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PULMONARY EMBOLISM IN THE OUTCOME OF A NEW CORONAVIRUS INFECTION: A CLINICAL EXAMPLE

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ABSTRACT

It is known that with a new coronavirus infection (SARS-CoV-2), even despite the use of anticoagulant therapy, there is a high frequency of both venous and arterial thrombosis, often leading to the death of the patient. Our publication presents a case of treatment of right-sided post-pneumonic pleural empyema (as a result of a new coronavirus infection and right-sided polysegmental destructive pneumonia) complicated by pulmonary embolism. Despite the successful treatment of the underlying disease, the fatal outcome came quickly and suddenly. This case shows that the risk of thrombosis in patients after COVID-19 can persist for a long time even when the presence of the virus in the body is no longer determined. Additional studies of the pathophysiological mechanisms and clinical features of these patients are needed to select the optimal therapeutic strategy.

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Introduction

COVID-19 is associated with endothelial activation against the background of a powerful inflammatory reaction and a state of hypercoagulation. The result of this thromboinflammatory condition is an excess of thrombotic events, in particular venous thromboembolism. Pulmonary embolism (PE) is of particular interest to patients with COVID-19, given its association with respiratory impairment, increased risk of hospitalization in the intensive care unit, and prolonged hospital stay. The pathophysiology and clinical characteristics of a PE associated with COVID-19 may differ from a normal PE not associated with COVID-19 **(Figure 1)**. In addition to the embolic phenomena of deep vein thrombi, pulmonary thrombosis *in situ*, especially in small vascular beds, may be relevant in patients with COVID-19. Thus, proper prevention of thrombotic events in COVID-19 has gained critical interest.

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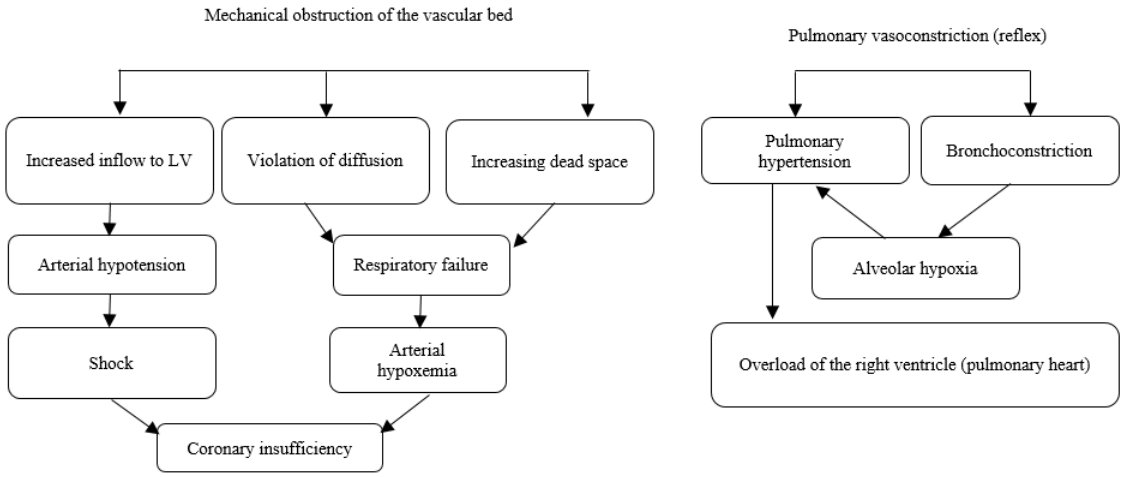

Figure 1. Classical pathogenesis of PE

Thrombotic phenomena are one of the common features of COVID-19 [1]. The underlying pathophysiological mechanisms are complex and involve two different mechanisms, namely thromboembolism and immunothrombosis. The first is characterized by activation of the coagulation cascade due to damage to endothelial cells, and the second is characterized by intense inflammatory and immune reactions that cause massive activation of the coagulation cascade and intense and prolonged degradation of fibrin [2, 3]. However, understanding this connection and timely treatment are crucial for effective treatment of this condition. It is known that the frequency of PE in COVID is at least 15% [1]. However, the incidence of PE in COVID-19 is widely unknown and requires further research to assess it. Some clinical signs indicating the severity of PE, such as obstructive shock and the nature of right ventricular deformity (VR), are associated with increased mortality [4]. It was found that mortality from COVID-19 itself is associated with concomitant diseases, as well as with PE [5, 6]. Overall mortality from PE in patients with COVID-19 has also not been systematically studied in larger studies.

Materials and Methods

Patient Z. has been ill since the beginning of November 2021. She received treatment in an infectious diseases hospital for Covid-19 from 05.11.2021 to 17.11.2021. She was not vaccinated against COVID-19. Concomitant pathology: hypertension 2st, risk 4. Further, after receiving negative smears, she was transferred to the Rostov Regional Hospital, where she continued to receive treatment for bilateral viral-bacterial pneumonia. On 26.11.2021, a right-sided hydropneumothorax was detected and transferred to the CGB. The pleural cavity was drained at two points. On 30.11.2021, thoracocentesis was performed, drainage of the pleural cavity on the right.

On 21.12.2021, the patient entered the department of purulent surgery of Volgograd Regional Hospital with complaints of shortness of breath, weakness, and discomfort in the place where the drainage tubes are standing. The treatment plan includes NSAIDs (ketonal), mucolytics (ambroxol), anticoagulants (heparin), and proton pump inhibitors (omeprazole). There are 2 drainage tubes in 6 and 8 intercostals on the right along the scapular line. On 22.12.2021, due to the severity of the condition, under conditions of O_2 insufflation, the patient was transported to Anesthesiology and Intensive Care Unit No. 1 of the Volgograd Regional Hospital. The patient's condition is severe, due to respiratory failure on the background of post-pneumonic empyema of the pleura on the right, pneumothorax, and post-COVID-19 fibrosis. R-graph of chest organs from 22.12.2021: signs of right-sided hydrothorax, right-sided destructive pneumonia, drained right pleural cavity.

But already on 23.12.2021, the condition stabilized and was transferred to the specialized department. There is scant serous discharge through drains on active aspiration. On 24.12.2021, against the background of drainage management, there was a clinically positive dynamic. R-graph of chest organs from 24.12.2021: drained right pleural cavity, atherosclerosis, R-signs corresponded to right-sided polysegmental destructive pneumonia in the developmental phase with an outcome in pneumofibrosis.

On 6.01.2022, drainage from the pleural cavity is migrating, it was not possible to restore it through the old channel. R-graph of chest organs from 10.01.2022: there were areas of post-pneumonic pneumofibrosis in both lungs. On 13.01.2022, after drainage removal, a small residual cavity remained in the posterior sections on the right. According to ultrasound indications for a puncture, drainage of the liquid formation was not found.

From the next day, the patient noted a slight increase in shortness of breath. On 17.12.2022, a resuscitator was called to the specialized department about the progression of cardiovascular insufficiency, namely paroxysm of atrial fibrillation. Prevention of the feasibility study was immediately prescribed: heparin 5000 units 3 times a day. The patient was transferred back to the OAR due to an increase in respiratory failure. Against the background of drainage management, the lung is straightened, and surgical complications are stopped. On the same day, respiratory support begins to be carried out using a ventilator in PCV mode with SpO_2 of 80%, against this background SpO_2 of 92-94%. Hemodynamics becomes unstable,

supported by the introduction of 4ml of norepinephrine + 16ml of 5% glucose at a rate of 10-12 ml/h. The state becomes terminal. The procalcitonin level of 7.31 ng/ml, C-reactive protein (CRP) increased to 295 mg/l. Prescribed: tigacil (100mg and 50mg 2 times per day) and broadsef (1.5g 2 times per day). General blood test results are showed in **Table 1**.

Table 1. General Blood Test

Index	17.12.2021	Standard
RBC	3.32	3.50-5.50
HGB	103	115-165
HCT	32.6	35-55
MCV	98.3	75-100
MCH	31.2	25-35
MCHC	317	310-380
PLT	166	100-400
WBC	18.6	3.5-10

Results of biochemical blood analysis are presented in **Table 2**.

Table 2. Biochemical Blood Analysis

Index	17.12.2021	Standard
Creatinine	45	44-80
Total bilirubin	6.4	0-17
AST	24.3	3-32
ALT	22.2	3-31
Glucose	6	4.1-5.9
Total protein	42.13	66-87
Urea	5.3	2.1-8.3
CRP	295	0-5
Procalcitonin	7.31	0-2

Results and Discussion

Despite the positive dynamics of treatment, following all clinical recommendations, the constant use of anticoagulants 18.01.2021 the D-dimer level was 6 micrograms/ml. It was stated that the patient was not transportable to confirm it. Resuscitation measures without effect, biological death was established at 13:45.

Clinical and pathoanatomic epicrisis: an aged patient after undergoing a new coronavirus infection developed diffuse pulmonary fibrosis with the formation of an abscess of the lower lobe with pleural empyema. Multiple foci of ischemic strokes in subcortical structures on both sides and the bridge with the development of cerebral insufficiency weighed down the patient's condition. The immediate cause of death of the patient was: progressive respiratory and cardiovascular, cerebral insufficiency.

The pathophysiology of PE in COVID-19 is complex and multifactorial. A distinct angiocentric feature of COVID-19 was identified relatively early in the pandemic [7, 8]. Two different mechanisms of the general pathogenesis of thrombosis in COVID-19 have been identified. The first mechanism is classical thromboembolism, which occurs due to sepsis and endothelial dysfunction, leading to the expression of tissue factors, activation of the thrombosis cascade, and, finally, classical thromboembolism [9]. The second mechanism, somewhat new, included microthrombosis due to the activation of immune pathways that cause serious damage to organs in the lungs, kidneys, skin (blue toes), and other organs [10]. It was reported that the last severe type, causing widespread immuno-mediated microthrombs, was found in patients receiving a prophylactic anticoagulant. We found that three publications (a total of six patients) mentioned PE despite preventive anticoagulant therapy [11-13]. PE, one of the consequences of the angiocentric activity of the disease, was detected in most patients with COVID-19 at autopsy.

The PE associated with COVID-19 has some specific clinical characteristics compared to the usual non-COVID-19 PE, which suggests that it may include a different phenotype of the disease. Further research is needed to clarify its true predictive value for fatal and non-fatal outcomes. Major scientific organizations give conditional recommendations in favor of full intensity over the standard intensity of preventive anticoagulation in non-critically ill hospitalized patients with COVID-19 with a low risk of bleeding. Although the treatment of acute PE associated with COVID-19 is generally similar to treatment before COVID-19, close attention needs to be paid to the potential drug interaction between COVID-19 therapy and oral anticoagulants.

Conclusion

This clinical example shows that the risk of thrombosis in patients after a new coronavirus infection can persist for a long time, even when the presence of the virus in the body is no longer determined. Only one marker of hypercoagulation was found in the patient - a high level of D-dimer. There was no increase in prothrombin time and thrombocytopenia.
Thus, thrombotic complications in patients with COVID-19 can occur in the late stages of the disease, when the SARS-CoV-2 virus is not detected, but the state of hypercoagulation persists. This indicates the need for further study of the pathophysiological mechanisms and clinical features of these patients to choose the optimal preventive and antithrombotic therapy.

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