographic examination revealed pericarditis with moderate pericardial effusion that did not lead to the collapse of the heart cavities, with a mild overload on the right ventricle after pulmonary thromboembolism - a slight increase in right ventricular systolic pressure (RVSP) and mildly tricuspid regurgitation (TR).

It did not have elevated biomarkers of myocardial damage, which indicated isolated pericarditis with effusion without myocardial lesion, as a complication of COVID-19 lung infection and pulmonary thromboembolism. Additional diagnostics of the colour-duplex scan of blood vessels of the lower extremities did not show signs of deep and superficial venous thrombosis, which could indicate that pulmonary thromboembolism developed in-situ as part of COVID-19 infection. Anticoagulant therapy (DOAC) was continued with the inclusion of colchicine in the therapy according to the protocol for the treatment of pericarditis with effusion. Due to the use of anticoagulant therapy, the patient shouldn't take aspirin or NSAIDs (as first-line therapy for idiopathic pericarditis), due to increased risk of bleeding (12).

At the control examination after 6 weeks of hospitalization, echocardiographic examination revealed regression of pericardial effusion with a reduction in the overload on the right ventricle and regular biomarkers of inflammation and D-dimer values.

After 3 months of hospitalization our patient with mild respiratory symptoms, bronchopneumonia of the right lung developed with slightly elevated biomarkers of inflammation and normal values of D-dimer. The finding of the nasopharyngeal swab on SARS-CoV-2 was negative. With prescribed antibiotic therapy and current therapy (DOAC and colchicine), there was a withdrawal of symptoms and regression of pericardial effusion and a reduction in right ventricular overload. It is proposed to continue colchicine therapy for up to 3 months from the start of the drug according to the recommendations, and anticoagulant therapy (DOAC) was extended after 3 months of pulmonary thromboembolism, given the new infection and possible increased risk of thromboembolic complications, with the low individual risk of bleeding.

At the follow-up examination five months after hospitalization, our patient was asymptomatic. The echocardiographic examination confirmed the complete regression of pericardial effusion with normal biomarkers of inflammation and D-dimer values. Since there was no increased risk of thromboembolic events, it was advisable to exclude anticoagulant therapy (DOAC) with continued low-dose aspirin therapy.

Conclusion

During SARS-CoV-2 infection with dominant respiratory symptoms, cardiac complications may be manifested, the most common of which is pulmonary thromboembolism as a consequence of the thromboinflammatory process during COVID-19 infection.

Significantly elevated D-dimer values may have a predictive value for thromboembolic complications. Pericarditis with pericardial effusion as a cardiac complication may follow the respiratory symptoms of COVID-19 infection or occurs isolated, which clinicians should consider when diagnosing and monitoring patients with COVID-19 infection.

References

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020; 395 (10223): 497–506.
2. Al-Ani F, Chehade S, Lazo-Langner A. Thrombosis risk associated with COVID-19 infection. A scoping review. Thromb Res. 2020; 192: 152–160.
3. Danzi GB, Loffi M, Galeazzi G, Gherbesi E. Acute pulmonary embolism and COVID-19 pneumonia: a random association? Eur Heart J. 2020; 41(19):1858.
4. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJHLH Across Speciality Collaboration, UK. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 2020; 395(10229): 1033–1034.
5. Abou-Ismail MY, Diamond A, Kapoor S, Arafah Y, Nayak L. The hypercoagulable state in COVID-19: Incidence, pathophysiology, and management. Thromb Res. 2020; 194: 101–115.
6. Ranucci M, Ballotta A, Di Dedda U, Bayshnikova E, Dei Poli M, Resta M, et al. The procoagulant pattern of patients with COVID-19 acute respiratory distress syndrome. J Thromb Haemost. 2020; 18(07): 1747–1751.
7. Leisman DE, Deutschman CS, Legrand M. Facing COVID-19 in the ICU: vascular dysfunction, thrombosis, and dysregulated inflammation. Intensive Care Med. 2020; 46(06): 1105–1108.
8. Zhang Y, Xiao M, Zhang S, Xia P, Cao W, Jiang W, et al. Coagulopathy and antiphospholipid antibodies in patients with Covid-19. N Engl J Med. 2020; 382 (17): e38.
9. Miesbach W, Makris M. COVID-19: coagulopathy, risk of thrombosis, and the rationale for anticoagulation. Clin Appl Thromb Hemost. 2020; 26: 1-7.
10. Inciardi R. M, Lupi L, Zaccone G, Italia L, Raffo M, Tomasoni D, et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). JAMA Cardiol. 2020; 5(7): 819–824.
11. Imazio M, Brucato A, Lazaros G, Andreis A, Scarsi M, Klein A, et al. Anti-inflammatory therapies for pericardial diseases in the COVID-19 pandemic: safety and potentiality. J Cardiovasc Med . 2020; 21(9): 625–629.
12. Imazio M, Adler Y. Treatment with aspirin, NSAID, corticosteroids, and colchicine in acute and recurrent pericarditis. Heart Fail Rev. 2013; 18(3): 355–360.
13. Konstantinides SV, Meyer G, Becattini C, Bueno H, GeersingGJ, HarjolaVP, et al. ESC Scientific Document Group 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J. 2020; 41: 543–603.
14. Manolis, AS, Manolis, TA. Cardiovascular complications of the Coronavirus (COVID-19) infection. Rhythmos. 2020; 15: 23–28.
15. Chi G, Lee JJ, Jamil A, Gunnam V, Najafi H, Memar Montazerin S, et al. Venous thromboembolism among hospitalized patients with COVID-19 undergoing thromboprophylaxis: a systematic review and meta-analysis. J Clin Med. 2020; 9(8): E2489.

16. Whyte MB, Kelly PA, Gonzalez E, Arya R, Roberts LN. Pulmonary embolism in hospitalised patients with COVID-19. Thromb Res. 2020; 195: 95–99.
17. Ackermann M, Verleden SE, Kuehnel M, Haverich A, Welte T, Laenger F, et al. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. N Engl J Med. 2020; 383(2): 120–128.
18. Al-Samkari H, Karp Leaf RS, Dzik WH, Carlson JC, Fogerty A E, Waheed A, et al. COVID-19 and coagulation: bleeding and thrombotic manifestations of SARS-CoV-2 infection. Blood. 2020; 136(4): 489–500.
19. McFadyen JD, Stevens H, Peter K. The emerging threat of (Micro)thrombosis in COVID-19 and its therapeutic implications. Circ Res. 2020; 127(4): 571–587.
20. Bikdeli B, Madhavan MV, Jimenez D, Chuich T, Dreyfus I, Driggin E et al. COVID-19 and thrombotic or thromboembolic disease: implications for prevention, antithrombotic therapy, and follow-up: JACC state-of-the-art review. J Am Coll Cardiol. 2020; 75(23): 2950–2973.
21. Patell R, Bogue T, Koshy A, Bindal P, Merrill M, Aird WC, et al. Postdischarge thrombosis and haemorrhage in patients with COVID-19. Blood. 2020; *136*(11): 1342–1346.
22. Zhai Z, Li C, Chen Y, Gerotziafas G, Zhang Z, Wan J, et al. Prevention and treatment of venous thromboembolism associated with coronavirus disease 2019 Infection: a consensus statement before guidelines. Thromb Haemost. 2020; 120(6): 937–948.
23. Ramacciotti E, Macedo AS, Biagioni RB, Caffaro RA, Lopes RD, Guerra JC, et al. Evidence-based practical guidance for the antithrombotic management in patients with coronavirus disease (COVID-19) in 2020. Clin Appl Thromb Hemost. 2020; 26: 1-8.
24. Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O, et al. Potential effects of coronaviruses on the cardiovascular system. JAMA Cardiol. 2020; 5(7): 831–40.
25. Farina A, Uccello G, Spreafico M, Bassanelli G, Savonitto S: SARS-CoV-2 detection in the pericardial fluid of a patient with cardiac tamponade. Eur J Intern Med. 2020; 76: 100–101.
26. Chiabrando JG, Bonaventura A, Vecchié A, Wohlford GF, Mauro AG, Jordan JH, et al. Management of acute and recurrent pericarditis: JACC state-of-the-art review. J Am Coll Cardiol. 2020; 75: 76-92.
27. Asif T, Kassab K, Iskander F, Alyousef T. Acute pericarditis and cardiac tamponade in a patient with COVID-19: a therapeutic challenge. European J Case Rep Intern Med. 2020; 7: 1–5.